THE MAKING OF THE CLINICAL TRIAL
IN BRITAIN, 1910-1945:
EXPERTISE, THE STATE AND THE PUBLIC.

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DECLARATIONS

Declaration required under Regulation 7 of the Regulations for the Ph.D., M.Sc. and M. Litt. degrees.

I hereby declare that my thesis entitled: *The Making of the Clinical Trial in Britain, 1910-1945: Expertise, the State and the Public*, is not substantially the same as any that I have submitted for a degree or diploma or other qualification at any other University.

I further state that no part of my thesis has already been or is being concurrently submitted for any such degree, diploma, or other qualification.

Date: 
Signed: 
This thesis has been compiled from published and unpublished sources. For citations of sources in footnotes, I have compiled a convention in which bibliographic information is kept to a minimum; full titles and publication details are provided in the Bibliography. More complete details of unpublished manuscript sources, contemporary periodical articles, and items in official publications are given in the footnotes.

**Abbreviations and Sources**

<table>
<thead>
<tr>
<th>Abbreviation</th>
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<tr>
<td>Hansard</td>
<td>Hansard Official Publications</td>
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<tr>
<td>ABCM</td>
<td>Association of British Chemical Manufacturers</td>
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<td>BJHS</td>
<td>British Journal of History of Science</td>
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<td>BMA</td>
<td>British Medical Association</td>
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<td>BMJ</td>
<td>British Medical Journal</td>
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<td>BHM</td>
<td>Bulletin for the History of Medicine</td>
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<td>CMAC</td>
<td>Contemporary Medical Archives Centre</td>
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<td>FRCP</td>
<td>Fellow of Royal College of Physicians</td>
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<td>FRCS</td>
<td>Fellow of Royal College of Surgeons</td>
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<tr>
<td>GMC</td>
<td>General Medical Council</td>
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<td>Lancet</td>
<td>The Lancet</td>
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<td>LGB</td>
<td>Local Government Board</td>
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<td>MRC</td>
<td>Medical Research Council</td>
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<td>MRCP</td>
<td>Member of the Royal College of Physicians</td>
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<td>MRCS</td>
<td>Member of the Royal College of Surgeons</td>
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<td>NIMR</td>
<td>National Institute for Medical Research</td>
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<td>PRO</td>
<td>Public Records Office</td>
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<tr>
<td>RCT</td>
<td>Randomised (Controlled) Clinical Trial</td>
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<td>TTC</td>
<td>Therapeutic Trials Committee</td>
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**Notes**

1  Anonymous articles from medical journals are given in full in the relevant footnotes, and take the following form: title, source, date, volume number, page numbers, e.g. 'The Quacks who quack', *BMJ* (1910), 1: 331.

2  Archival correspondence will appear in the following form: source, correspondent to recipient, date (day/month/year), e.g. PRO: FD1/335, T. Brown to B. Jones, 31/3/37.

3  In cases where photocopies have been taken from published sources and enclosed in archival files, the published work will be given along with the archival file number as follows: author, title, date, publication details (archival source). e.g. 'The Quacks who quack', *BMJ* (1910), 1: 331; or Hansard, 3/5/31, vol. 269, col. 222 (PRO: FD1/335).
ACKNOWLEDGEMENTS

This thesis has been about so much more than I could possibly say here. First I would like to thank my family for their unstinting support particularly during some difficult times these past four years. In these past few years I have come to draw on the lessons they have taught me about life. I would also like to thank Ken Palmer and Sam Green and Kirk Culmer for their loyal support particular in those years when I was only a kid of humble ancestry, growing up on the small island of Nassau in The Bahamas.

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Desirée Cox-Maksimov, 26 September, 1997.
**SUMMARY**

The randomised controlled clinical trial (RCT) is hailed as one of the most revolutionary medical innovations this century. It is a method for determining the therapeutic efficacy of medicines. This thesis is a socio-cultural history of how the clinical trial was made in Britain during the first half of this century. Previous histories have argued either that the RCT is simply the culmination of a very ancient history of therapeutic testing, or that it is the product of the rise of medical statistics this century. Both kinds of history focus on the medical statistician Austin Bradford Hill, who imported randomisation into the streptomycin trials of 1946-48.

This thesis, in contrast, shows what has been taken as a strictly medical methodology as part of other developments and contests in medicine and in British society. Not only does it show that all the procedural elements of the RCT were put into place before 1946, but that the stakes for defining therapeutic value were high for medical authorities such as the British Medical Association and the Ministry of Health and state bodies like the Medical Research Council. One layman, Major Chas Stevens, who took these authorities on year after year, for some thirty years, forced authorities to show what was at stake in creating a 'standard' system for defining the therapeutic value of medicines. This was the Dreyfus Case of the making of the clinical trial in Britain. What was at stake for these authorities was nothing short of the future of the nation. I focus on this extreme case, and I analyse three additional clinical trials in detail (ranging from the 1920s to the 1940s) to examine the moral management of pharmaceutical companies, physicians and patients in defining expertise for therapeutic testing. These cases also show the role of state institutions in legitimising this system.

The thesis is divided into three parts. Part I, entitled *Therapeutic Values*, is about the battles of Major Chas Stevens with medical and state authorities in his attempts to have his tuberculosis remedy legitimised by these authorities. The case, which runs from the turn of the century to the 1940s, introduces the central figures and institutions, particularly the Medical...
Research Council (MRC), involved in making the clinical trial. I demonstrate that 'character', 'trust', and 'standards' were crucial in determining who were excluded from the MRC's trial machinery as well as in defining expertise for determining efficacy. The themes of expertise and efficacy are developed further in Part II, *Standards, Moral Management and the State*, which connects them with state authority and public interest, through appeals to efficiency and standardisation on the part of an influential group of medical scientists and administrators within the MRC. I show how, in the 1920s, the highly publicised insulin trials were used to facilitate the MRC's becoming the legal authority in the biological standardisation of therapeutic substances.

Part III of the thesis is entitled *Human Machines*, and shows how clinical trials were standardised and managed by the MRC's Therapeutic Trials Committee, and how contests regarding the serum pneumococcal trials in the 1930s were crucial in defining standard trial procedure. Through a detailed examination of the 1940s mass trial of the drug Patulin for the common cold, I show how, in the context of war-time mobilisation, the system of clinical trials was mechanised. The large scale of this trial provided the statistician Major Greenwood with a unique opportunity to justify the essential role of statistical tools in managing and mechanising clinical trials. I conclude the thesis with discussion about the moral and cultural meanings of defining expertise for determining the therapeutic value of drugs within the state. I comment on the ways in which the ‘public’ had to be created in order to make a standard system for generating verdicts about the efficacy of medicines. Finally, I examine the implications of opening up this medical methodology as a cultural critique of twentieth century Britain. The Epilogue about post-war streptomycin trials connects this cultural history with the medical statistician Austin Bradford Hill's use of 'randomisation' as a specifically statistical tool of mechanisation. It also points to the way in which this now famous RCT was made a monumental success in the wake of, and perhaps in part because of, the highly public failure of the mass Patulin trials. Overall, the thesis offers a novel perspective on how and why medical
authorities, driven by and appealing to major national concerns, used particularly British
cultural values to define a methodology for defining therapeutic efficacy, for the public good.
INTRODUCTION

Who should represent the public interest? When ordinary citizens, lay members of the public, become patients, who should speak for them? Should doctors and scientists defend patients' interests? Should a state body represent them? Or should committees be established to represent their interests? These issues become especially focused where drugs are concerned. And they can become emotive national issues when those drugs are unstandardised, risky or experimental.

Today, debates on such matters often revolve around the question of whether a particular drug has been put through a 'proper', randomised controlled clinical trial (RCT) and, if so, which groups of society were represented in that RCT. The RCT is a method for determining the therapeutic efficacy of medicines by randomly dividing patients who are equal in all relevant respects into 'control' and 'test' groups which are well balanced. The standard, orthodox treatment or the placebo was given to the 'control' group while the therapy being investigated is given to the 'test' group of patients. Defended as an unbiased, scientific method for determining the therapeutic value of medicines, the RCT is hailed as one of the most revolutionary medical innovations this century. However, in the public domain, it has also become a battleground, and many argue that, in practice, the commercial interests of pharmaceutical companies, the professional interests of physicians, the public interests of the state, and the private interests of citizens, are in direct conflict in the conduct of therapeutic trials.

It may seem that these issues about expert representation of citizens who are patients have become public because of a) advances in modern medicine which have widened the choice of treatments available to patients, b) public scandals about deaths caused by unsafe, inadequately tested and frankly dangerous drugs, and c) the increasing individualism which the dismantling of the British Welfare State and the National Health Service symbolise. This is not the case. Questions about which citizens should receive which medical therapies, whether the state should be responsible for legitimising certain medicines and sanctioning them as safe for
public consumption were moral, political and national questions for early twentieth century scientists and doctors.

This thesis is a socio-cultural history of how the clinical trial was made in Britain during the first half of this century, by which I mean the way in which it was made within the domain of the state, and how its making was influenced by national concerns such as efficiency and standardisation. It shows that the clinical trial, the state and the public have always been intertwined. More specifically, the study is about how a group of physicians and scientists, doubling as national and international statesmen, explicitly set out to define national issues as the domain of the department of the state which they were trying to shape. This state body was the Medical Research Council (MRC). It was a body which was itself born out of national concerns about efficiency. I argue that after the Great War, Walter Fletcher (the first Secretary of the newly-formed MRC) tried to create a new class of citizen with a duty to define the meaning and nature of the 'practical' needs of society, to determine public policy and find solutions to national concerns through 'medical research'. I show that Fletcher and MRC colleague Henry Dale (a scientist and international spokesman for biological standardisation) chose biological standardisation as one of their primary causes, not least because this was an issue of general concern at the time. The crisis over toxic Salvarsan during the Great War, and the rise of unstandardised, unsafe patent medicines and secret remedies made biological standardisation a subject which they could frame as a matter of public interest. These scientists campaigned for the MRC to be established as the department of the state with the moral responsibility and legal authority for standardising drugs for the public.

I show that in establishing a system for the biological standardisation of certain therapies, Fletcher and Dale cultivated a certain type of person to judge the efficacy of medicines on patients in clinical trials for the public good. They did this by establishing social contracts with physicians they trusted to standardise medicines and test those medicines on patients. The MRC defined the expertise needed to determine the efficacy of drugs fairly based on the 'character' of physicians and whether they could be trusted, thus linking the shaping of the clinical trial during the early part of this century to older Victorian ideals of altruism and public virtue. I propose the label 'noble scientists' to describe this new class of citizen.
Crucially, I show that by cultivating 'noble scientists', and establishing separate contracts with select pharmaceutical manufacturing companies, the MRC produced a system for determining the therapeutic efficacy of medicines through the moral management of physicians and drug manufacturers. This ultimately involved the moral control of patients.

The clinical trial system which the MRC organised was a corporate system managed by ad hoc committees through social contracts and moral management during the 1920s. I argue that during the 1930s, the clinical trial system was managed by the Therapeutic Trials Committee and was designed to run like a 'human machine.' I show that because physicians formed the components of this 1930s 'human machine', statistics and statistical tools played an insignificant form of the expertise for determining therapeutic efficacy. However, at the outbreak of World War II, the Therapeutic Trials Committee was disbanded. I argue that during the 1940s the clinical trial, which began as a human machine, became mechanised. In the context of war-time mobilisation the MRC's clinical trial was reconfigured as a mass trial in which statisticians like Major Greenwood and, later, Austin Bradford Hill (both of whom had been offering statistical critique of MRC research projects for over a decade) were invited onto ad hoc committees to help organise the new mass trials. Statisticians helped to mechanise the clinical trial, and randomisation -- explicitly defined as a statistical tool when it was introduced in the streptomycin trial -- was one of the tools which mechanised the human machine that was the clinical trial. Thus the making of the clinical trial provides an excellent case of mechanisation of various human activities in society during the first half of this century.

One can find physicians in earlier periods testing the efficacy of drugs or medical methods by dividing patients into control and test groups in alternation.¹ In some cases they said that they were conducting trials, or even clinical trials of a drug. And there is no shortage of historical examples of groups of physicians and factions of scientists promoting their actions as being in the public interest, and the new bodies (or medical approaches) they wanted to establish as being institutions for the public good. In Part I of the thesis in particular, I point to

¹Lilienfield (1982); Bull (1959).
the ways in which Fletcher's focus on character (in selecting trustworthy physicians to test drugs) was reminiscent of earlier periods. I argue that what is novel about the making of the clinical trial in the first half of this century and, indeed, why the clinical trial should be periodised as a process which occurred during the first half of this century, is as follows. It was only during the first four decades of this century that there was a deliberate attempt to establish and manage a coordinated system for determining therapeutic efficacy which brought together a network of trustworthy characters to create a standard approach for testing worthy drugs through clinical trials. It is this system which I propose is the clinical trial.

**Why write a history of the clinical trial in Britain?**

A history of the clinical trial which focuses on Britain should allow us to gain a better understanding of how adequate explanations evolved in modern medicine and British society during this century. It might also persuade those within the medical body politic who engage in reforming medical practice to think about their task in a different way.

The clinical trial is now a methodology applied all over the Western world. The received wisdom (in Britain at least) is that the RCT was an essentially British invention, made by Austin Bradford Hill, and that it was promoted by Hill and his allies and thus spread throughout the world.  

Harry Marks, however, has written a history of the clinical trial in the United States of America which suggests that the RCT had a separate evolutionary path in that country. 

There is no comprehensive history of the clinical trial in Britain, Germany, or France for that matter. This history of the clinical trial in Britain thus takes us closer to being able to address wider issues about the globalisation of the clinical trial this century.

There is a further reason for writing a history of the clinical trial in Britain. History has become a player in contemporary battles about the trial. The production, form and use of existing historical accounts of the trial have implications for the making of the history of the

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2 Armitage (1982).

3 Marks (1997).
clinical trial. In the contemporary context, those who defend randomisation and the RCT use existing historical accounts in their defence. These histories are also used in arguments that promote more rigorous employment of statistics in clinical research. They stand as evidence of the virtue of statistical tools and quantification in bringing about progress in modern medicine. On the other hand, critics of the methodology and conduct of the clinical trial tend to draw on philosophical or trans-historical traditions to construct their arguments. This is particularly true of debates about the ethics of randomisation, the ethics of excluding certain sectors of the population (particularly women) from clinical trials, clinical equipoise, the necessity of large samples in trials, informed consent, stopping rules for trials, and the use of meta-analysis in the interpretation of trial results. Indeed, 'patients' rights' and the 'ethics' of the clinical trial in general are subjects of public debates of a trans-historical and folk-philosophical nature. The issue here is not that the existing histories of the clinical trial are not the works of professional historians. Neither is the fact that such accounts may be seen as so-called 'winners' histories a matter of primary concern. The principal issue at stake is that these histories are in the process of being made into standard accounts, and master narratives of the clinical trial. They are not just the histories of the winners. They are the work of those who have promoted and continue

4 In Vico's words 'men like to make their own history and that what they know is what they have made.' The idea of people writing histories for their own purpose has been discussed at length in general debates about the uses of history elsewhere. See Said (1978); White (1973); Berlin (1990); Young (1990).

5 Most of this use of history occurs in oral addresses about the clinical trial. See R. Peto, 'Moderate effects and large-scale randomised evidence: the introduction of meta-analysis for clinical trials' in Wellcome Sound Archives of the Proceedings of Symposium on Mathematics and Medicine, held at the Wellcome Institute for the History of Medicine, 21/3/96. For a written example of this, see Armitage (1982) and (1983); Friedman, Furberg and DeMets (1982); Fletcher and Fletcher (1979); Editorial, 'Cochrane Legacy', The Lancet (1992), 340: 1131-2; Binns (1981); Chalmers (1974); Doll (1982); Holland, Breeze, and Swan (1982); Sackett and Cook (1993); Peto (1978).

6 For discussions about the epistemology of trials and the Bayesian versus Frequentist battle, see Kadane (ed. 1996); Spicker, Alon, DeVries and Englehardt (eds 1988); Berry (1991); Whitehead (1991); Urbach (1991); Earman (1992); and Machin (1994).

7 AIDS and the clinical trials of drugs for AIDS have caused patient advocacy and patients' rights, as well as many other ethical and methodological issues, to come into sharp focus. For the works on patient advocacy and 'patients rights' in trials in general, and AIDS in particular, see Rothman (1991); Garfield (1994); Fee and Fox (1989); Epstein (1993) and Treichler (1991).
to promote trials in order to win the trial an untainted place in history. Writing the history of
the RCT, therefore, has political implications.

**Previous histories**

The clinical trial has only recently become the subject of scholarly attention and there is little
in the way of published work on the RCT. Histories of this medical innovation are transmitted
orally by those who remember early clinical trials, or who remember Austin Bradford Hill, or
by those who are involved in the shaping of the present-day RCT. Many of the short historical
articles published on the RCT written by physicians and statisticians have taken the form of
master narratives which place a heavy emphasis on the origin of randomisation and on Austin
Bradford Hill. And the issue of the origin of randomisation is ultimately connected with the
question of who should be given a place in the history for introducing the innovative RCT. Hill
is credited as the person who brought randomisation to the trial of streptomycin between 1946-
48, and this clinical trial is defined as the first proper RCT. Accounts by the physicians John
P. Bull and Harry F. Dowling, by the medical statistician Peter Armitage, and the
epidemiologist Abraham Lilienfield have become significant examples of these early histories.9

Some scholars concerned with how particular therapies acquired cultural meanings
have produced historical and sociological studies of specific clinical trials.10 Clinical trials have
also been recruited as evidence in thematic histories about human experimentation, the design
of therapeutic experiments, quantification and trust. Most of these studies focus on the USA.11
However, the making of the clinical trial in other countries, particularly Britain, invites

8 Below I use 'History', to refer to master narratives of the clinical trial, as opposed to 'histories'
implying a pluralist stance in which there are a number of histories or historical accounts each
written from a different perspective. An excellent discussion of this subject can be found in Duara
(1995). (I am grateful to B. J. Andrews for drawing my attention to this source.)

9 For examples of histories written by physicians, medical statisticians and other non-historians, see
Armitage (1983) and (1992); Bull (1959); Dowling (1975); Hill (1951); Lilienfield (1982). See also
Witts (ed. 1959); Hill (1990).


they should expose moral issues of the method. Crucially, many of the historical issues about how the clinical trial was shaped by, and helped to shape, the state and the relationship between trial, state and public have yet to be addressed. At present, the historical accounts by John P. Bull, Peter Armitage, Abraham Lilienfield, and the historian of medicine, Harry Marks, are established as standard texts on the subject. For this reason it is worth discussing these histories in turn.

John Prince Bull, a physician who was involved in non-randomised clinical trials on burns patients of plasma substitutes at the MRC Burns Unit in Birmingham during the late 1940s and 1950s, wrote his history of the clinical trial in 1951. He argued that the conduct of 'clinical trials' can be traced back to the ancient Egyptians. Bull's history is based on the premise that experiments designed to assess the value of therapeutic procedures on patients have always been an essential feature of medicine, and that therapeutic procedures have always been 'clinical trials'. Highlighting historic moments such as Avicenna's rules for testing drugs, Francis Bacon's suggestion of a committee of physicians to judge therapeutic efficacy, James Lind's comparative trial of scurvy 'cures', and P. C. A. Louis' application of his numerical method in the clinic, Bull presents a linear account of these as historical inputs to the clinical trial. The implication in this master narrative is that, cumulatively, these inputs make the clinical trial progressively more scientific. The discovery of new drugs (such as Salvarsan, digitalis, insulin and penicillin) and the advent of the First World War provided the materials and the opportunity for the conduct of more sound clinical trials in the twentieth century.

Although Bull notes that Bradford Hill's introduction of randomisation modernised the clinical trial, it is only one of the many historical inputs.  

Focusing on Austin Bradford Hill, Armitage connects Bradford Hill's personal history with the evolution of the clinical trial in Britain. Armitage is a medical statistician who knew Bradford Hill. He remembers a time when statisticians took what work they could get, and when medical statistics was not widely recognised as a separate or independent field. Armitage takes Bull's account as the pre-history of the RCT. As a past president of the Royal Statistical

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Society, and now a retired Professor of the Department of Biomathematics at Oxford University, Armitage presents the RCT as a crucial part of the making of medical statistics. Armitage notes that Hill learned his statistics from Karl Pearson and Major Greenwood, and argues that, as a member of the MRC's Statistical Committee, Hill was first involved in advising on the statistical analysis of the therapeutic trials organised by the MRC's Therapeutic Trials Committee during the 1930s. He does not provide archival evidence for this, nor does he show how the Statistical Committee or the Therapeutic Trials Committee made their judgements about the therapeutic efficacy of substances that they accepted for clinical trial. Armitage argues that Hill clarified his ideas about the design and benefit of randomisation in therapeutic trials during the 1930s, and published many of them in his series on statistics and medicine in *The Lancet* in 1937. Significantly, he claims that although randomisation was introduced by the statistician R. A. Fisher in 1923, 'Hill would have accepted randomisation on common-sense grounds and would have been unimpressed by Fisher's sophisticated advocacy.'\(^{13}\) Armitage argues that in 1946, in the context of rationed supplies of streptomycin donated to the MRC from America, Hill, who sat on the MRC's *ad hoc* committee set up to organise the streptomycin trials, suggested the randomisation of patients and treatments. He offers Bradford Hill's promotion of the RCT during the 1950s and 1970s as an explanation for the institutionalisation the RCT.\(^{14}\)

Abraham Lilienfield conceives of the clinical trial as comprising separate components, namely, comparative therapeutic analysis, randomisation, and blind or masked therapeutic assessment. He treats these so-called historical variables not unlike the factors of an epidemiological equation for how the RCT came into being. Systematically charting evolutionary paths for each of these components separately, he argues that the main goal of each of these approaches and their fusion in the clinical trial is to achieve *ceteris paribus*, 'all other factors being equal'. These different species of therapeutic trial were united in the clinical trial during the twentieth century. In tracing the history of comparative studies hinted at in the

\(^{13}\) Armitage (1982).

\(^{14}\) Armitage (1982).
Old Testament, but actively pursued in the comparative studies of Lind in the eighteenth century through to the twentieth century, Lilienfield argues that it is from this strand that controls, alternating controls and controlled series originate. He demonstrates that the idea of controls can be found in the late nineteenth century. While Lilienfield stands with Armitage in crediting the introduction of randomisation to R. A. Fisher, he dates J. Burn's trial of Sanocycin (gold therapy) for pulmonary tuberculosis in Michigan as the first recorded randomised controlled trial. This was also the first blind trial.\(^{15}\)

Harry Marks has written an intellectual history of the clinical trial, which focuses mainly on the USA. In his book Marks examines the beliefs and activities of a disparate group which he labels 'therapeutic reformers' who, operating through institutional structures (such as the Council of Pharmacy and Chemistry, the US Food and Drug Administration and various universities), used the science of controlled experiments to direct medical practice. In so doing they framed the randomised controlled clinical trial during the first half of the twentieth century, and furthered its institutionalisation in America from the 1950s onwards. In this history Marks argues that while laboratory sciences provided the standard of the 'well-controlled' experiment for medicine, during the second half of the century the clinically based randomised controlled trial offered a new standard of scientific excellence.\(^{16}\)

**The approach and scope of this thesis**

My approach to the history of the clinical trial in this thesis is to situate therapeutic trials in their social and cultural contexts by examining individual trials as events and stories of how people negotiated relationships between each other, and how they manipulated public and national concerns to further their goals and ambitions. I focus on particular trials as historical cases which exemplify the crucial issues and themes in the making of the clinical trial. This history thus links micro-historical studies of crucial trials, special cases, cases of exclusion and 'ordinary' trials. The cases I have selected also demonstrate: a) what was at stake in making

\(^{15}\) Lilienfield (1982).

\(^{16}\) Marks (1997). See also Marks (1988).
judgments about the efficacy of drugs; b) why it mattered who stood as judge and jury in this process, as well as how and where those judgments were made; and c) who was excluded from this process. By examining clinical trials which received considerable attention, and were treated as public events at the time, I open up clinical trials as accounts which speak about British society during the first half of this century.

I begin the thesis with a 'test' case which begins in 1910 with a court trial. The case spans the period in which the clinical trial system was developed to determine therapeutic efficacy. I end around 1945 with the clinical trial of the drug Patulin (which was one of the first mass trials by the MRC), the end of the Second World War, and the year before the clinical trial of streptomycin with which Austin Bradford Hill was involved. In the Epilogue I show how Bradford Hill and others defined this as the first randomised controlled clinical trial, but I have deliberately not focused on Bradford Hill. This is not because I have intended to write him out of its history. Quite the contrary. His crucial role in introducing randomisation as a statistical tool into the clinical trial, in promoting and encouraging refinements of that tool, and in the 'History' of clinical trial has been assured (as I mentioned earlier) by others. I have focused on this earlier period, which I define as the making of the clinical trial, because I aim to show how and why the clinical trial was made, and that by the time of the famous streptomycin trial of 1946, the MRC had established a grammar of therapeutic testing through clinical trials without which the streptomycin trial would not have been possible. Even so, I have not been concerned with listing the details of which clinical trial followed what procedure, or engaging in contemporary debates about which trial was really the first RCT. My primary aim has been to write a history of the clinical trial with a societal focus which shows how the making of this medical methodology related to contexts beyond the doctors, in order to open up this subject as a broader history of modern British society during the first half of this century.

My exposition is not an institutional history of state bodies such as the MRC, the National Institute of Medical Research or Ministry of Health. Nor, of course, can it be a full account of the activities of the commercial, medico-scientific or domestic spheres of British society regarding therapeutic matters in the early part of this century. It is the nexus between these worlds that concerns me in this study. This is where one finds the conflict and consensus
that drove the technology. Here one sees the way in which the making of the clinical trial, determining therapeutic efficacy, and the production, control, and use of 'safe' medicines were given meanings in contexts beyond the doctors. While the extent to which the MRC's judgements influenced the therapeutic practice of individual doctors working in hospital wards during this period is undoubtedly important for an account of the effect of the clinical trial on therapeutic practice, it is beyond the scope of this thesis. I have not taken a thematic view of the clinical trial as an example of the rise of statistics in medicine or of the use of human beings as experimental objects. Neither have I explicitly framed it as an example of the rise of the laboratory in medicine during the first half of this century. This thesis does, however, draw on scholarship in all these subjects and may inform research in these areas. My aim has been to shift the ground on which existing histories of the trial have previously rested, in order to raise and address a different set of questions about the place of the clinical trial in British society, and the role of the state, the public, and public interest in the making of the trial.

**The structure of the thesis**

I begin with the public. The thesis is divided into three parts and six chapters. Part I is entitled: *Therapeutic Values*; Part II, *Standards, Moral Management and the State*; Part III, *Human Machines*. Part I of the thesis opens with Chapter 1, 'The Case of Major Chas H. Stevens and the Umckaloabo Treatment for Tuberculosis'. This is the case of a layman who tried to have his therapy for tuberculosis legitimated by medical authorities and eventually by an MRC clinical trial. The case runs from the turn of the century through to the 1940s, covering the period of making of 'the' clinical trial, and it introduces the central figures in that process. Stevens was a layman and his case became a matter of public debate. It became a focus of a Select Committee on Patent Medicine before the Great War, the subject of discussion in the House of Commons, not to mention the public press, during the inter-war period. It has even been identified as the inspiration for H. G. Wells' novel, *Tono-Bungay*. The MRC created several files on this case, which are now held in the Public Records Office at Kew Gardens. In so doing they preserved the records for public viewing which tell the story of how eminent figures like Walter Fletcher, Henry Dale, Professor T. R. Elliott, and F. H. K. Green were
trying to create a 'just' process for judging therapeutic efficacy. The public records were also
designed to show how eminent MRC figures felt obliged to protect the system they were
creating by controlling access to MRC clinical trials. Beginning with this case thus introduces
the different senses and meanings of 'public' which were being negotiated at the time and the
people who claimed to be representing the public. Chapter Two, 'The Commentary of the Case:
Themes in the Making of the Clinical Trial' presents an analysis of the case and discuss its
meaning in the context of the making of the clinical trial itself. In particular, I focus on
'character', 'trust' and 'standards' and connect these themes with the thesis. I show how these
themes connect Expertise, the State and the Public, which are unifying themes of the thesis as
a whole.

Part II, Standards, Moral Management and the State, comprises two chapters.
Chapter Three, 'Bringing the State Back in: Characters, Standards and the MRC', locates the
clinical trial within the domain of the state. In this second part of the thesis I show how the
making of the clinical trial began within the Medical Research Council (MRC), and that trials
were implicitly sanctioned by the state. Walter Morley Fletcher and Henry Hallett Dale were
two of the most influential figures in this process. Principally, I argue that Fletcher intended to
define or shape the Medical Research Committee (later the MRC) as a unique department of
the state which addressed national concerns and solved important practical problems of
government and industry through medical research. In this part of the thesis, I demonstrate that
Fletcher used national concerns about efficiency and the Medical Research Committee's
coordinating role in war-time research to serve this end. I also indicate how Fletcher's focus on
biological standardisation after the war, and his campaign to authorise MRC control of
therapeutic standards through the Therapeutic Substances Act, was also aimed at fashioning a
unique place for the MRC within the state. Crucially I argue that for Fletcher, the burden of
defending such claims for the MRC came to rest on public demonstrations of its practical
value. I also show how organising a fair and efficient system for testing therapies on patients
was a part of the biological standardisation of drugs.

Chapter Four, 'Biological Standards, Patients and the 'Noble Scientists' of the MRC in
the Insulin Trials: A Public Affair' examines the way in which the MRC framed the early
research to standardise insulin and the clinical trials of that drug on patients in Britain as a public event. I show how Fletcher and Dale tried to cultivate a new kind of MRC research citizen, a clinical scientist duty-bound to improve the welfare of the nation through research. I show how they did this by a) establishing social contracts between the MRC and the physicians trying insulin in the clinic, and b) the moral management of manufacturers who made insulin and of the patients on whom it was being tested. In focusing on how the MRC made and managed insulin trials as a public event, I examine the moral economy of standardising a drug through clinical trials and also how defining the meaning of a fair and moral manager made the clinical trial.

Part III, *Human Machines*, begins with Chapter Five, 'Principles, Fairness: the Therapeutic Trials Committee'. This chapter examines the way in which negotiations between members of the so-called legitimate pharmaceutical industry (representing commercial interests) and representatives of the Medical Research Council (who claimed to be defending national interests) shaped the trial. Both parties claimed to be acting in the interest of the public. I argue that the Therapeutic Trials Committee (TTC) was established partly at that request of the pharmaceutical industry to organise a system of clinical trials to determine the efficacy of their medicines. I show how that Committee established standard trial methodology and how they managed competing interests in the interest of fairness.

Chapter Six, 'The Common Man's Cold: Mobilisation and the Masses in the Patulin Trials', is about trials of the drug Patulin as a cure for the common cold. In this chapter, I show how the power relations between the MRC and the major British pharmaceutical companies changed after the disbanding of the Therapeutic Trials Committee. This trial demonstrates that *prima facie* evidence was not a static piece of evidence produced before conducting a mass clinical trial; it was in fact produced during that clinical trial as a part of the justification for conducting a trial on this massive scale. I also examine how the methodology was shaped by the special circumstances of conducting a large-scale trial during the war, and how the trial, which mobilised masses of factory workers, was mechanised.

Finally the Conclusion: 'Evidence, Trust, the Trial and the Public'. I draw conclusions about the moral and cultural meanings of defining expertise for determining the therapeutic
value of drugs within the state. I also comment on the ways in which the public had to be created in order to make a standard system for generating verdicts about the efficacy of medicines, and examine the implications of opening up this medical methodology as a cultural critique of twentieth-century Britain. I end with an Epilogue about the Streptomycin Trial and the post-war evolution of the trial.
PART I

THERAPEUTIC VALUES

What was at stake in assuring a future in which the British public would know which medicines were genuine and safe? Why was it so important to establish rules of best conduct for the medical profession, the pharmaceutical industry and the public when it came to assigning value to therapies? How far were authorities willing to go to ensure that all of these players followed the proper rules of the game? This is the subject of Part I of this thesis. The stakes were high for medical and state authorities like the British Medical Association, the Ministry of Health and the Medical Research Council. So when a layman named Major Chas Stevens had the temerity to take them on one by one, again and again, year in and year out, for over thirty years, these medical and state authorities pulled out all the stops to make sure that this man would have no place in the worlds they were trying to create. To the BMA, Stevens threatened the professional authority of doctors to judge whether a medicine was effective against a particular condition or not. It was the duty of the Ministry of Health to protect the public health against the likes of Stevens. But what was at stake for influential MRC figures like Walter Fletcher and Henry Dale in creating a 'standard' system for determining the therapeutic efficacy of medicines, was nothing short of the future of the nation. When the MRC embodied this system with codes of fair conduct, and carried out clinical trials with the moral virtue of doing medical research for the nation, they made their system the very epitome of what it meant to behave with British integrity and discretion, and what it meant to uphold proper 'standards' in public affairs.

And so the case of Major Chas Stevens was not merely a case of a layman who tried to have his remedy legitimated by medical authorities: this was trench warfare. With each trench, they drew another boundary to exclude characters like Stevens, and the element of society he represented, from their system. With each direct hit, Stevens recruited new allies to his cause, and gathered more ammunition in his quest for legitimacy. The MRC kept a
number of files on Stevens recording this trench war. Official histories of clinical trials never mention this in their accounts of trials as a part of the rise of statistics, the triumph of randomisation, Austin Bradford Hill, and the like. It is in the detail of these files buried in the MRC’s now public records that one sees the energy authorities put into building a system to evaluate therapies. It is through the evidence of the sheer wilfulness of Stevens that one sees the lengths they were prepared to go to build and protect their system by excluding people like Stevens from it. The ways in which authorities embodied systems for judging therapeutic efficacy with their moral virtues are also buried in the subtitles of how they waged their battles against Stevens. And so I examine these battles in great detail in Chapter 1, placing the events of the trench war in contexts of the period as the history evolved. It is precisely because this was the war of attrition that the key people and authorities in the making of the clinical trial are introduced in this chapter. In Chapter 2, I offer a commentary and analysis of the Stevens case, bringing the details of the case together under the themes ‘character’, ‘trust’ and ‘standards’ to show how these unifying themes of the case are strands in the making of the trial as a whole. I also show how they connect the central themes of the thesis: the expertise, the state and the public.
On 27 July 1910, in the Basingstoke County Court, a widow took legal action against Major Charles Henry Stevens. She wanted to force the said `consumptive curer', to pay the 'guarantee bond' he had issued along with his medicament. According to this bond, the widow was entitled to a refund from Stevens, if she had not been cured by his remedy. She claimed that she had received no benefit from the Stevens Umckaloabo treatment for tuberculosis and demanded he refund her money. When Stevens refused to repay her, she took him to court. The judge found in favour of the plaintiff and refused leave to appeal, describing the transaction as `an intentional and well-considered fraud'.

It was rare for a case like this to make it to court, and even more remarkable for the proprietor to be convicted of fraud. When such matters did make it to court, the prosecution's case was often destroyed because of the difficulty in proving guilty knowledge, or as it was referred to in legal terms -- 'wilful' misstatement. Furthermore, defendants could be rescued from conviction by witnesses who testified to the personal benefit of the therapy. This guilty verdict did not stop Stevens from peddling his Umckaloabo treatment. He continued to advertise the miraculous curative powers of his medicament also known as Stevens' Consumptive Cure, despite this mishap, and to sell it to any tuberculosis sufferers who would pay for a course of this treatment.


18 The Select Committee for Patent Medicines concluded that 'successful prosecutions for fraud in connection with the sale of secret remedies have been so few as to be negligible'. See Note 1, p. viii.

19 It was clear by the end of the Select Committee hearings that false pretences in respect of Secret Remedies were not adequately dealt with, either by Common Law or by certain existing Acts, and that there were not adequate powers of prosecution vested in officials and Departments of State. For all practical purposes it was not legally possible to prevent any mixture, be it potent or therapeutically ineffective (provided it did not contain a scheduled poison), from being advertised in decent terms as
Charles Henry Stevens was born in Birmingham, England. In 1897, at the impressionable age of seventeen, he was diagnosed with 'weakness of the lungs'. He happened to be in South Africa at the time. According to Stevens, a Dutchman introduced him to a witch doctor who, adorned in leopard skin, gave him a decoction. Stevens took this drink twice a day for two months and was cured of his lung condition. The cure so impressed Stevens that he returned to England with a small consignment of the remedy, and conducted his own personal clinical trials of it, treating 22 consumptives with it, free of charge. Stevens claimed that the consumptives did well as a result of his Umckaloabo treatment.

After the Boer War began in 1899 Stevens travelled to South Africa again. He fought on the British side, rising to the rank of major. But when the war was over, Stevens decided to stay on in South Africa and set up a business there -- the New Hudson Cycle and Motor Agency. Misfortune struck, the business was destroyed by fire, and Stevens turned to selling the Umckaloabo treatment. But he ran into trouble with doctors in Johannesburg and fled the country. Some time during 1907, he appeared at 204 Worple Road, Wimbledon, where he began a thriving business. Wimbledon became the headquarters of the C. H. Stevens Consumptive Cure Company. His company employed some fifty people who were paid to make, pack and post Umckaloabo. He advertised the consumptive cure in the newspapers, magazines, through letters to doctors, and leaflets to the general public. In addition to packaging the remedy and advertising it, his employees also helped to prepare and post the personalised letters he sent to patients, and manage the company accounts.20

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20 See F. B. Smith (1988), 155-65. See also The Times, 22/7/12, and The Times, 28/10/12.
I. 1. i. Secret remedies and proprietary medicines, and standardised drugs

By the turn of century, the trade in patent medicines and secret remedies had become a source of grave concern to many Britons, particularly professional physicians and intellectuals.\textsuperscript{21} Chas Stevens epitomised the kind of character medical authorities were trying to marginalise and ultimately remove from the public sphere. Stevens (and his kind) threatened their livelihood and profession by selling proprietary medicines to 'cure' diseases only proper doctors were supposed to treat. And yet, his was the precisely the kind of remedy most Britons purchased. In 1908, it was estimated that the British public spent some £2,500,000 per annum on proprietary mixtures.\textsuperscript{22} Most of these medicines carried no statement of their formula or composition, and were thus known as secret remedies. According to the Stamps Act, manufacturers of proprietary medicines were required to register these medicines and pay a duty for a government stamp which they then displayed on the items. The British Government collected a considerable revenue from issuing stamps for remedies like Stevens’ Umekaloabo treatment, revenue which, in 1908 alone, amounted to £334,142.\textsuperscript{23} Newspapers also profited from this trade. Over £200,000 a year was being spent on advertising secret remedies and proprietary medicines to the public. For some provincial newspapers and sundry religious papers such advertisements had become their life-blood.\textsuperscript{24}

\textsuperscript{21} For details about the history of the trade in patent medicines up to the turn of century, see Holloway (1995), 77-96; Berridge and Edwards (1987); Saks (ed. 1992), 101-11; The Editor of Health News, (1896), 1-2; Fraser (1981), 134-46; Richards (1991), 169-204.

\textsuperscript{22} Saks (ed. 1992), 102.

\textsuperscript{23} The increase is noteworthy. In 1860 the government was estimated to have collected £43,366 from this source. By 1890 the amount had risen five-fold: Saks (ed. 1992). It was estimated that the government was collecting up to £250,000 each year from the sale of secret remedies at the turn of the century. See The Editor of Health News (1896). The revenue from secret remedies continued to increase throughout this century until the stamp duty was abolished as a result of the Pharmacy and Medicines Act of 1941. For more about the amount of money raised by the Government in the trade of patent medicines and secret remedies, see 'Secret Remedies', \textit{BMJ} (1909), 2: 1174; 'Patent medicines (Revenue), \textit{BMJ} (1909), ii, 813; Bartrip (1990), 189; \textit{BMJ} (1895), 1: 95; \textit{BMJ} (1904), 2: 1599; Berridge and Edwards (1987), chapters 10 and 11. For specific details of figures collected during this period, and the details of amendments of the Stamp Acts and the revenue collected on each stamp for a proprietary medicine, see Chapman (1941), 138, and (1955), 207-9; Matthews (1986), 2-5; \textit{The Select Committee on Medicine Stamp Duties} (1937). See also Note 1, pp. ix-x.

\textsuperscript{24} See Fraser (1981); Turner (1953), 143-76; Note 1, p. ix; Nevett (1982).
It may have suited the British government, the press and those who manufactured proprietary medicines to support this trade, but the BMA (encouraged by the majority of doctors who regarded this industry as a menace and a threat to both their pockets and their status) launched a campaign to stamp it out. These medical men found it particularly irksome that the government supported this scandalous trade.\footnote{Lloyd George in particular was criticised by the BMA for failing to impose heavier taxes on proprietary medicines in his 'People's Budget'. See Bartrip (1990), 196; \textit{BMJ} (1909), 1: 1134-5.} Their professional claim was that secret remedies and proprietary medicines were harmful to the public.\footnote{The BMA had begun its campaign against proprietary medicines in the 1880s. For more about the campaign see Bartrip (1990), 190-1; WIHMCAC: SA/BMA/C353, Alfred Cox, 'Action taken on the question of patent medicines', in 'Unqualified practice general. Minutes, and extracts 1918-1943'. See also BMA (1909), Introduction; and BMA (1912).} The doctors and their allies campaigned for legislation to force proprietors to print the contents of secret remedies on their labels, insisting that people who manufactured and sold poisonous proprietary medicines should be taken to court. Initially, the BMA simply publicised instances where proper doctors believed that these secret remedies might have caused deaths to support their claims.\footnote{The General Medical Council (GMC), the Pharmaceutical Society and other medical bodies supported the BMA in its campaign against secret remedies. The Pharmaceutical Society, encouraged by Ernest Hart (editor of the \textit{BMJ} between 1867-98), took legal action against guilty traders. The GMC appointed a committee to investigate the law for the prevention of medical practice by unqualified practitioners (in Britain and the colonies). See Bartrip (1990), 190-1; \textit{Reports from the Commissioners, Inspectors and Others on the Practice of Medicine and Surgery by Unqualified Persons; Parliamentary Papers}, vol. 43 (1910). See also WIHMCAC: SA/BMA/C353, Alfred Cox, 'Notes on the action taken by the Association in the matter of the practice of medicine by unqualified persons'. For more on the GMC's attempts to protect the profession from unqualified practice in general and to deal with this issue of proprietary drugs as it affected practice of orthodox medicine during this period, see Stacey (1992); Carr-Saunders and Wilson (1933), 419; MacAlister (1906); Pyke-Lees (1958).} But in 1904 the \textit{British Medical Journal (BMJ)} initiated its own campaign to expose the contents of these remedies by publishing a series of short weekly articles on the composition and cost of particular secret remedies. These articles continued through to 1908, and were collected and published by the BMA in book form during the following year (\textit{Secret Remedies: What They Cost and What They Contain}). A second volume of these expositions, entitled \textit{More Secret Remedies}, was released in 1912.\footnote{See BMA (1909) and (1912). These books seem to have been widely read. The 1909 text was sold out in less than a month of publication, despite the fact that popular newspapers such as the \textit{Daily...}
While the BMA were campaigning against secret remedies, so-called legitimate pharmaceutical firms such as Allen Hanbury and Burroughs Wellcome (which had begun as family businesses and apothecary's shops, not many decades before) were busily buying scientific expertise to standardise and produce pure unadulterated drugs.\textsuperscript{29} E. M. Tansey's account of the early career of Henry Dale at the Wellcome Physiological Research Laboratories (WPRL) at the turn of this century, is a case in point. Dale (who will emerge as an important figure in this thesis) had trained as a scientist in Cambridge around the turn of the century before going on to St Bartholomew’s Hospital to become a physician. Unhappy as a physician, he was snatched up by the (WPRL) soon after qualifying as a doctor. This well-paid job with a commercial company allowed him to do the original scientific research which eventually led to him receiving a Nobel prize, but one of his most important tasks when he began with the company, was to standardise the diphtheria anti-toxin which was one of its main commercial products.\textsuperscript{30}

There was not much difference between pharmaceutical firms and patent medicine manufacturers at the turn of the century. Apart from the fact that many of them had begun as apothecary's shops, their records of drug adulteration was as unimpressive as their competition -- the proprietary medicine manufacturers. By adulteration Victorians meant thus: 'any procedure that produces an alteration in strength or purity, or both, from the avowed standard of a drug, whether through intent or neglect'.\textsuperscript{31} In his \textit{Treatise on Adulterations} of 1820, Frederick Accum concluded that 'nine tenths of the most potent drugs and chemical

\textit{Express, The Graphic, The News of the World, The Daily Chronicle, and The Star} refused to accept advertisements for it. See also 'The profitable "proprietary"', \textit{BMJ} (1909), 1: 556; 'Methods of quackery: All of the ills of humanity', \textit{BMJ} (1909), 1: 671; 'Quack medicines', \textit{BMJ} (1909), 2: 721; Patent medicine labels', \textit{BMJ} (1909), 2: 905. The \textit{BMJ} also reported on efforts to stamp out quackery in Europe and America as part of its campaign, demonstrating that their actions were entirely in line with the rest of the civilised world. See 'A German anti-quackery bill', \textit{BMJ} (1908) 1: 960, (here the editor of the \textit{BMJ} talks about the legal methods designed to stop the sale of quack remedies); 'Quacks in the press', \textit{BMJ} (1905), 2: 1607 (the editor laments about quacks in New York, USA) 'Suppression of quacks', \textit{BMJ} (1905), 2: 730 (the suppression of quacks in South Africa is praised); 'War against quacks in Philadelphia', \textit{BMJ} (1905), 2: 1825; 'Quackery in Italy', \textit{BMJ} (1907), 1: 210; 'Suppression of quackery in the USA', \textit{BMJ} (1907), 1: 103; 'Ophthalmic quacks in America', \textit{BMJ} (1907), 1: 892.

\textsuperscript{29} Liebenau (1981), Ch. 1; Beer (1958).

\textsuperscript{30} Tansey (1990).

\textsuperscript{31} Abraham (1995), 37. See also Stieb (1966); and Blake (ed. 1970).
preparations used in pharmacy (in England and Wales were vended in a sophisticated [i.e. adulterated] state).\textsuperscript{32} British pharmaceutical companies (such as Burroughs Wellcome and Allen Hanbury), like their American counterparts (e.g. Smith, Kline and French, Mereck, Parke Davis, Eli Lilly), tried to set themselves apart from patent medicine manufacturers by advertising that they sold higher quality medicines, and that they sold these medicine to physicians.

These firms based their respectability on their ability to reassure the consumer that he or she could rely on the quality of drugs their company had produced. Physicians also fuelled the demand for standard commodities when they appealed to measured doses and pure standard preparations to impress patients with a scientific approach to treatment which was quite apart from that of the drug peddler or unqualified practitioner.\textsuperscript{33} In short, there were competitive advantages (both commercially and professionally) for standardising drugs. Crucially, the drugs which the legitimate drug companies were producing became known as 'ethical' pharmaceuticals. And while this word 'ethical' initially meant 'honest', the term began to be used to define medicines which were advertised only to doctors, and not to the public. This latter development occurred during the first decades of the twentieth century.\textsuperscript{34} I should also like to draw attention to the term 'patent' at this point because, during this same time, the term patent, which originally meant 'open' in common language, came to mean 'secret' in the context of proprietary medicines: i.e. 'patent' medicines meant 'secret remedies'. I shall expand on this relationship between secrecy and disclosure in Chapter 2, as it has far-reaching moral implications, and implications for standardisation in general. It will also become evident as I detail this Stevens case that this in itself reflected the way in which issues of honesty and trustworthiness were directly linked to the reputations of people who sold drugs, and the kinds of drugs they sold.

\textsuperscript{32} Stieb (1966), 114.

\textsuperscript{33} Liebenau (1981), 13, 52-3.

\textsuperscript{34} Liebenau (1988); and Abraham (1995), 37-86.
I. 1. ii. Stevens and the Select Committee

The BMA and the General Medical Council (GMC) managed to convince the government to appoint a Royal Commission into the 'evil effects' of unqualified persons engaging in medical practice and surgery in 1910.\textsuperscript{35} Two years later, a House of Commons Select Committee on Patent Medicines conducted an inquiry into the sale of patent medicines, medical preparations and appliances, and the way in which they were advertised. This Select Committee inquiry was spectacularly public. The Committee held 33 public sittings, and directed over 14,000 questions at 42 witnesses over 2 years. The public interest it aroused was comparable to that generated by the Dreyfus trials, and of the American public's interest in the trial of president McKinley's anarchist assassin, Czolgosz.\textsuperscript{36} Popular newspapers (like the \textit{Daily Dispatch}) and special interest groups such as the Proprietary Medicine section of the London Chamber of Commerce, defended the manufacturer's right to protect his commercial interests by keeping the composition of his drugs secret. They accused the doctors' campaign against patent medicines as being an attempt to give doctors a monopoly over the medical market. These drug manufacturers were unashamed of the mass advertising campaigns. They claimed that they, like other commercial companies, were simply allowing 'the public' to judge the therapeutic efficacy of the medicines they consumed for themselves.\textsuperscript{37}

It was in the context of this public inquiry that Chas Stevens again came under scrutiny. Again, it was a patient who drew the Committee's attention to Stevens. A tuberculosis sufferer who had been treating himself with a patent medicine from a London firm was alerted to the existence of the Committee through the newspapers. He wrote to the Select Committee for advice about his situation. After some correspondence, and the promise that his identity would be kept confidential, he decided to give evidence before the Committee. He was therefore referred to as Mr A.\textsuperscript{38}

\textsuperscript{35} See \textit{Reports from the Commissioners, Inspectors and Others on the Practice of Medicine and Surgery by Unqualified Persons}.

\textsuperscript{36} See Richards (1991), 172-5; see also Note 1.

\textsuperscript{37} Saks (ed. 1992), 102.
Mr A told the chairman of the Select Committee (Sir Henry Norman) that 'he had found himself suffering from tuberculosis on the diagnosis of his medical man'. He recounted the story of how he had spent a considerable period of time in a sanatorium under treatment for tuberculosis. Mr A said that he had received some benefit for his treatment, but that shortly after his convalescence he had relapsed into what his doctors diagnosed as a nervous condition. It was during his relapse that Mr A's attention was drawn to an advertisement of Stevens' consumptive cure. He contacted Chas Stevens, hoping that Stevens might cure his condition. Without examining him, Stevens sold this man a three-month course of the treatment guaranteed to cure him.

Mr A told said that he had paid his money and had taken Stevens' Umckaloabo treatment as instructed. But after three months passed without him being cured of his condition he had sought the advice of a specialist, only to be told that his chest was worse than before. Convinced that he had been cheated, Mr A wrote to Stevens, asking for his five guineas to be returned in accordance with Mr Stevens' guarantee. Stevens replied, suggesting that Mr A had been misguided in his understanding of the agreement between them. 'First he (Stevens) had never in any case guaranteed to cure a patient in three months'. Secondly, Mr A had taken advantage of the agreement as he had never mentioned his lack of benefit before this point. Thirdly, he, Mr A, had broken the conditions of the guarantee by not giving Stevens a weekly report of his progress. Concluding with 'an offer to examine the patient if he would come to Wimbledon,' Stevens also offered Mr A 'another three months treatment which he would not have to pay for unless he [Mr A] was satisfied that he was on the right road for a complete cure'. Mr A would not be seduced. He continued to demand the return of his money.

38 See Note 1, p. xxi.
39 See Note 1.
40 Stevens seems normally to have treated his patients by correspondence. See PRO: FD1/163, 'Emancipation for tuberculosis after awful suffering: grateful tributes', Health Logic (October 1931), 14. In this article, which effectively presented a series of cases designed to promote the cure, two of the cases mentioned treatment by correspondence. For numerous other examples of quacks treating their patients by correspondence and diagnosing them through questionnaires, see BMA (1909). See also 'Methods of quackery: all the ills of humanity', BMJ (1909), 1: 671-2.
41 See Note 1, p. xxi.
would not give him a refund.\textsuperscript{43} It was only after several letters, Mr A's testimony before the
Select Committee, and the threat of further action, that Stevens returned Mr A's five guineas
with the following words:\textsuperscript{44}

Dear Sir,
I received your letter this morning, and cannot help but think that you are a most
unreasonable chap. Although, I had fully made up my mind when I wrote you on the
28th ultimo, I do not want you to think me as unreasonable as I think you. Therefore I
am returning your 5 guineas herewith, which I shall be glad if you will acknowledge.

Very truly yours

C. H. Stevens.\textsuperscript{45}

The way in which Chas Stevens behaved towards Mr A was enough to label him a disreputable
man and a commercially-driven drug peddler. He defended himself against these attacks with
testimonial evidence from satisfied consumers just as he had done in the case of the
Basingstoke widow, a ploy typical of patent medicine manufacturers. Stevens even went so far
as to challenge the Brompton Hospital to inoculate him with the worst tuberculosis, on the
condition that when he cured himself by his own remedy, the hospital would adopt his
treatment as their cure for consumption. The Brompton Hospital did not take up this
challenge.\textsuperscript{46} But while these particular cases suggested that Stevens' treatment did not cure
tuberculosis, the Select Committee decided that this was insufficient evidence to determine the
efficacy of this consumptive cure. It may have been that the remedy was ineffective on Mr A's
consumption, but that it had an observable therapeutic effect on other cases of the disease. So,
having taken this evidence for Mr A, the Committee initiated their own investigation of
Stevens' treatment.

\textsuperscript{42} See Note 1, p. 365.
\textsuperscript{43} See Note 1, p. 365.
\textsuperscript{44} See Note 1, p. 365.
\textsuperscript{45} See Note 1, p. 365.
\textsuperscript{46} See Note 1, p. xxi.
The Committee asked Stevens to submit two bottles of the remedy. They, in turn, recruited expert witnesses to examine its contents for evidence of active ingredients which might explain whether the treatment worked, and if so, how. The Committee then sent these bottles to a trustworthy government chemist. The chemist found that the contents of these bottles were the same neither in volume nor proportion. He found 'no alkaloids or resins, typically associated with medical therapies with active ingredients, and he concluded that 'the solid matter corresponding with the colouring and extractive substances are therefore essentially mixtures of wine and glycerol.'

The Committee members were clear about three main points: Stevens was an unscrupulous character whose remedy had failed to cure at least two people and had most likely duped many others; the chemical analysis of the medicament suggested that it was unstandardised (and therefore unreliable); and the remedy contained no specific chemical (or derivative thereof) which was identifiably therapeutic in tuberculosis. Indeed, the positive identification of wines and glycerols as the primary components of the remedy suggested that it was a typically quackish remedy. And yet it seemed that lay people were still willing to entertain the possibility of the Umckaloabo treatment as an effective remedy against tuberculosis. The Select Committee's chairman was particularly struck by the credulity of the average layman:

It is instructive as illustrating the credulity of the public, that Mr A., although an intelligent man, believed that Stevens' lithographical letters were written by Stevens' own hand, with reference to his case, and that in spite of our efforts to enlighten him, he was obviously still impressed when he left us by Stevens 'challenge' to the Brompton Hospital for Consumptives.

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47 The government chemist they chose was James Dobbie. The Committee had noted with some dismay that there was considerable inconsistency as far as scientific opinion on chemical evidence was concerned. During the course of the two years of evidence they came to prefer some chemists over others. See Note 1, pp. xi-xii.

48 See Note 1, p. xxi.

49 For more about therapeutic effect in tuberculosis, see F. B. Smith (1988), 137-66, and 97-135; and Bryder (1988). For more on the association of certain chemical groups, such as alkaloids and glycerides, with therapeutic effect in the first half of the century, see Grier (1937), 49-57, 140-63, 193-203, 247-52; Liebenau (1984); Slinn (1984) and (1989); Matthews (1962); Robson (1989). See also Note 1, pp. xxxvi-xl.

50 See Note 1, p. xxi.
Thus it would seem that the public were impressed by medical treatment which seemed especially tailored for their needs. Also, testimonies from ordinary people went a long way to convince patients of the curative value of a treatment, especially when (as one often saw in advertisement labels) these testimonies were corroborated by physicians who had spoken out courageously in favour of the treatment, apparently against professional advice.

I. 1. iii. Stevens the quack: unqualified practice, secret remedies and moral conduct

H. G. Wells' novel *Tono-Bungay* is said to have been based on Chas Stevens' story.\(^{51}\)

Published in 1909, the book is about how a patent medicine manufacturer named Edward Ponderevo made and sold a fraudulent secret remedy named Tono-Bungay. The story is told by his nephew George Ponderevo. George was the son of a housekeeper of aristocrats who lived in a manor house named Bladesover in the Kentish countryside. Because he was raised at Bladesover, he had been socialised to understand the order of things, and thus served as Wells' moral voice for describing the proper social order of Edwardian England. But the young George found himself being banished from Bladesover, and shunted off to his uncle Edward after an incident in which the gentrified children accused him of behaving unfairly during a fight. The charismatic and energetic Edward took George in as a fully indentured apprentice at his patent medicine company. The business was situated at Wimblehurst, where Edward himself lived.

After a few years, the business went bust, so Edward moved to London. At first he lived in relative obscurity, but with time Ponderevo began to market the secret remedy, Tono-Bungay. He advertised the medicine in the newspapers, on posters and through personalised letters posted all over the country. Tono-Bungay was 'THE SECRET OF VIGOUR'.\(^{52}\) There was 'Tono-Bungay Hair Stimulant'. There was 'Tono-Bungay Chocolate' with 'extraordinary

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51 F. B. Smith (1988), 156.

52 Wells (1946), 122-3.
nutritive and recuperative value, in cases of fatigue and strain'. And, 'regiments of school teachers, revivalist ministers, politicians and the like' had been drawn to use the 'Tono-Bungay Lozenges' by the advertisement which featured a 'barristerish barrister' talking at a table with the words: 'A Four Hours' Speech on Tono-Bungay Lozenges and as fresh as when he began'. Tono-Bungay brought Edward Ponderevo money and fame. He soon became a rich celebrity who dressed and behaved like a gentleman. The business eventually went bust, but Ponderevo emerged as something of a hero.

Wells' *Tono-Bungay* was not only about the rise and fall of patent medicine manufacturer and a secret remedy, it was a social commentary of the changing class structure and social order which concerned physicians, elites and intellectuals. Wells' patent medicine manufacturers slip in and out of character and across class boundaries, all the time challenging social and cultural norms and boundaries of their day. Edward never revealed the contents of the secret remedy. Only once, in a guarded conversation to his nephew (George), did Edward reveal the contents of his brew noting the therapeutic value each ingredient was supposed to mimic:

> You see, said my uncle in a slow, confidential whisper, with eyes very wide and creased forehead, 'it's nice because of the' (here he mentioned a flavouring matter and an aromatic spirit), 'it's stimulating because of' (here he mentioned two very vivid tonics, one with a marked action on the kidney). 'And the' (here he mentioned two other ingredients) 'makes it pretty intoxicating. Cocks their tails...' 'Then there's' (but I touch on the essential secret). 'And there you are. I got it out of an old book of recipes -- all except the' (here he mentioned the more virulent substance, the one that assails the kidneys), 'which is my idea. Modern touch! There you are!' 

But George remained convinced throughout the Tono-Bungay affair that the business of making and selling this secret remedy was unethical and morally wrong. He had accepted his uncle Edward's offer of a partnership in the business only because, as he said, it offered 'a life of scientific research, no passionate service to humanity could ever have given me'.

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53 See Note 36, 145.

54 See Note 36, 124.
used George to state that the commercial venture was morally wrong because they were selling the Tono-Bungay 'slightly injurious rubbish [sold] at one-and-three-halfpence and two-and-nine a bottle, including the Government stamp.'

Whether Wells' *Tono-Bungay* is about the Stevens story is secondary. The point is that it could have been. There are certainly striking similarities between Stevens and Wells' Ponderevo. Both were infamous patent medicine manufacturers, both advertised in similar ways and made their fortunes by selling a suspicious secret remedy with an unusual-sounding name they appeared to have concocted. Stevens lived and operated out of Wimbledon, Ponderevo operated out of Wimblehurst; Ponderevo had colonial links (his brother had emigrated to South Africa), Stevens had lived in South Africa and fought in the Boer War. People from all walks of life bought Ponderevo's Tono-Bungay and Chas Stevens' Umckaloabo. This, and the money Ponderevo earned, was the currency he used to travel across class boundaries. Stevens, too, was able to sell his remedy to people of all classes.

Stevens' Umckaloabo treatment may seem a strange name. Its African-sounding name was a creation of the phonetic pronunciation of the Zulu words for 'cold' and 'flu', and was designed to have natural appeal. Like Wells' Tono-Bungay, it would have sat well amongst other proprietary medicines of the time, many of which had unfamiliar names. 'Pure colourless kalamas', 'salith leaves', 'stallax', 'pheminol', 'pergofl', 'pure bisurated blossom', 'tennaline' and 'carmarole' were just some of the names proprietary drug-makers created with botanical nuances to suggest botanical, biological and chemical effect.

Most proprietary medicine-makers tried to legitimise their product just as Stevens did, by printing testimonies of alleged patients and doctors on the label. Some even made the remedy itself a physician's testimony. The 'Roulet injection' (advertised as a treatment for gonorrhoea at the time), which was guaranteed by the facsimile signature of an imaginary 'Dr Roulet', was a famous example. Stevens chose to stick with the 'Umckaloabo' brand name for the

55 See Note 36, 139.

56 See Note 39.

57 See Note 1, p. xix.
treatment despite being prosecuted for fraud in 1910, and humiliated by the Select Committee inquiry of 1912. It was perhaps because of the success of the Umckaloabo treatment that he did, but he would not have been unique if he had decided to change the name of his product. Manufacturers of proprietary medicines were not averse to changing the names of their drugs or adopting an alias to boost drug sales, or to rescue an unsuccessful or disreputable product. Famously, an unqualified American named Skinner, who operated in Britain, was successively Scott, Symonds, London Stores, Professor Dana, Professor Pollock, and Horatio Carter. Similarly, Nelson Lloyd, an Englishman who sold a 'fat cure', was in reality an advertising agent named Derry.  

Stevens diagnosed and treated his clients by post. Again, this was not uncommon amongst proprietary medicine manufacturers, but it was marked by physicians as the sign of a 'quack'. Patients, it seems, were not so concerned about distinctions between qualified and unqualified practice, and with good reason, or so George Bernard Shaw believed. In his popular play The Doctor's Dilemma (produced in London in 1906, and published in 1911, just two years after the publication of Tono-Bungay), this famous critic of the medical profession claimed that:

the distinction between a quack doctor and a qualified one is mainly that only the qualified one is authorised to sign death certificates, for which both sorts seem to have about equal occasion. Unqualified practitioners now make large incomes as hygienists, and are resorted to as frequently by cultivated amateur scientists who understand quite well what they are doing as by ignorant people who are simply dupes. Bone-setters make fortunes under the very noses of our greatest surgeons from educated and wealthy patients; and some of the most successful doctors on the register use quite heretical methods of treating disease and have qualified themselves solely for convenience. Leaving out of account the village witches who prescribe spells and sell charms, the humblest professional healers in this country are the herbalists... I have never been able to perceive any distinction between the science of the herbalist and that of the duly registered doctor.  

58 See Note 1, p. xxii.

59 See Note 1, pp. xxii-xxiii.

60 J. Byers, 'Quackery: with special references to female complaints', BMJ (1911), 1: 1239-42; see also Note 1, p. x; Digby (1994). See also 'Unqualified practice in the name of the law', BMJ (1911), 1: 1277-81; 'Unqualified practice through the post', BMJ (1911), 1: 1281-4. Comments from physicians about unqualified practice can also be found in WHMCAC: SA/BMA/C355, 'Unqualified practice: 1906-1925'. See also Bartrip (1990), 41-6 and 184-94; Thompson (1928), 345-6; and Carter (1903), 222-44. For more on the medical practice of these elite physicians, see Lawrence (1985) and (1994).
Stevens posed a problem for doctors in some respects because although he behaved like an unqualified practitioner and had access to their patients, he had never claimed to be a doctor and could not therefore be taken to court for impersonating a doctor. Some physicians also took the view that this distinction was purely theoretical. The point was that unqualified practitioners or laymen like Stevens fuelled the trade in proprietary medicines, and that members of the public were being duped into engaging their services and using their remedies.  

However, when BMA officials began their initiatives to expose people like Stevens with the view to eliminating the trade in proprietary medicines, they were confronted with a more complex reality. Not only did patients knowingly engage unqualified practitioners, Sir Alfred Cox of the BMA found that many qualified doctors prescribed proprietary medicines and secret remedies and recommended them. In the years that followed, Stevens

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61 Shaw (1948), 25-6. See also Löwy (1988). For more on concerns about the medical profession descending into a trade, see Parry and Parry (1976).

62 For cases of unqualified practitioners which the BMA and GMC brought to legal trial, see: 'Status of an unregistered practitioner', BMJ (1929), 1: 281 and 371; 'A bogus doctor', BMJ (1920), 2: 456; and 'Offences under the Medical Acts', BMJ (1921),1: 324; 'A coroner on an unqualified practice', BMJ (1922), 1: 615; 'The practices of an unregistered medical practitioner,' BMJ (1932), 1: 266.

63 The case of Mr Roche is particularly noteworthy. The Society of Apothecaries of London attempted to prosecute Roche. The case was as follows: In November 1928, Mr C, a patient suffering from cancer of the stomach, consulted Mr Roche (an unqualified person with a considerable practice in the area), who prescribed for him a certain medicine. Mr C died shortly afterwards. At the inquest, in which Mr Roche's medicine was implicated in Mr C's death, it was revealed that Mr Roche admitted to having practised for fifty years as a consulting specialist in drug action, but that he only took cases incurable for the ordinary doctor. Although Mr Roche was not found guilty of Mr C's death, the Society of Apothecaries wanted to bring him to trial under the Apothecaries Act. Recalling a court ruling in which Mr Justice Cresswell had defined an apothecary as 'a person who professes to judge internal disease by its symptoms and applies himself to cure that disease by medicines', they reasoned that Mr Roche, though he had not been masquerading as a qualified doctor, had been falsely acting as an apothecary. They were disappointed when they were advised to refrain from taking such action, not on legal but on policy grounds. For Mr Roche had, it was understood, 'a very considerable practice. His name and methods had been given wide publicity in Truth and the Daily Telegraph to mention only two journals, and it is that any proceedings the object of which would curtail his activities, would incur strong resentment from those sections of the press.' They feared that the argument promoted by these papers would be that: 'Mr Roche is evidently a very clever person able to hold his own in controversy with doctors who have criticised him', that 'he claims to have discovered methods of medicinal treatment which the ordinary doctor does not know, and he backs up his belief in his methods by being able to produce a considerable number of people who have benefited by his administrations after doctors - some of them eminent men - have failed.' It was suggested that the legal action which was being contemplated would seem to be due to jealousy.
manipulated these complex relationships between unqualified practitioners, doctors and patients, as he tried to have his Umckaloabo treatment accepted as a legitimate class of drug.

I. 1. iv. The campaign for legitimacy and an official investigation of the Umckaloabo treatment

The Select Committee on Patent Medicines referred to Major Stevens as 'a well-known consumptive curer'. Over the next two decades Stevens became positively infamous. He doubled his efforts to promote the value of the Umckaloabo treatment. He advertised in newspapers, journals and pamphlets, wrote to physicians, tuberculosis medical officers, and doctors treating tuberculous patients in sanitoria throughout the country, and invited doctors up and down the country to try his remedy on their patients. Advertising brought him

64 The case of Cox and the Cicfa Company demonstrated this only too well. The case events are as follows: the BMA Ethical Committee was informed in 1920 that a certain Cicfa company was marketing a proprietary medicine which it claimed cured a number of digestive ailments. On the advertisement for the drug, the company stated that: '16,000 British doctors have taken up Cicfa. Very many of them have written to us privately of the splendid result which they have obtained by its use'. Cox investigated the case. After a cross-fire of angry letters between Cox and the proprietor, Cox was eventually invited to visit the company and view the evidence for himself. On 8 March 1920, he reported that he had found evidence that nearly 18,000 doctors had written in to the company, a number of whom had (as the advertisement stated), tried the remedy and were pleased with the result. He said: 'I read over 200 original letters. He [the Managing Director of the Cicfa Company] was all ready to produce the others but I had seen enough.' This discovery so alarmed Cox that he publicised it within the BMA and informed the GMC. The case prompted the GMC to issue a recommendation in the BMJ 'that a registered practitioner should not make use of, or recommend any remedy the composition of which he is not aware.' See WIHMCAC: SA/BMA/D176, Extract from Council Agenda of April 14th 1920. (4) Secret Remedies. Minute 97, 'Secret remedies, Minutes, Correspondence 1920-1942.' See also 'New and non-official remedies', BMJ (1922), 1: 927-8. For accounts of quacks around this period, see Schupbach (1985); Smith (1985); and Petersen and Markle (1975).

65 See Note 1, p. xxi.

66 At the time of the Select Committee's hearings, the Committee reported that Stevens had been inserting full-page advertisements of his consumptive cure in London daily newspapers up to the year before the report was written. See Note 1, p. xxi. This practice was continued after the hearings and into the 1920s. For evidence of the treatment being promoted in the papers, see 'Will two state departments help?', South of England Advertiser: Sussex, Surrey and Hampshire, 4 June 1931; Gordon Howe (on behalf of the Committee of Investigation on Treatments for Tuberculosis), 'Tuberculosis', letter to the editor, The Times, 4 April 1936; Gordon Howe, Northern Daily Telegraph, 13 July 1936; Gordon Howe, 'Tuberculosis', Western Daily Press, 13 June 1936. For evidence of the books and pamphlets which Stevens and his allies published to attract customers and to increase his campaign for doctors to use and medical authorities to investigate his Umckaloabo treatment, see Stevens (1938). See also Sechelhaye (1931) and (1938).

publicity. With publicity came more customers, more money,\(^68\) and more testimonials from ordinary Britons, who in turn, it seems, spread the word about the Umckaloabo cure.\(^69\) Since Stevens also wanted to be respected and credited by medical and state authorities for discovering an efficacious cure for tuberculosis, he actively sought to have his Umckaloabo treatment recognised as a legitimate consumptive cure by these authorities.\(^70\)

Stevens was unrelenting. Between 1914 and 1931 he approached the Ministry of Health, the Local Government Board (LGB), the British Medical Association (BMA), and the General Medical Council (GMC).\(^71\) He petitioned the Minister of Health for much of the first decade of the Ministry's existence. On some occasions he approached this department directly, on other

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\(^68\) PRO: FD1/163, 'Emancipation for tuberculosis after awful suffering: grateful tributes', *Health Logic* (October 1931). With regard to Stevens' own self-promotion, it is worth noting that by the second half of the 1930s, Stevens had managed to sell his treatment in Europe where it was produced by Messrs J. Brun and Son, chemists, place Longmalle 18, in Geneva; and by Mr Revel, chemist, rue St Lazare 34, Paris, IXe, in France. See Sechehaye (1938). One physician, Dr Lissant Cox, Central Tuberculosis Officer for the County of Lancashire, did (perhaps as a result of this propaganda) try Stevens' preparation on a number of his tuberculosis sanatorium patients. Cox, however, seems to have acted on his own initiative. He reported to the Ministry of Health that his investigation did not substantiate the claim that the remedy had curative properties. See PRO: FD1/163, A. S. MacNalty (Chief Medical Officer of the Ministry of Health) to E. Mellanby (Secretary of the MRC) and A. B. Maclachlan (Ministry of Health), 22/2/36 and 25/2/36. See PRO: FD1/163, Report of the Central Tuberculosis Officer of the Lancashire County Council (1924), 13. For more about Dr Lissant Cox and his views on tuberculosis treatment and the coordination thereof, see Bryder (1988), 72, 91-2, 103, 113, 117.

\(^69\) The introductory course of the treatment was sold at £2 12s 6d; further bottles went at 5s. Although the price was sometimes adjusted, the sale of the treatment, along with the sale of his pamphlets would have provided Stevens with a decent income. He claimed to have made £6,000 per year from it between 1903-1907 in South Africa, £5,000 of which he claimed to have given to the poor of Cape Town. Stevens himself was reported to have admitted to 'making such a good thing out of [the Umckaloabo treatment] as a secret remedy.' See PRO: FD1/163, Record of F. H. K. Green's meeting with Dr Frank Deas, 12/1/32. Another indicator of Stevens' comfortable economic standing was his ability to afford to pay the £2,000 legal fees incurred as a result of a legal action in which the BMA challenged the efficacy of his remedy. See PRO: FD1/163, E. Mellanby (MRC) to A. W. Hill (Royal Botanic Gardens, Kew), 18/3/36; and PRO: FD1/163, minutes A. S. MacNalty to E. Mellanby, 22/2/36, and 25/2/36. For more about Stevens' finances and financial dealings, see F. B. Smith (1988), 155-60.

\(^70\) Evidence of the fact that Stevens seized every opportunity he could to promote both the treatment and himself can be found in the copies of the books about the treatment which he distributed. Also, on the inside jacket of Sechehaye's (1938), *The Treatment of Tuberculosis Affections with Umckaloabo*, he placed a red sticker with the words: 'The headquarters of Umckaloabo, where the remedy is prepared, are at 204-6, Worple Road, Wimbledon, London, SW20. The Laboratory is under the personal supervision of Chas H. Stevens, the discoverer, from whom supplies can be obtained.'

\(^71\) PRO: FD1/163, F. Slator (for the Minister of Health) to T. P. Ritzema, 8/3/24; and T. P. Ritzema to T. Lindsay (Principal Assistant Secretary, Ministry of Health), 28/4/30.
occasions his allies approached the Ministry on his behalf. In February 1924, Stevens' ally, T. P. Ritzema of the *Northern Daily Herald*, wrote to the Minister of Health and its predecessor, the LGB, requesting a systematic inquiry into Stevens' remedy. He suggested that a scientific clinical investigation would demonstrate that the remedy did in fact cure people of tuberculosis. Acting on Stevens' behalf, Ritzema passed his request on to the Minister. The Ministry replied with this:

The claims made in regard to the results obtained in consumptive patients from the use of this remedy do not differ in character from those made for many other so-called remedies for tuberculosis, which have been advertised from time to time and afterwards found to be valueless; and after consideration of all the information available, the Minister is of the opinion that there is no sufficient ground for instituting a systematic clinical investigation into the value of this alleged remedy. The Minister is, however, advised that there is nothing to prevent any tuberculosis officer of a Local Authority or Medical Superintendent of a Tuberculosis Sanatorium from making trial of the remedy in the treatment of tuberculosis patients if he thinks fit to do so.

The letter infuriated Stevens. He believed that he was being treated unfairly, and wrote to the Ministry, making it plain that he had interpreted their reply to Ritzema to mean that

even though the Local Government Board, the Ministry of Health, the British Medical Association and our apathetic Government generally have persistently refused and still refuse to even allow me the opportunity of proving to them that my remedy for Tuberculosis does positively cure this insidious disease, the fetters have been somewhat removed that have prevented so many Medical Men from using my remedy, not only in their private practices but State Institutions.

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72 PRO: FD1/163, Minutes from A. S. MacNalty to E. Mellanby and Mr A. Maclachlan, 22/2/36, and 25/2/36.

73 For more on the history of the creation of the Ministry of Health and its aims and responsibilities, see Jones (1994), 76-8; Honigsbaum (1970); and Grant (1994). See also Gilbert (1973); Hay (1957); and Thane (1982).

74 No copies of Stevens' original letter to the Ministry of Health or to Ritzema seem to have survived. However, it does seem from the Ministry's response that Ritzema wrote to the Ministry on Stevens' behalf. See PRO: FD1/163, F. Slator to T. P. Ritzema, 8/3/24. It is noteworthy that although Stevens became persistent in his campaign to have authorities set up a clinical investigation of his therapy, he was no stranger to the Ministry in 1924. According to MacNalty: 'since about 1909 the Local Government Board and the Ministry have been aware of the claims made for Mr Stevens' consumptive cure'.


76 Stevens typed these words in red ink.
Stevens continued his pressure on the minister to conduct a clinical investigation of Umckaloabo both in the House of Commons and outside of it. At the same time he wrote to doctors and members of the general public to send written testimonials about his treatment to the Minister of Health. He did this by typing his challenge at the bottom of a copy of the letter from the Minister of Health perhaps as a ploy to demonstrate ministerial backing for his challenge.

The above, is I am satisfied, as far as any Minister of Health in his official capacity could reasonably be expected to go, and it is up to the Superintendents of T.B. Institutions and medical practitioners generally to wipe out tuberculosis or stop me from distributing the medicament which I claim is capable of bringing about this result. Umckaloabo is either a remedy for tuberculosis, or a damn fraud. If the former, it obviously should be used and the thirty thousand yearly victims in England alone saved from the living death they now endure; if the latter, I, Charles Henry Stevens, should be stopped, arrested, ostracised, imprisoned -- yes, hung, drawn and quartered as well. I knew you would agree with that, so if you will dear doctor, take a seat on the jury, collect at my expense some direct personal evidence, and not judge by hearsay, prejudice, or the opinions of those wise-heads who know it is no good, because they have never tried it! Then vote as your conscience dictates, the Minister of Health will, am sure, welcome your evidence.

Stevens gathered support for this treatment from all classes, professions and stations in British society. By the 1930s, the case had become a political issue. The newspaper man T. P. Ritzema and Waldron Smithers, the M.P. for Chislehurst, were two of his more prominent allies. While Smithers was keeping the case alive in the House, Ritzema was supporting him in the papers. In July 1931, Smithers put the Minister on the spot in the House of Commons: had his department investigated the Umckaloabo treatment for tuberculosis? and if so, with what results? At first, the Minister replied in much the same terms as he had to Ritzema. But by

77 See letter from Stevens to Miss L. Waddington, 29 Ice St, Off Whalley Range, Blackburn, Lancashire, 4 November 1932. There, in 1932, he admits to having waged a campaign for a clinical investigation of his cure since 1924 without success: "the details of the questions that have been asked in the House by captain Elliston and his "brother members" show that whatever Government is in power, the Ministry of Health adopts the same attitude as it has shown since 1924."

78 The words 'they have never tried it!' were underlined in the original document. See PRO: FD1/163, T. Lindsay to T. P. Ritzema, 28/4/30.
this stage, Stevens' 'challenge' to doctors and victims of tuberculosis had caused a large
total of testimonial letters about the treatment to be directed to the Ministry. Smithers knew
about this evidence. He rose again, this time asking whether in view of the national significance
of
finding a cure for this important disease, he would reconsider his decision and instruct his
experts to re-examine this method of treatment and to use every means at his disposal to
make this treatment known to the public.\footnote{PRO: FD1/163, Official reports of the Parliamentary Debates, 'Questions and Answers given in the House of Commons regarding the Umckaloabo treatment for tuberculosis', 30 July 1931, col. 2442, vol. 255.}

The response: 'there was insufficient ground for instituting a clinical investigation into the
value of this alleged remedy for tuberculosis.'\footnote{PRO: FD1/163, C. H. Stevens to F. H. K. Green, 30/11/31.}

I. 2. Bringing the case to trial: doing battle with the MRC

By 1931, when Stevens approached the MRC's newly-established Therapeutic Trials
Committee (TTC), he had been campaigning for an official investigation of his treatment for
over a decade. That November he wrote to the Secretary of the TTC:

having unsuccessfully approached every known authority that could have investigated the
matter for nearly thirty years now, I am not approaching you with any great confidence of
success. Nevertheless, I am sending you two books that have recently been published about
a remedy that I have been informed you would probably like to investigate.\footnote{Hansard, July 1931, vol. 255, col. 758 (PRO: FD1/163). See also PRO: FD1/163, C. H. Stevens to Miss L. Waddington, 4/11/32.}


\textsuperscript{80} PRO: FD1/163, Official reports of the Parliamentary Debates, 'Questions and Answers given in the House of Commons regarding the Umckaloabo treatment for tuberculosis', 30 July 1931, col. 2442, vol. 255.


\textsuperscript{82} PRO: FD1/163, C. H. Stevens to F. H. K. Green, 30/11/31.
F. H. K. Green (Frank Green, the secretary of the TTC) immediately contacted the Chairman, T. R. Elliott. On Elliott's authority Green rejected the application 'toute suite', without explanation.\(^\text{83}\) Elliott had heard about Stevens' treatment. The MRC's response did not come as surprise to Stevens. He wrote:

> This is just exactly the kind of answer I expected to get to my last letter, and shows quite clearly that your so-called Therapeutic Trials Committee is not concerned in finding a cure for so wretched a disease as tuberculosis should there be any chance of such [a cure] springing from a layman.\(^\text{84}\)

Meanwhile, back at the MRC, Elliott, perhaps suspecting that the matter would not end here, advised Green to 'seek the pleasure of a conversation with Dr [Frank] Deas, a physician working in the Wimbledon area where Stevens' company was based, to learn what he thinks of the remedy and its maker.'\(^\text{85}\) Deas called Green at MRC headquarters. In early January, after their meeting, the administrator Green, recording this conversation with Deas for the files, wrote:

> [Dr Deas] told me how he had impersonated a patient and consulted Stevens. Stevens told him to go to a doctor friend of his for diagnosis, and then, if thought tuberculous, to come back for treatment and 'I will guarantee to cure you, old man'. Deas later challenged Stevens to publish his formula, telling him that even if it cured 25% of tuberculous cases, he would have the whole world at his feet. Stevens replied that he was making such a good thing out of it as a secret remedy, that he had no intention of disclosing its nature. Deas said there was no evidence available at the trial, or since, that Stevens ever received any material from Africa, as he alleged. Botanists and others in the district of Africa from which the 'plant' was supposed to come denied its existence; nor was anybody except Stevens familiar with the native 'lore' on which the alleged treatment was stated to be based.\(^\text{86}\)

\(^{83}\) 'Toute suite' was underlined in the original document. PRO: FD1/163, T. R. Elliott to F. H. K. Green, 18/12/31. PRO: FD1/163, extract from a letter from F. H. K. Green to T. R. Elliott, 21/12/31.

\(^{84}\) PRO: FD1/163, C. H. Stevens to F. H. K. Green, 22/12/31.

\(^{85}\) For further evidence of the MRC's correspondence about Stevens' treatment, see PRO: FD1/163, F. H. K. Green to F. Deas, 22/12/31. In that letter Green says: 'Professor Elliott told me, however, that, if I would like further information about Mr C. H. Stevens and his works, I should apply to you. I hasten to do so, not only for my personal edification, but also because we often receive inquiries from one source or another about this alleged remedy.'

\(^{86}\) Typed record of meeting between F. H. K. Green and Deas, 12/1/32.
Green may well have felt that his brief on Deas had served him well, because the matter did not rest here.

Stevens' aristocratic allies and parliamentarians had already begun to petition the MRC for a clinical trial. If the therapy was indeed worthless, then surely a proper scientific clinical trial would demonstrate this without question. The exasperated M.P., Captain Elliston, pleaded the case with Walter Fletcher directly.

The quack contends again and again that his 'remedy' is dismissed without trial investigation. The credulous public protest that medical jealousy is *denying the man fair play*. Is there sufficient reason why the MRC should not arrange for such a laboratory and clinical investigations e.g. at a municipal hospital as would justify them [the MRC] in saying that the remedy has been given a trial?

Fletcher's reply to this request is revealing, not least because versions and excerpts of his reply to Elliston appeared in subsequent rejections of requests for an MRC trial. The letter has therefore been quoted in full in Appendix 1.

Fletcher told Elliston while he could sympathise with the M.P.'s situation, the MRC

would not be helped by the examination of claims which have neither a *rational basis* nor the support of any *trustworthy practical evidence*.

He insisted that clinical trials were for testing 'new remedies of an authentic kind', and that, if the MRC moved away from this policy, they would forfeit their arrangement to test remedies in

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88 Italics are mine. PRO: FD1/163, Capt. G. S. Elliston to W. M. Fletcher, 11/11/32. In some cases M.P.'s would be asked by their constituents to raise the matter in the house. See PRO: FD1/163, M.P. (unnamed) to M. Mears, 17/3/33. The letter, originally addressed to her M.P., eventually made its way to Mr Balfour, and then later to the MRC. See PRO: FD1/163, A. L. Thomson to A. R. Walford, 22/3/33; A. L. Thomson to Walford, 27/3/33.

89 For evidence that versions of and excerpts from this letter appeared in other responses from the MRC and the Therapeutic Trials Committee, correspondence between W. M. Fletcher and A. B. Howitt (M.P.), namely: PRO: FD1/163, A. B. Howitt to W. M. Fletcher, 26/11/32; W. M. Fletcher to A. B. Howitt, 28/11/32; A. B. Howitt to W. M. Fletcher, 29/11/32 W. M. Fletcher to F. H. K. Green, 14/3/33; A. R. Walford to A. L. Thomson, 22/3/33; A. Thomson and A. R. Walford, 27/3/33.

90 Quoted from Fletcher's letter (See Appendix 1). Italics are mine.
hospitals. Fletcher's primary objection to the Umckaloabo treatment was that it was a secret remedy:

To test such a remedy is to report upon a substance which is identified only by the invented name attached to it by the makers, and of which the composition may therefore be privately changed by them at any time. Apart from that, a secret preparation may contain dangerous components, and at best it usually consists of substances of which the medicinal properties are already well known... A machinery for testing genuine new remedies already exists, in our Therapeutics Trial Committee. *91*

Finally, he ended by suggesting that the Umckaloabo remedy was neither *new* nor *authentic*:

*[The] active principle was nothing more than the well-known drug Krameria. There was no evidence at the trial that the inventor ever received consignments of material from Africa, and botanists there have denied the existence of the plant from which the preparation and its name are alleged to be derived.* *92*

This was Fletcher's attempt to settle the matter, but the situation took an unexpected turn.

I. 2. ii. Credible allies and the politics of evidence

An independent body, presenting itself as a disinterested party, took up the case. This was the Committee of Investigation on Treatments of Tuberculosis (CITT). In May 1935, this Committee decided to conduct a clinical trial of Stevens' Umckaloabo treatment. This distinguished body consisted of Lady Malcolm of Poltalloch, who served as honorary treasurer, members of parliament (Lt. Col. J. Sandeman Allen, Robert Bernays, W. Craven Ellis, A. M. Lyons, and Sir Waldron Smithers), and other eminent people such as Lady Mount Temple, T. K. Dobson, George Parsons, Major Gordon Home and Brig. Gen. J. J. H. Nation, C.V.O, D.S.O.* *93* Theirs was to be a fair and scientific clinical trial. *94*

*91* See Note 74.

*92* See Note 74.

*93* For a list of Committee members, see PRO: FD1/163, circular letter (undated) attached to a letter from R. Hill to Dr E. Mellanby, 27/2/36. The composition of the Committee did, however, change over the next few years with Col. C. Kerr, M.P. and Lawrence Kimball, M.P., Capt. W. F. Strickland, M.P., being added to the list by March 1936. PRO: MH55/1170, letterhead of letter from the G. Parsons (Secretary to the Committee) to E. Mellanby, 5/3/36. According to G. Parson: *'This
The Committee launched its own campaign for the Umckaloabo treatment to be investigated. Its members petitioned the Ministry of Health, the BMA and the MRC. They informed the medical press that their Committee included members of parliament, and the Committee also informed the public that they had acquired mainly private funds (not government donations) to conduct a clinical trial of the Umckaloabo treatment. However, they implied that to spend the money on anything but an official trial would be morally unjustified.

Our committee have not thought it right to ask the generous donors to permit us to spend their money on this test unless it be officially observed by the Ministry of Health, the British Medical Association, and the Medical Research Council.

In their quest to gain the support of official medical bodies, the Committee took the following approach. First, they sent an official letter of introduction setting out the Committee's agenda to the authority concerned. Then they set up a meeting so that both parties could discuss the matter in person. George Parsons (the secretary of the Committee), visited Sir Kingsley Wood (the Minister of Health). Wood told Parson that:

Committee has been founded based on Dr Adrien Sechehaye's remarks [about the Umckaloabo treatment]; it is to have the support of Members of Parliament alive to both the public and medical aspects of the question. Dr Sechehaye had apparently visited London not long before Parsons made this comment to address a meeting convened by Lady Malcolm. At that meeting he had spoken about the treatment of tuberculosis with Umckaloabo, with examples of numerous cures he had effected.

94 For the Committee's desire to conduct a scientific clinical trial of the Umckaloabo treatment, see circular letter mentioned in Note 77.

95 G. Home, 'Letter to the Editor', The Times, 4/4/36; and see circular letter (Note 77). Several persons, accustomed to consulting the Charity Organisation Society (COS), about whether to donate to a particular cause or not, wrote to the COS for their advice about this cause. The COS's secretary (Rev. J. C. Pringle) in turn wrote to Fletcher requesting advice. Again, A. L. Thomson referred to the letter from Fletcher shown in Appendix 1. See PRO: FD1/163, J. C. Pringle to E. Mellanby, 11/2/35; A. L. Thomson to Secretary of the Charity Organisation Society, 13/5/35; J. C. Pringle to E. Mellanby, 16/5/35. For a more general discussion about charities and charitable funding of medical causes (particularly by aristocratic ladies) during the late nineteenth century and first half of the twentieth century, see Barry and Jones (1991); and Prochaska (1988).


97 PRO: FD1/163, Circular letter (undated) attached to a letter from R. Hill (Private Secretary to Lord Linlithgow) to Dr E. Mellanby (Secretary of the MRC), 27/2/36.
if the composition of the remedy were disclosed and there were some scientific evidence making out a *prima facie* case for investigation [he] would have no objection to observing a test.

In February 1936, Lady Malcolm sent word (via Lord Linlithgow) to Dr Edward Mellanby (who by then had succeeded Fletcher as Secretary of the MRC), informing him of the Committee's intentions. She urged Lord Linlithgow to set up a meeting between herself and Mellanby with a view to persuading him to endorse Committee trial.

[All] I want is a line from you to Dr Mellanby asking him to see one or two members of our committee say myself and one other. I have been a member of the Finance and House Committee of the West--- Hospital for Nervous Diseases for 25 years! So I am no newcomer to the world of medicine and fully realise the position [your] Medical Research Council occupies and for that reason we are specially anxious to get in touch with it.99

Linlithgow passed this note on to Mellanby.100 After several reminders Mellanby arranged to meet her.101 In the meantime, Mellanby had begun making his own inquiries into the case. He had contacted the Ministry of Health, where he was given the history of the case. Mellanby was also informed by Dr A. S. MacNalty (a medical officer to the Ministry of Health who had been advising the Minister on the case) that the Minister had rejected any legitimate inquiry,

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99 PRO: FD1/163, Lord Linlithgow to Mellanby, 27/2/36. See also the attached handwritten note from Lady Malcolm (undated) and the circular letter which had been sent to various medical associations in the country to inform them of the therapy, the evidence of efficacy, and the Committee's desire of their monetary support to conduct an official trial of the remedy. By 18 April 1935, they had received more than 198 individual donations 'from all kinds of pockets', reaching over 300 pounds. For quotation and list of subscribers, see letter and attached list on PRO: MH55/1170, Parsons to Ministry of Health, 18/4/36.

100 PRO: FD1/163. See circular letter which the Committee had sent to various medical associations in the country.

101 It should be noted that less than a week had passed between Lord Linlithgow's secretary's letter to Mellanby and the Committee Secretary's reminder to Mellanby. See PRO: FD1/163, Lord Linlithgow to Mellanby, 27/2/36. This included a handwritten note from Lady Malcolm (undated) and the circular letter which had been sent to various medical associations in the country. See also the letter from Lord Linlithgow to Mellanby, 28 February 1936 (PRO/FD1/163) saying: 'it would help me a lot if you will see Lady Malcolm and one other for a few minutes. She is a very charming and capable lady'. Other reminders can be found in: PRO: FD1/163, Mellanby to Parsons, 28/2/36 (PRO/FD1/163); and Parsons to Mellanby, 5/3/36. Mellanby did not state his reasons for his delay in replying to George Parsons.
and that he believed that an 'experimental home (for the Umckaloabo treatment) should be discouraged.'

MacNalty also told him that the Minister was going to see Sir Waldron Smithers (who sat on the Committee for the Investigation of Tuberculosis) to express an opinion to this effect.

On 11 March, Lady Malcolm called on Mellanby. Mellanby recorded his impression of that meeting immediately after it took place:

Lady Malcolm called, and brought with her Sir Waldron Smithers and four other people, one of whom was a Mr Thomas Dobson of Weybridge, who was one of the patients who claimed to have been cured of phthisis by this drug. They pointed out that they were completely disinterested financially in the matter, and only wanted to see whether there was anything in the great number of claims being put forward in regard to the curative action of this substance in tuberculosis. They had at their disposal a sum of £10,000 to carry out tests, and were thinking of taking a house and filling it with tuberculosis patients for this work. They asked if we would assist in any way, either by suggesting the best means for carrying out such work, or by appointing observers in the investigation. After much discussion I told them that it was impossible for the MRC to take any interest in remedies which purported to have therapeutic properties so long as there was any question of secrecy involved, that all the cards had to be on the table before we acted on the matter: we would have to know exactly the name of the plant and to be in possession of all other information in connection with the preparation of the compound. If all the necessary conditions were fulfilled, I said, I was prepared to ask the opinion of my advisers, and even to put the matter before the Council as to whether we should assist in this inquiry. I informed them that we did, as a matter of fact, carry out therapeutic trials for manufacturing chemists, and if all the conditions under which such tests were made were fulfilled in the present case, there seemed no reason why therapeutic trials should not be arranged. I gave them a copy of the Conditions of Investigation, as drawn up by the

102 PRO: FD1/163, Private and Confidential Memo 1. Mr. Maclachlan, 2. Secretary, 'Umckaloabo', 22/2/36.

103 More specifically, MacNalty's memo informed Mellanby that 'since about 1909 the Local Government Board and the Ministry [had] been aware of the claims made by Mr Stevens' consumption cure'. The memo noted that the remedy was of the nature of a 'secret remedy', and that it supposedly contained 80 grams of 'Umckaloobo' root and 13 grains of Chijitse, but that although samples purporting to be the Umckaloabo root had been examined by pathological experts, the parts of the plant necessary to identify its botanical nature had never been submitted for expert judgement. Mellanby was also informed of the 1912 and 1914 libel cases involving Stevens and the BMA. He also mentioned that various well-known chemists had analysed the remedy without finding any active ingredient which would be likely to have any curative effect on tuberculosis. The claim by Stevens, that the remedy was a germicide and that it destroyed the tubercle bacillus was, MacNalty noted, also found to be untrue. For the medicine in full strength failed to kill the tubercle bacillus after exposure to it for six days. Finally, Ritzema's and others' attempts to persuade the Ministry to initiate a clinical investigation of the remedy were mentioned, as were the Minister's categorical rejection. In fact Ministry officials, MacNalty noted, had already begun to take steps to discourage the Committee for the Investigation of Tuberculosis from engaging in this enquiry into Steven's Umckaloabo treatment. (He referred specifically to the Minister's intention to see Sir Waldron Smithers, on 25 February 1936, to dissuade him from campaigning for this cause.). See PRO: FD1/163, Private and Confidential Memo 1. Mr. Maclachlan, 2. Secretary, 'Umckaloabo', 22/2/36.
Therapeutic Trials Committee. Smithers suggested that if we were prepared to take this interest, we might be able to make use of the £10,000 and carry out the investigation under our own aegis. I said that also was a possibility. ¹⁰⁴

The BMA, Ministry of Health, and MRC were, therefore, united in the position that they would consider either overseeing or conducting a clinical trial of the Umckaloabo treatment for tuberculosis on the following two conditions: a) that the composition of the remedy was disclosed, and b) that the Committee could produce scientific evidence making out a *prima facie* case for investigation. The Minister of Health promised that his department would have its advisors examine the therapeutic evidence and the chemical analysis of the Umckaloabo treatment. ¹⁰⁵ If the Committee satisfied these two conditions, the remedy would be given a clinical trial. The BMA's Secretary, Dr Anderson, decided however that 'in view of the political support given to the nostrum (it would perhaps be prudent) to set up a small advisory committee including tuberculosis specialists like Dr R. A. Young, and Dr R. R. Trail on which the Ministry [of Health] might also be represented.' ¹⁰⁶ Mellanby, on the other hand, had suggested that an application satisfying these two conditions would be considered by the MRC and processed through the appropriate channel, namely the Therapeutic Trials Committee.

What, then did the Committee submit as evidence for the efficacy of the treatment? Moreover, how did the BMA and the Ministry of Health assess the Committee's evidence?

¹⁰⁶ PRO: MH55/1170, MacNalty to Rucker, 6/3/36. The Committee was in fact formed and met on at least three occasions. Only the records of the second and third meetings which were held at BMA House on Friday, 3 April 1936 and Monday 19 October 1936 have survived. The BMA advisory committee consisted of Dr C. O. Hawthorne (Chairman), Dr G. C. Anderson (Medical Secretary to the BMA), Dr R. A. Young, Dr Lissant Cox, Dr E. Ward, Dr R. R. Trail, Dr Norman Smith (clinical advisor to the Ministry of Health, who had been asked to assess the clinical evidence of the Umckaloabo case on this occasion), four officers of the BMA, and five members of the Committee for the Investigation on Treatment of Tuberculosis, including Major Gordon Home (Vice-Chairman), Sir Waldron Smithers (M.P.), Brig. Gen. J. J. H. Nation, Mr George Parsons (Secretary). See PRO: MH55/1170, Private and Confidential Memo, 'Committee re: Umckaloabo', compiled by Dr Norman Smith, 6/4/36. This note records the second meeting. See also records of the third meeting, Private and Confidential Memo, 'Committee re: Umckaloabo', compiled by Norman Smith, 27 October 1936, PRO: MH55/1170. At that meeting Dr A. Macrae (Assistant Medical Secretary of the BMA), Sir Humphrey Rolleston and Mr Bishop Harman, three people not present at the second meeting, were present, replacing R. R. Trail and R. A. Young. Only two BMA officers were present in this instance and there was no representative from the Committee for the Investigation of Tuberculosis.
What conclusions did these bodies come to? The Committee claimed that it had received 'a considerable volume of personal evidence' from persons who were 'satisfied that while suffering from tuberculosis, they have been cured or greatly benefited while taking Umckaloabo.' To convey that these were real patients, bearing testimony, they noted that 'among these are some sufferers who are personally known to certain of our members'. They were also fully aware of the fact that a certain percentage of testimonials 'may have been erroneous or exaggerated', but they stressed that it remained true that, at least in the lay mind, there was 'weight of moral evidence' to establish a claim that Umckaloabo should be made the subject of exact investigation. The testimonials from satisfied patients, which formed the 'weight of moral evidence', stood alongside evidence from Dr Sechehaye acting as a scientist, and evidence from the same doctor in his role as a clinician. Taking my cue from the body of evidence submitted to the Committee for the efficacy of Umckaloabo, I propose that there were three kinds of evidence: moral evidence, scientist's evidence, and clinician's evidence. I present them thus, but I do not intend to imply a hierarchal relationship between these three kinds of evidence. The relationship between these forms of evidence will become evident with the development of this thesis as a whole.

I. 2. ii. Three kinds of evidence

First, moral evidence. Moral evidence was the accumulation of personal testimonies of patients who had been cured by Umckaloabo. These testimonies were related in part by the patient and his or her family, and observed at various stages by doctors and nurses and

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107 PRO: MH55/1170. This quotation is from an undated document, prepared jointly, it seems, by the Committee for the Investigation of Tuberculosis and the confidential BMA advisory committee mentioned previously. The document was entitled, 'The Case for Investigating Committee', and is attached to a document entitled: 'Comment on the Case Presented by the Investigation Committee', in which the comments of the BMA Committee were outlined. Minute of the Second Meeting of the BMA Advisory Committee, held at BMA House, Friday 3 April 1936, p. 3.

108 See Note 91.

109 See Note 91.

110 PRO: FD1/163, 'Report to Medical Research Council', prepared by the CITT, 11/3/36. This document, which was in many ways a summary of Dr Sechehaye's book, served along with the book itself, as a document of evidence for the efficacy of the Umckaloabo treatment.
recorded by a medical doctor. Once these testimonies were aggregated, the patients became anonymous. Moral evidence therefore comprised anonymous voices. But for this body of evidence to have moral weight, the Committee had to demonstrate that these testimonies were true.\textsuperscript{111} As I mentioned earlier, authorities often suspected that the testimonies appearing on the labels of medicine bottles did not come from real patients. Lady Malcolm's Committee selected a total of eight cases and presented them as examples of moral evidence for the efficacy of the treatment. These were demonstrably unique case-stories of patients who, having been unsuccessfully treated by many doctors and at several institutions, had been cured by the Umckaloabo remedy. The fact that they had tried many other orthodox therapies before being cured by Stevens' cure was a statement about the therapeutic value of the treatment. The uniqueness of each story, and Committee members' personal knowledge of these patients was supposed to substantiate these truth claims.\textsuperscript{112}

The \textit{scientist's evidence} consisted of both `a chemical analysis of the composition of the Umckaloabo treatment', made by Mr Jules W. Burn, at the request of Dr Adrien Sechehaye, and `scientific experiments', some of which were conducted by Sechehaye and some of which had been reported to him. Sechehaye was a Swiss doctor in the Faculté de Médecine de l'Université de Genève. Like Stevens, this Swiss doctor had been so impressed with the workings of the treatment that he had continued to use and test the therapy on his patients. He had received at least some of his supply of the Umckaloabo treatment from Stevens in London. After `more than twelve years experience of Umckaloabo', and curing `several hundred cases', he had published a book defending the treatment.\textsuperscript{113}

\textsuperscript{111} In one case, it was even noted that the patient would be `willing to appear before a medical committee for examination. See PRO: FD1/163, `Report to Medical Research Council', prepared by the Committee of Investigation on Treatments of Tuberculosis, 11/3/36; P.35.A., pp. 4-5. See also the comments of Major Gordon Home and Sir Waldron Smithers of the CITT, Minutes of the Second Meeting of the BMA Advisory Committee, 3/4/36, pp. 2-3.

\textsuperscript{112} Although only eight cases were presented in detail in this report the Committee boasted of having collected some 511 cases in the book of evidence -- Sechehaye's book. These cases, it seemed, could be divided into several groups.

\textsuperscript{113} PRO: FD1/163, Report to Medical Research Council, prepared by the Committee of Investigation on Treatments of Tuberculosis, 11/3/36. See also his writings in the formerly anonymous publication, \textit{The Treatment of Pulmonary and Surgical Tuberculosis with Umckaloabo. Internal Medication}
The chemical analysis of Umckaloabo involved describing the drug as seen with the naked eye, observing it under a microscope, and then applying various tests and procedures to identify its components. Chemical tests were then performed on the drug. These revealed that it contained mineral substances, was rich in tannin, but contained no alkaloids. However, it was not easy to determine whether the drug extract contained glycosides. Here, the analyst claimed that, since there was no general method for isolating glycosides, hydrolysis was as good a method as any. Then there were Dr Sechehaye's `scientific experiments' which consisted of a case of self-experiment, referred to as `an experiment on a healthy man', and a few experiments on guinea-pigs and rabbits. The experiments were set up to answer two main questions about the drug: Was the Umckaloabo toxic? And did it have an effect on tuberculosis? The toxicity issue was crucial since the drug needed to be safe for human consumption. A human would therefore be the best subject for a toxicity test. Dr Sechehaye, the experimenter, donated his body for the experiment. The implication was that if the drug was found to be non-toxic in a healthy subject, it would certainly be safe for a sick patient. A toxicity test which was the self-experiment of a doctor would be a noble and reliable report that this drug was safe. Sechehaye's animal experiments, on the other hand, were designed both to test toxicity, and to give some indication about the efficacy of Umckaloabo. His justification for conducting these experiments on different types of animals was as follows. Animal groups were variable. There was variability within an animal group, variations between species, and between individual human beings within any given group. It was therefore impossible to determine from a drug's effect on a healthy or sick animal what its effect on a sick patient might be. One could only ever draw analogies from the behaviour of one group or one context to another but conducting experiments on different types of animals would enable one to do this more confidently. However, in the end, it had to be recognised that the laboratory


115 See Note 98, pp. 4-5.
investigator could never prove absolutely that the drug was non-toxic or effective in human beings solely from the results of the experiments.

Beginning with the human experiments: Sechehaye presented these first. There were two such experiments. The first he reported as an experiment in which he had injected himself intra-muscularly with 1 cc of the Umckaloabo and had then undergone a full clinical and laboratory examination.\(^\text{117}\) His clinical history showed him to be: a 68 kg man in a ‘very good state of health ... with no abnormal findings on examination with no symptoms or signs of tuberculosis.’\(^\text{118}\) Having subjected himself to a full clinical examination and submitted his blood and urine for analysis at the end of May 1928, the doctor proceeded to experiment ‘upon himself [again] from June 15th to September 17th 1928’.\(^\text{119}\) This time he investigated the effects of taking the Umckaloabo drug by mouth. Sechehaye recorded the experiment as if it had been conducted on an ordinary man.

Umckaloabo, in the form of liquid extract was taken from June 15th 1928, at the dose of 20 drops twice a day half an hour before the morning and evening meals; the dose was increased every week by 5 drops at each time of taking, up to 50 drops twice a day. It must be admitted that the medicine could not be taken very regularly on account of professional occupation. However, during the August holidays, the dose of 100 drops a day was taken fairly regularly; the maximum dose was 120 drops a day towards the close of the experiment, which ended on September 17th. It, therefore, lasted three months; the total quantity of fluid extract of Umckaloabo absorbed was 113 grammes.\(^\text{120}\)

After these experiments, the subject underwent a final examination. Apart from a weight gain of 1 kg, his medical status was unchanged. Sechehaye concluded that although the

\(^{116}\) See Note 98, pp. 8-12.

\(^{117}\) See Note 98, p. 6.

\(^{118}\) See Note, 98, p. 7. It was noted on p. 7 of the report, however, that although the doctor had no manifestation of tuberculosis, ‘on the radiograph, the hila present a few calcified glands, and near the left base there is a spot which might admit a former, well-localised, bacillary injury. Pirquet test positive; Besredka reaction negative.’ This included an examination of the circulatory, respiratory, digestive, nervous and muscular systems, with blood differential count and urine analysis, all of which were considered to be normal. His sublingual temperature was also considered to be within normal range (36 to 36.5 C.).

\(^{119}\) See Note 98, p. 7.

\(^{120}\) See Note 98, pp. 8-9.
fluid extract of Umckaloabo produces a strong reaction if introduced into the muscular tissues; if swallowed it is absolutely non-toxic, and does not give rise to any trouble in any system, even if the maximum dose prescribed to patients is exceeded.\textsuperscript{121}

Sechehaye's animal experiments resembled the experiments he had performed on his own body. He injected Umckaloabo intramuscularly into a rabbit and a guinea-pig. Then with the aid of his post-mortem examinations, he was able to determine the maximum and minimum toxic doses. Taking a second set of rabbits and guinea-pigs, he fed the animals successively smaller doses of the liquid form of Umckaloabo to confirm his toxicity test results. Regarding the efficacy of the drug, however, Sechehaye ended as he began, namely, that he could make no conclusions on the question of efficacy based on these animal experiments.\textsuperscript{122}

Sechehaye presented clinician's evidence of his own as well as that reported by other doctors. There were two forms of clinical evidence: a) the clinical observations of the signs and symptoms in successful cases, and b) an analysis of the effects of the Umckaloabo therapy on certain specific symptoms of tuberculosis.\textsuperscript{123} The clinical cases (observational evidence) were presented from the doctor's perspective with the following material: notes about the clinical investigations (e.g. radiographic and bacteriological tests), the case history prior to the administration of Umckaloabo, and a note about clinical symptoms and signs which the patient had presented.\textsuperscript{124} The date and dose at which the Umckaloabo treatment was initiated marked the beginning of the patient's recovery. The constitutional changes that followed this event were noted, as was the course of the patient's tuberculous symptoms.

The treatment regime was not standardised: each patient was managed on an individual basis.\textsuperscript{125} In one case, for instance, a patient who received a few doses of the Umckaloabo

\textsuperscript{121} See Note 98, p. 10.

\textsuperscript{122} See Note 98, pp. 12-17.

\textsuperscript{123} These sections of the documents of evidence (‘Report to the Medical Research Council’, and Dr Sechehaye's book) were entitled ‘Examples of clinical observations’ and ‘Effects of Umckaloabo on symptoms of tuberculosis’. See Note 98.

\textsuperscript{124} See Note 107.
treatment noticed an improvement in her condition. She therefore decided to stop taking the
treatment. Following this cessation, her condition, Sechehaye reported, took an immediate turn
for the worse. The patient's decline, however, reversed after the Umckaloabo treatment was
resumed, thus showing that her improvement had been caused by the treatment. Another case
concerned a patient who, after being relieved of her symptoms, took leave of Dr Sechehaye's
care. On examination several months later she was found to have remained well without having
taken any subsequent or boosting doses of the remedy. The doctor also demonstrated that the
treatment even worked on a patient who, 'on account of having to maintain his own family
could never take the rest that his condition demanded'. The patient, as a result of his situation,
had therefore had long periods during which he had 'worked ten hours and more a day'. This,
on its own, might have removed the possibility of any recovery, irrespective of medication.
And yet, it seemed, the Umckaloabo treatment 'cured' people. In other cases, patients treated
with Umckaloabo under Sechehaye's care had returned to their original doctors in such good
condition that their doctors had felt compelled to congratulate Sechehaye on the 'marvellous
effect' that his remedy caused.

Careful symptomatological analysis formed part two of the clinical evidence of the efficacy
of Umckaloabo. In his report on 'Effects of Umckaloabo on the symptoms of tuberculosis',
Sechehaye noted that while Umckaloabo 'produces its effect upon all manifestations of
tuberculosis infection ... its influence upon certain symptoms must be emphasised'. Fever,
cough, expectoration, haemoptysis, night-sweats, anorexia, weight, pain, stethoscopic signs,

125 PRO: FD1/163, 'Report to Medical Research Council', prepared by the Committee of Investigation
on Treatments of Tuberculosis, 11/3/36, pp. 18-31.

126 See Note 98.

127 See Note 98.

128 See Note 98.

129 The predominant view during this period was that rest was essential for the recovery from
tuberculosis. See Bryder (1988); and Smith (1988).

130 See Note 98. See 'Case of fibro-caseous tuberculosis of both apexes', pp. 29-32.
The quotation comes from p. 32.

131 PRO: FD1/163, 'Report to Medical Research Council', prepared by the Committee of Investigation
on Treatments of Tuberculosis, 11/3/36, p. 33.
and fatigue (and other associated nervous symptoms) were the symptoms on which Sechehaye's
probing eyes were focused.132

To analyse these symptoms the doctor noted the nature, extent, duration and time of the
symptomatological changes which followed after his patients had begun taking Umckaloabo.
There were roughly two symptomatological courses: a) symptoms which improved
immediately (within hours or a day or two) after the treatment was begun, and b) symptoms in
which these changes were either unremarkable, occurred only occasionally, or were only
observed some time after the treatment had begun. The first category comprised the following
symptoms: fever, night sweats, anorexia, weight, pain, fatigue and nervous symptoms. Cough,
expectoration and haemoptysis fell into the second category.133

Sechehaye supplemented his observational evidence of direct effects in certain symptoms
with information accumulated through his clinical experience of the following: other drugs,
patients' comments about the evolution (or improvement) of their symptoms, and the results of
some of the experiments he had conducted on himself. This supportive evidence was not,
however, applied in a consistent manner. In the case of fever, for example, the doctor
compared his experience of Umckaloabo with the speed at which he had seen other drugs
reduce fever. He also cited striking cases of the drug's effect on fever in the case of
tuberculosis, Umckaloabo's failure to have an effect on fevers caused by other diseases, and
the results of his self-experiment.

In the case of anorexia, however, the doctor supplemented his observational evidence of
the immediate effect of Umckaloabo on weight and appetite with patient's comments, remarks
about the extreme cases in which the drug had still had an effect, and the elimination of other
possible explanations for the increase in appetite in these cases.134 Interestingly, in the case of
fatigue and nervous symptoms, Sechehaye allowed a patient's account to serve as the weight of
evidence for the direct effect of the drug on this symptom because the patient was a doctor.135

132 See Note 115.
133 MRC Report Section, 'Effects of Umckaloabo on the symptoms of tuberculosis', pp. 33-45.
134 See Note 117, pp. 37-8.
Symptomatological changes which were either unremarkable, rare, or only observed some time after the treatment had begun, were given less attention. 136

In the case of haemoptysis, however, a rational physiological argument was used to rescue this as a weak effect. 137 Finally, the argument for the Umckaloabo having a direct effect on certain symptoms was strengthened by uniting these symptoms under one explanatory umbrella -- phase 1 of the therapeutic effect. The symptoms in which only an indirect effect had been observed fell into phase 2 of the therapeutic process. 138 It is important to note at this point that this corpus of evidence, though divided and presented here (and in the documents presented to medical authorities at the time) in three separate forms -- moral evidence, scientific evidence and clinical evidence -- within each form the evidence is heterogeneous. The relationship between the three forms of evidence was not hierarchical. Indeed, the way in which each form refers to, defers to and depends on the others maps a social and geographical world of evidence through which a course of therapeutic efficacy could be navigated rather than a ladder ascending to therapeutic truth. The significance of this will be discussed in the commentary of the case in Chapter 2.

I. 2. iii. The wrong kind of evidence

The Committee of Investigation on Treatments of Tuberculosis comprised laypeople who believed that they had presented a strong prima facie case for the efficacy of the Umckaloabo treatment. 139 MRC authorities did not see this as prima facie evidence for the efficacy of the remedy, neither did the Ministry of Health, or the BMA’s Advisory Committee. They each had

135 See Note 117, pp. 40 and 45.
136 See Note 117, p. 35.
137 See Note 117, p. 36.
138 See Note 118, pp. 45-7.
139 At the second meeting of the BMA Advisory Committee, Sir Waldron Smithers, in response to the suggestion that whether there was prima facie evidence for efficacy rested with the medical profession and not the layman, retorted: ‘We as laymen feel there is prima facie evidence.’ See PRO: MH55/1170, Minutes of the 2nd meeting of the BMA Advisory Committee, 3/4/36.
different reasons for rejecting this lay Committee's evidence. The significance of this will be
addressed in the commentary of this case and themes on the thesis as a whole in Chapter 2.

For the MRC the absence of a detailed chemical analysis that showed that the Umckaloabo
root had an identifiable active ingredient which could be isolated from the extract was
unacceptable.140 Mellanby had told the Committee on previous occasions that the MRC's
Therapeutic Trials Committee required information about who had manufactured the drug,
what its purpose and special advantages were, how it was administered, and in what doses.
The members of the MRC's trial machine also needed to know the chemical formula and
physical properties of Stevens' cure, whether or not its manufacturing process had been
patented, experimental evidence of the value of the remedy which included pharmacological
and toxicity tests, as well as particulars about any clinical trials that had either already been
conducted or were being arranged, and details of scientific publications on the subject.141 When
Mellanby received the Committee's evidence he replied to Parsons (Secretary of the CITT)
with this:

I think I have already told you that it is quite impossible for the MRC to take any steps in
this matter until they know exactly what the substance is with which they are dealing.142

Mellanby also complained that this evidence had not come in, or on, the application form for a
clinical trial.143

140 For evidence of the crucial role of chemical analysis for the MRC in this instance see: PRO:
MH55/1170, Minutes of the Third Meeting of the BMA Advisory Committee, held at BMA House,
19/10/36, pp. 1-2; undated document entitled: The Case for the Investigating Committee and
Comment on the Case Presented by the Investigating Committee. See PRO: FD1/163, Mellanby to
Parsons, 14/4/36; and untitled note by Mellanby about a meeting with A. Macrae (Assistant Secretary
of the BMA), 2/10/36.

141 For Mellanby's comments about the requirements of the Therapeutic Trials Committee, see PRO:

142 PRO: FD1/163, Mellanby to Parsons, 14/5/36.

143 This was what he said in a letter to Lord Horder after Horder was asked by certain members of the
Committee to speak to Mellanby about the request for an official trial after had submitted their
evidence to the MRC. See PRO: FD1/163, Mellanby to Lord Horder, 21/1/37.
Mellanby initiated his own inquiry on the matter, just as he had done when the Committee
first approached him. He focused on the ontological status of the Umckaloabo treatment. Did
Umckaloabo exist? And if so, what was its botanical identity was. What did the plant consist
of? Was there any evidence that supplies of this plant had been or were being shipped into
Britain from South Africa? He inquired about the identity of the Swiss doctor with the view to
finding out whether he existed or whether this was Stevens under another identity. Sechehaye
did exist. Mellanby wrote to Sir Arthur Hill, a respected botanist at the Royal Botanic gardens,
at Kew. Hill, in turn, asked his colleagues in South Africa to assist him in his investigation of
the true identity of the Umckaloabo plant. MRC officials also contacted the British Customs
Services to find out whether there was evidence of Umckaloabo being imported into the
country. According to the Kew botanists Umckaloabo was `probably a species of Rumex,
although the possibility of its being Polygonum was not excluded'. However, the botanists also
pointed out that an authoritative text on the medicinal uses of the species of Rumex and allied
genera occurring in South Africa (namely The Medicinal and Poisonous Plants of Southern
Africa, by Professor J. Mitchell Watt, M.B., Ch.B., and M. G. Breyer-Brandwijk) had not
mentioned `Umckaloabo'. Moreover, Hill noted:

We have ourselves long been curious as to the real identity of this plant, alleged to have
such wonderful properties. If a herbarium specimen could be obtained, i.e. a pressed plant
of portions of the plant with leaves, flowers and if possible, fruits, it should be a simple
matter to arrive at its true identity.

The Committee members, it seems, did not produce the herbarium specimens which had been
requested for further analysis.

144 For inquiries about the identity of the Umckaloabo root, see PRO: FD1/163, Mellanby to Sir A. W.
Hill, 18/3/36; and Hill to Mellanby, 24/3/36. See also Mellanby to George Parsons, 27/3/36, and Hill
to Mellanby, 'Umckaloabo', 1/4/36. For communications between South African botanists, Royal
Botanical Gardens, and Mellanby, see PRO/ FD1/163, E. Percy Phillips (Divisions of Plant Industry,
Botanical Section, Pretoria) to Hill, 21/4/36; Hill to Mellanby, 12/5/36; Mellanby to Hill, 14/5/36. See
note by Mellanby concerning customs inquiries.


146 Mellanby asked the Committee to supply this specimen. See PRO: FD1/163, Mellanby to Parsons
from Mellanby, 27/3/36. In this letter Mellanby asks for `a herbarium specimen, i.e. a pressed plant or
South African botanists were similarly mystified by Umckaloabo's identity. The Principal Botanist of the Division of Plant Industry, Botanical Section, in Pretoria wrote:

For years past this Division has attempted but unsuccessfully to trace the Source of the so-called 'Umckaloabo' cure. Just after the Boer War it was advertised in Cape Town and since then we have constantly had enquiries about it. Professor Watt of the Pharmacological Department, Witwatersrand University, wrote us a short while back: 'I do not believe Stevens' tuberculosis cure or Umckaloabo from which it is said to be made to be of any value in the treatment of tuberculosis. From information which have I think the remedy contains tamins (sic.) and nothing else.'

As far as the MRC were concerned, the Committee had failed to fit their evidence into the categories fixed by the MRC's Therapeutic Trials Committee (TTC). Crucially, they had not demonstrated the authenticity of the plant from which Umckaloabo was supposed to have originated. Indeed, there was no firm evidence that a plant by that name was being shipped into Britain from South Africa. In short, the existence of an active ingredient was in question because its source could not be traced.

The Ministry of Health's advisors, Dr E. W. Adams and Dr Norman Smith, also rejected the Committee's evidence. Their main objections revolved around the fact that this was a secret remedy. More specifically, Adams pointed to the following problems with the supporting evidence for the Umckaloabo treatment: a) the chemical analysis they presented did not 'constitute a "disclosure" of the composition of the drug';\(^{147}\) b) the experiments on the drug's physiological action did not throw any light 'on its therapeutic properties';\(^{148}\) and c) the case evidence provided 'no material upon which a medical or scientific opinion [could] be formed.'\(^{149}\) Regarding the chemical analysis, Adams reviewed the evidence on the composition of Umckaloabo and the experiments on the physiological action of the drug. He argued that the portions of the plant with leaves, flowers and if possible fruits', in order for Hill to make a complete diagnosis.) However, there is no documentary evidence to suggest that they did.


\(^{148}\) See Note 134, p. 3.

analysis did not constitute a true disclosure of the identity of Umckaloabo because there was nothing in the list of components to suggest that Umckaloabo had any pharmacological action. He based his argument on the knowledge that certain substances, such as alkaloids and glycerides, were pharmacological groups known to have therapeutic action. The absence of such substances, then, went against this drug being a valuable treatment for tuberculosis. Adams went on to state what, in his view, would be real disclosure.

A real disclosure would give the botanical name of the plant used, or if the plant is at present unknown to botanical science, a careful description of the plant with furnishment of samples so that its botanical relations could be determined.

Broadly speaking then, Adams, representing the Ministry of Health, stood with Mellanby and the TTC. Giving the botanical name would be 'real disclosure', because 'such information might at once give valuable pointers as to the likelihood of any therapeutic properties being present' in the Umckaloabo plant. Finding the plant, or the universal failure to find the so-called plant, was an important key to 'real disclosure'. 'If the plant were well-known it is highly probable that its medicinal virtues had already been investigated', if it was truly an unknown entity, 'a study of its relations might afford a valuable clue to its possible therapeutic properties, if any'. Certainly he found Sechehaye's animal experiments and trials useless attempts to provide a physiological basis for the efficacy of the remedy. According to Adams these experimental exploits simply showed that the substance was 'very irritating and, in the case of animals, even toxic'. They did not demonstrate any therapeutic value as such. As for the 'experiments on the healthy man by ingestion' these 'merely showed that by mouth

151 See Note 134.
152 See Note 134.
153 See Note 134.
154 See Note 134, p. 2.
155 See Note 134.
Umckaloabo is apparently non-toxic, but they [furnished] no evidence that the drug [was] other than inert.\textsuperscript{156}

Norman Smith took up the issue of the case evidence for Umckaloabo, gathering the bulk of the testimonials forming the weight of moral evidence and Sechehaye's clinical evidence together for examination. Smith was unimpressed with the testimonial evidence. Of these he said: 'the "protocols" of the 170 cases put forward by the Committee of Investigation on Treatments of Tuberculosis make tedious and melancholy reading'.\textsuperscript{157} He considered this testimonial evidence to be valueless because of the nature of the cases presented, and because of the way in which these cases had been reported. He found four main problems with this evidence: 1) the 'stories set out are of the usual patent medicine testimonial type of literature',\textsuperscript{158} 2) basic 'data such as age and sex of the results of sputum examination are lacking',\textsuperscript{159} and 3) the remedy had only been used on a select type of case, and on patients of an untrustworthy persuasion.

The miracles recorded on almost every page must, I fear be seen to believed. One cannot but ask why this remedy has apparently been used solely upon the serious or hopeless cases... Many of the patients were of the well-known 'difficult' type who disobey doctor's orders, criticise the administration of the sanatorium, refuse to enter a sanatorium, etc. They were in fact the very type most liable to be blown about by every wind of doctrine and to lose no opportunity of advertising their latest faith.\textsuperscript{160}

Finally, 4) there was 'no record of any attempt to follow up these reported cures and to ascertain their present condition'.\textsuperscript{161}

As for the clinical evidence, while Smith found Sechehaye's clinical approach generally scientific, he found this evidence nevertheless unsatisfactory.\textsuperscript{162} It was unsatisfactory because it

\textsuperscript{156} See Note 134.
\textsuperscript{157} See Note 134, p. 1.
\textsuperscript{158} See Note 134.
\textsuperscript{159} See Note 134.
\textsuperscript{160} See Note 134.
\textsuperscript{161} See Note 134, p. 2.
lacked certain details about the patients, such as 'sputum tests after history or collateral orthodox treatment' in general, but he also believed that the absence of such details reduced the value of the symptomatological analysis in specific ways.\(^{163}\) For example:

> exposition of the effects of Umckaloabo on the symptoms of tuberculosis -- particularly the abatement of fever and night-sweats -- cannot be assessed in the absence of data as to the patient's mode of life while undergoing the Umckaloabo treatment.\(^{164}\)

The BMA Advisory Committee also focused on the case evidence. They expressed particular concern about the insecure footing of testimonial evidence, the benefit of chemical and bacteriological information, in this case evidence, and the need for stronger clinical case-based evidence. As far as testimonial evidence was concerned, the Committee reported that such evidence was open to many qualifications, suggesting that the case for inquiry would be greatly strengthened if:

> a certain number, say 50 to 100, of the persons alleged to have been cured by Umckaloabo were examined and reported on by an experienced physician with a view to [determining] the present condition of such persons.\(^{165}\)

Significantly, the BMA Committee's assessment also linked concerns about the inadequacy of the evidence presented in this case of the Umckaloabo treatment with issues about the consequences of collecting evidence, testing remedies on patients, and using therapeutic evidence (obtained from any number of available sources) in the treatment of patients in the clinic. Indeed, they made it clear that whether the BMA sanctioned an official trial of Umckaloabo or not was as much a function of its position on these issues surrounding the question of evidence, as an analysis of the evidence itself. In a memorandum entitled

\(^{162}\) See Note 134.

\(^{163}\) See Note 134.

\(^{164}\) See Note 134.

Memorandum by a Committee of the BMA for Presentation to the Committee of Investigation of Reported Cures for Tuberculosis, the BMA Committee outlined some general principles.

The points made in this document expressed precisely what these surrounding issues actually were.

According to these general principles every practitioner was perfectly free to use in the treatment if any patient whatever methods or drugs he honestly believes to be for the patients benefit. There is no `standard' or `orthodox' treatment to which he must conform and no practice which he might follow. No council or college or association pretends to exercise authority either over methods or treatment or over the therapeutic judgment of a practitioner. 166

Further, it was stated that the medical profession ought not to spend valuable time in testing clinically, enterprises which are devoid of adequate presumptive evidence in their favour. Doctors, alike in the laboratory and in clinical practice, have serious and urgent responsibilities, and to leave these on insufficient nomination would be a dereliction of a duty. 167

The BMA Committee also stated that the medical care of a patient could not be arranged as a pure scientific experiment; it has to be commanded by consideration for the patient's interest and benefit and not by a desire to prove, aye or no, a particular scientific doctrine or to demonstrate aye or no, a reputed drug value. 168

The Committee concluded therefore, that

it would be impossible for a medical practitioner set in charge of patients to agree in advance to use in treatment some selected substance and no other... The conditions which apply to the scientific pursuit of truth in a laboratory cannot be applied to the inmates of a hospital ward or nursing home. This does not mean that a new drug or method of treatment cannot be systematically studied. Either one or the other can be systematically studied provided that in each patient, and throughout the investigation, the interest of the individual, not the completeness of the experiment, is the deciding factor. 169

166 See Note 149.
167 See Note 149.
168 See Note 149.
169 See Note 149.
Finally, then, the BMA Advisory Committee gave the proposal ‘cordial recognition as a practical effort dictated by a humane desire to relieve suffering and banish a widespread disease’, but suggested that an investigation be undertaken with the following conditions. First, that the Committee of Investigation on Treatment of Tuberculosis strengthened their case along the lines mentioned above; second, that they abandoned their plan to establish a special home for their investigation with £10,000 of funds; and third, that they consent to the clinical experimental trial being run within an existing clinical institution.

I. 2. iv. How the case ends

In the end no official clinical trials were conducted. The Committee on Investigation of Treatments of Tuberculosis (CITT) approached other eminent clinicians (such as Lord Horder) on subsequent occasions about the possibility of assisting them in arranging and conducting a scientific clinical trial of Umckaloabo during the late 1930s and 1940s. This they did with the hope that a few respectable physicians be employed to ‘watch' and report on patients being given Umckaloabo; thus, they might achieve something approaching an official clinical experiment. The Committee even managed to persuade a Dr E. T. W. Starkie to donate his sanatorium, complete with patients, for the experiment. But, in the final analysis, Horder was concerned about what seemed to him to be an unwillingness on the Committee's part to

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170 See Note 149, p. 2.

171 The BMA Advisory Committee had discouraged the idea of the £10,000 being spent to set up a separate home. They objected to it on the grounds that the cost of equipping such a home would be too high to allow a valuable clinical experiment to be run. This, they believed, would consist of no less than twenty beds being allocated for this purpose for three or so years. A separate home might also endanger the patient. See Note 149. See also, PRO: MH55/1170, Minutes of the 2nd meeting of the BMA Advisory Committee, 3/4/36; Minutes of the Third Meeting of the BMA Advisory Committee, held at BMA House, 19/10/36; and undated document entitled: The Case for the Investigating Committee and Comment on the Case Presented by the Investigating Committee.

172 See PRO: FD1/163, Lt. Col. C. Kerr (of the Committee on Investigation of Treatments of Tuberculosis) to Lord Horder, 25/2/37; Kerr wrote: ‘Dr. E. T. W. Starkie, who has a sanatorium at Creaton, Northampton, is prepared to collaborate with Major Stevens in every case of the word, and to place a certain portion of his sanatorium at our disposal for that purpose.'
recruit MRC and BMA support, and went to see Mellanby about the matter. After this meeting Horder withdrew his support, informing the Committee that, in his opinion:

If you really want to convert the profession you must not do this (i.e. omit to involve the MRC in the proceedings). And you must choose your 'watching' committee (the group of doctors to observe the treatment being tried on patients) more selectively.\footnote{PRO: FD1/163, Horder to Kerr, 15/3/37.}

By the 1940s the rules of best conduct for the medical profession, the pharmaceutical industry, and the public in assessing therapeutic values had already been established. The authorities had won the war not because Stevens' remedy was never given a clinical trial, but because these rules of best conduct for assessing therapeutic value were now connected with moral issues of character, trust and standards in contexts quite beyond medicine. The clinical trial was merely a configuration or expression of this. It was a means of playing the game, not an end in itself. How therapeutic values were connected to other societal issues, and how the Stevens case epitomised this, is the subject of Chapter 2.
CHAPTER 2

Commentary on the Stevens Case:
Themes in the Making of the Clinical Trial

There was a reflexive relationship between Stevens' trustworthiness and his ability to speak the truth. This, I propose, was the 'Quack's Regress': a disreputable man like Stevens could not be trusted because he had kept the nature of his remedy secret, and a untrustworthy man like Stevens could not disclose the contents of his secret remedy precisely because he could not be trusted to speak the truth. Neither the BMA, the Ministry of Health, nor the MRC could afford to have Stevens or his Umckaloabo treatment associated with the systems they had established and the systems they were trying to create. If they wanted to be seen as authoritative evaluators of therapeutic value, they had to take a clear stand against this man.

As I have shown throughout Stevens' battles, authority in these matters was based on the ability to distinguish what was genuine and authentic from the start to finish. And authenticity was about character: character and nature of a therapy, and character of the person who owned it. Medical bodies made a public play of refusing to conduct an official investigation of Stevens' Umckaloabo treatment. In refusing to do so in public, each medical body was staking a claim for authority in this area. Both the BMA and the MRC wanted their method of assessing therapeutic value to be authoritative. As the government department responsible for the public health, the Ministry of Health was supposed to represent the state in matters of therapeutic efficacy and value. But it was the MRC which successfully claimed the right to define therapeutic value as their own.

The MRC achieved this, first, by making therapeutic evaluation a part of the biological standardisation of medicines during the 1920s. Fletcher was concerned about character in his efforts to shape the clinical expertise for therapeutic testing within the MRC. During the same decade the MRC defended standard-setting as a moral virtue. Fletcher forged these connections between standard-setting and therapeutic value by inventing traditions which made therapeutic evaluation essential for the nation as a whole. The result: the same institution
that made therapeutic values was setting standards for the state in other areas. And, the same
'characters' Fletcher cultivated as the right sort of people to determine therapeutic efficacy and
standards, were setting MRC standards more generally. In a world where standardisation was
a national concern associated with the heavily debated issues of efficiency, scientific
management and rationalisation, the MRC argued that their work on therapeutic standards and
values was for the public good in a wider sense.

The Stevens case introduces the people who made the MRC's clinical trial. Fletcher, T. R. Elliott, Henry Dale and F. H. K. Green, for instance, will reappear throughout the thesis. I
shall open up the case in this chapter to show the importance of 'character', 'trust' and
'standards' as three important themes of the Stevens case, and in shaping a fair system for
judging the therapeutic efficacy of drugs. These strands also interconnect in the main themes of
the thesis: namely, expertise, the state and the public. I begin by exploring the quack's regress,
and the issues it raises about disclosure. I show how medical bodies had separate interests in
excluding Stevens and how these interests reflect the nature of the authority they hoped to
claim by excluding him. I focus on how the MRC came to dominate that authoritative space,
pointing to how this was done, how a system of therapeutic values was established, and where
these issues are addressed in more detail in the thesis. The national significance of
standardisation and its connection to efficiency and rationalisation are demonstrated in this
chapter. Again, I point to how the biological standardisation of therapeutic agents for the state
and the public were given moral meaning through Fletcher's focus on character.
I. The Quack's Regress: interests and authority

Social historians and sociologists argue that order within social groups and institutions depends upon trust. Trust is the moral bond between the individuals of a community which allows the knowledge of that group to be effectively accessible to the people within it. Untrustworthy persons cannot have the knowledge the community claims for itself. In Stevens' time (as remains the case today), orthodox physicians and medical authorities claimed to possess genuine knowledge about the value and efficacy of therapeutic agents. Stevens did not belong to their communities. As a layman, and proprietor of a secret remedy who was treating their patients, Stevens was vilified by the medical profession. The moral bond of trust between them excluded him.

While this may suffice as a simple statement of the state of affairs and the logic behind the Quack's Regress, attending to the dynamics of this case shows how and why this regress constrained Stevens, focused the struggle for medical authority, and why officials were forced into a display of fair play. Stevens was disreputable. His reputation had been tarnished by his conviction (of fraud) in the Basingstoke affair, and by the fact that this proprietor of a secret remedy had been named at, and tried by, the Select Committee on Patent Medicine's public inquiry. Stevens was also untrustworthy because he was commercially driven and because he refused to disclose the contents of his secret remedy. Add to this the fact that Stevens advertised both his remedy and himself with the crassness evident in mass culture, and one has

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174 A more recent (and controversial) book on this subject is Steven Shapin's (1994) *A Social History of Truth*, in which Shapin argues that truth is itself a social institution. Shapin's study takes the Royal Society of seventeenth-century England as the primary case from which he draws specific arguments about trust and early modern gentlemanly culture, and universal arguments about trust. In early modern English society it was the gentleman who was trustworthy. Gentlemen were trustworthy because of their moral virtue, their character. Shapin argues that the making of early modern science therefore depended on gentlemen trusting each other's testimonies. I do not wish to engage in the fracas over the title of the book, or debate whether Shapin's social constructivist account is a relativist tome couched as a 'liberal' analysis of truth. I wish quite simply to welcome the fact that it points to the moral aspects of the kind of knowledge which social groups and communities hold, they show that making scientific knowledge involves managing testimony and that decisions about which scientific testimonies to believe are largely (though not solely) a question of which people to trust. See also Gambetta (ed. 1990).

175 Shapin (1994) argues that twentieth-century science also depends on trust: the scientist promising that his word is his bond (i.e. giving true testimony) and accepting the testimonies of other scientists (trusting the word of others).
the kind of person medical officials would have found positively indecent. However, I should like to point out that these medical bodies -- the BMA, the Ministry of Health, and the MRC -- played an active role in framing Stevens as an utterly untrustworthy man.

Hearsay contributed to Stevens being type-cast in this negative way. Stevens became more disreputable and notorious with each private committee meeting, memo and letter that passed through medical institutions and government departments. T. R. Elliott, for instance, told F. H. K. Green about Dr Deas' encounter with Stevens; Deas then retold his story to Green of the Therapeutic Trials Committee; details of Deas' meeting were then passed on to Fletcher; and Fletcher was quoting from the doctor's report when he disdainfully told the parliamentarian, Captain Elliston (in his explanation of the MRC's position regarding Stevens) that the man admitted 'that he does too well out of it to reveal his formula.' Similarly, when the BMA approached government departments for specific facts about the case, they began by presenting Stevens' history of court cases, the Select Committee ruling and official responses to his persistent campaigns. They also reminded those concerned that Stevens advertised himself and his secret remedy with monotonous regularity. Letters and telephone conversations from MRC head office took the same line. And so the same messages were passed along to other societies and departments from Britain to South Africa, in official letters and in private meetings.

Transmitting these stories may have worked against Stevens in two ways: a) by giving him a negative label; and b) they may have had the knock-on effect of forcing Stevens to defend himself and his reputation even more aggressively in dramatic and demanding letters, thus unwittingly providing further evidence for the crass and unrestrained behaviour that had defined him as untrustworthy in the first place. What is more, by transmitting these accounts about Stevens, officials like Fletcher, Elliott, Green, not to mention the BMA and civil servants at the Ministry of Health, linked their own personal integrity to this labelling process. Once they had demonstrated their ability as authorities on what was genuine and authentic by

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176 Morris (1994).
assigning him the label of a disreputable and his remedy a fraud, they were then duty bound to dismiss him 'toute suite' on paper (refusing him an audience with them in person), and to tell him that his 'alleged remedy' was without value.

Stevens defended himself by recruiting credible allies. I demonstrated this in the previous chapter. The Committee of Investigation on Treatments of Tuberculosis (CITT), with its aristocrats and parliamentarians, was the most notable in that their involvement in these battles forced medical authorities to engage with Stevens. The M.P.s and Lady Malcolm appear to have been convinced by Dr Sechehaye's evidence and by the weight of testimonial evidence that the treatment worked. Stevens may have been an unscrupulous man, but he was also a member of the public the CITT believed was being treated unfairly by the medical world. Captain Elliston's approach to Fletcher about Stevens' case exemplified this. The M.P. saw no conflict in calling the man a 'quack' while defending Stevens' right to be treated fairly. The aristocratic committee's interests in defending this treatment may have been philanthropic (as they asserted) but doing philanthropic works had social and political currency, especially in the case of tuberculosis, arguably the single most important cause of national inefficiency.  

Furthermore, rejecting patients' testimonials as insufficient grounds for investigating the benefits of the remedy might imply that even intelligent patients were incapable of assessing the effects of medicines on their own bodies. By the same token, the testimony of their fellow Committee member, Mr Dobson of Weybridge, who had taken Stevens' cure (and a man who, in the Committee's ears, spoke the truth about his body), was also worthless. When the lay committee argued for patients' testimonials to stand as moral evidence, it was arguing for the intelligent layman's voice to be credited in official evaluations of therapeutic efficacy.

Dismissing Stevens directly and publicly as medical bodies did during the 1920s and early 1930s may have served to demonstrate their authority. By recruiting these credible allies, who presented themselves as advocates for the lay people in general, Stevens made it difficult for officials to dismiss him out of hand. The MRC's Secretary and the Minister of Health had to grant his aristocratic allies face-to-face meetings. Cultural codes of decency would have

177 Bryder (1988).
made it impossible for them to act otherwise. In short, if these medical authorities appeared to be unduly prejudiced against Stevens, they risked being labelled as selfish professionals who were simply protecting their own interests, and who could not therefore be trusted to protect the public interest. Medical men now had to demonstrate that they had established codes of best conduct and best practice which were fair and just for the sake of their own integrity. Once they had identified requirements for clinical testing, and established that any remedy meeting the requirements would be tested, this amounted to a promise which they then had to keep. Stevens had now become a ‘quack’ they were forced to deal with. Trapped by the Quack's Regress these bodies were now forced to at least give a public appearance of acting fairly towards Stevens.

The BMA and MRC responded in two ways: they conducted independent inquiries into the nature of Umckaloabo, and they changed the meaning of disclosure each time Stevens revealed more details about his remedy. By conducting their own separate and extensive search for the elusive Umckaloabo, or an active ingredient by any other name, these medical bodies might seem to have escaped this regress. But since officials doubted that Umckaloabo really existed even before their inquiry, these investigations were perhaps also intended to show that there was nothing to disclose. If there was nothing to disclose, their suspicions would have been justified: Stevens was untrustworthy and his therapy was therefore a fraud.

The BMA, the MRC and the Ministry of Health each claimed genuine knowledge about therapeutic efficacy for their respective community. Stevens became the foil they used to focus those interests. To the BMA, he was an unqualified person peddling a secret remedy at a time when they were campaigning to stamp out the trade in proprietary medicines. At the same time this body promoted the clinic as the place where therapeutic efficacy was judged through the critical eye of individual doctors with incommunicable knowledge.\textsuperscript{178} In the BMA's eyes the practitioner had the right to use whatever method or drug he believed would honestly benefit his patient. No 'standard' or 'orthodox' treatment or method should be imposed. And I propose that when the BMA set out in its principles on the matter that: 'No council or college or

\textsuperscript{178} Lawrence (1985).
association pretends to exercise authority either over methods or treatment or over the therapeutic judgement of the practitioner', they were referring to the MRC. As we shall see (in Chapters 4 and 5), even MRC controlled clinical trials were in truth idiosyncratic clinical experiments in the hands of doctors who tested those medicines in the clinic.

For the newly-formed Ministry of Health, occupying the middle ground between the MRC and the BMA as coordinator and arbiter in matters of public health, Stevens was a quack selling a proprietary medicine, which damaged the public health. On the other hand, he offered a treatment for tuberculosis, so that although they publicly denounced Stevens and his cure, the Ministry initially sanctioned Dr Cox's trial of the Umckaloabo treatment at a sanatorium. Moreover, the letter which the Minister addressed to Ritzema effectively licensed its use in tuberculosis sanatoria up and down the country.

To the MRC, Stevens was a layman who manufactured and sold a quack remedy for which there was no 'rational basis' (laboratory, scientific or clinical) or 'trustworthy practical' evidence for therapeutic efficacy. Furthermore, the remedy was neither 'new' nor 'genuine'. Unlike the BMA, the MRC was concerned about standardising therapeutic substances into reliable quantifiable units and ensuring that they were effective and safe for public consumption (Chapters 3 and 4). Born out of this interest in biological standardisation, this state institution had established a 'machinery for testing genuine new remedies'. The machinery was itself a standardising mechanism in which physicians had to become mere calibrators of therapeutic effect (Chapter 5).

Each time new facts were revealed, the medical bodies changed the meaning of disclosure. This made it impossible for Stevens to disclose the contents of his remedy. Disclosure was not simply a question of producing evidence. Stevens had listed the ingredients of his consumptive cure since 1909 during the BMA's campaign against secret remedies, and in the book the BMA published on secret remedies during that year. Two bottles of his remedy were also analysed by a government chemist at the Select Committee hearings. In 1914, the Select Committee reported that the remedy had no alkaloids or resins, and that the solid matter corresponding with the colouring and extractive substances were essentially mixtures of wine and glycerol; this counted as disclosure. By 1936, however, the CITT's analysis produced a
similar list of ingredients; this was not disclosure. In 1936, disclosure meant more than a list of ingredients. Judging from the reaction of the Ministry of Health advisor, and the BMA’s Committee, disclosure meant identifying the active ingredient by its Latin botanical name, not a local or native name, like Umckaloabo, and providing a sample of the plant for independent analysis. This would make it possible to verify and demonstrate the pharmacological effects claimed in private testimonies about the drug. Disclosure, one might argue then, was the highest form of evidence. By defining disclosure in these ways a character like Stevens could be excluded from official testing systems in ways which authorities could defend as disinterested, open and non-prejudicial.

II. Authority and disclosure

To laymen -- like Stevens -- all of these medical bodies appeared to be authorities. But I propose that it was only at the historical moment of consensus about Stevens' reputation and what this said about the Umckaloabo remedy he peddled, that these medical bodies became a united front one might call 'medical authority'. Establishing power and authority meant governing space. It also involved preventing other kinds of knowledge about therapeutic efficacy from being constructed. Here again, the point at which these medical bodies came together is significant. They all tried to prevent the CITT from establishing a separate 'experimental home' to test the Umckaloabo treatment, despite the considerable amount of cash at the Committee's disposal. An experimental home with separate resources would create its own networks and expertise, and would have allowed the CITT to become more powerful.

Both the BMA and the MRC tried to manage disclosure by staking claims to genuine authority. The BMA's way of managing disclosure was the physicians' way, i.e. by managing patients' testimonies. Recall the BMA's response to Dr Sechehaye's evidence. The aristocratic

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179 This was occurring at a time when zoologists and botanists in Europe were standardising the names of plants and microorganisms with classical names and codes. The replacement of the multiple local conventions by international codes is outlined in 'Symposium on Linnaeus and nomenclatorial codes', *Systematic Zoology*, 8 (1959), pp. 1-47. I am grateful to Nick Jardine for drawing my attention to this reference.

CITT had implied that testimonial evidence carried moral weight and that it was unjust to ignore so many patients' voices. But the physicians implied that lay people -- the patients -- were suggestible. After screening the evidence they concluded that whether patients said they had been cured or not depended on the sort of people they were. As Sir Norman Smith of the Ministry of Health put it, 'many of these patients were of the well known 'difficult type' who would lose no opportunity of advertising their latest faith''. The BMA then, tried to manage disclosure by arranging for a doctor (who would presumably have either been selected or approved by the BMA) to conduct a clinical examination of 50-100 of these cases. If they had made the official test, then the physician, and only the physician, would have the authority to disclose 'evidence' about whether the drug was effective or not.

The MRC's approach to managing disclosure was different. Their move was to bring disclosure inside, to make it something that was done in laboratories and, in the committee rooms of the MRC, and which was managed by MRC officials, scientists and physicians. This was more than a new construction of disclosure: it would also shape what it meant to do the MRC's work. Disclosure, interpreted in this way -- disclosure as that which occurs in an enclosure -- was how researching MRC scientists should behave in the course of their research on matters of national concern. When Frank Green (of the TTC) launched his separate investigation of Stevens (T. R. Elliott's advice, as the reader will recall), he brought Dr Deas' testimony into the MRC's domain, writing it down in their files for future reference. Later, Mellanby asked the botanist Dr Hill to identify the Latin term for this Umckaloabo plant for the MRC's records, enclosing Umckaloabo's folk identity in a Latin label would make European botanists (allied to the MRC) the authorities about the efficacy of this drug. 181

There was another notion of disclosure which ran counter to the MRC's approach of bringing disclosure inside, one which was being forged by the press, advertising agencies, marketing research agencies, for example, for whom disclosure was a public act. Disclosing in this sense involved throwing 'facts' (about this commodity, or that medicine) out to the public and allowing laypeople to make their own judgements. Disclosing invited public participation.

181 See Note 6.
This competing notion of disclosure was fuelled by advertising. It was because these two opposing constructions are occurring at the same time that the MRC and its allies had to exert such energy to defend their meaning of disclosure. As we shall see, particularly in the clinical trials of insulin (Chapter 4), Fletcher managed public disclosure (encouraged by the press) to defend clinical trials as being in the public's interest while shaping the rules of private disclosure (within committees, and by social contracts) to make the trials work.

III. Inventing traditions: character, standards and the state

At the beginning of this chapter, I said that Fletcher invented traditions which linked the character of those who judged medicines within the MRC, and that institution's standard-setting programs, to nation building (Chapter 3). Eric Hobsbawm has identified the late nineteenth and early twentieth century (just before the Great War) as a period when invented traditions sprang up 'with particular assiduity' across Europe.\(^{182}\) By invented tradition, Hobsbawm (and Terence Ranger) mean a set of practices normally governed by accepted rules of a ritual or symbolic nature in ways which inculcate certain values and norms of behaviour by repetition, and which imply continuity with the past. The late nineteenth- and twentieth-century invention of the pageantry which now surrounds the British monarchy was a classic example of this.\(^{183}\) Hobsbawm argues that these traditions were invented to establish new bonds of loyalty in a period of profound and rapid social transformations. Crucially he argued that 'the state' became the entity which linked invented traditions, providing the stage where the new public holidays, ceremonies, heroes or symbols recruiting a captive public were played out. For practical purposes, civil society and the state within which it operated became increasingly inseparable. State, nation and society converged.\(^{184}\)

I propose that the clinical trial was an invented tradition. I examine Fletcher's cultivation of what I define in Chapters 3 and 4 as 'noble scientists', with an altruistic commitment to scientific medical research, in more detail in this thesis. The MRC's approach

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\(^{182}\) Hobsbawm (1983), 263.

\(^{183}\) Hobsbawm and Ranger (eds. 1983).

\(^{184}\) Hobsbawm (1983).
of embodying its authoritative space with moral virtue by cultivating character and bonds of trust can be tied to a long narrative of trust and institutions in modern life. It is in many ways reminiscent of the Victorian ideal of character. Fletcher's and Dale's affirmation of this old ideal to create a new culture of medical research and 'noble scientists' through bonds of trust with physicians, drug manufacturers and patients represented the invention of a new tradition (Chapters 3 and 4). Historians (like Shapin and Gambetta) have focused on trust in the making of modern state institutions, arguing that questions about which testimonies to trust, and why, are moral issues, and that character remains a basis for discriminating trusts and managing testimony. But Fletcher and Dale (as we shall see, particularly in Part II of this thesis) also placed their trust in objectifying standard units. Again, historians (notably Theodore Porter) point to trust in numbers as a distinctly modern trend, arguing convincingly that, over the past few centuries, quantification has been used by governments, businesses and social research to minimise the need for intimate knowledge and personal trusts. The way in which this modern institution of the state assumed authority for determining therapeutic values through a process which involved making the clinical trial, shows that trust in people and character ran side by side with trust in numbers. This simultaneous process demonstrates (as I shall indicate in this section and throughout the thesis) that far from moral and cultural codes being frictional forces impeding the uptake of standards in modern life (as Porter's account implies), they were the vectors which propelled standards, making standardisation a moral act. Furthermore, I shall argue that commercial issues were not secondary to the moral issues of trust and character (as Shapin implies by his failure to attend to commercial matters), but were at the heart of the issues of standardisation and why standards were valued.

III. 1. Character and moral virtue

Fletcher's focus of 'character' connects the making of the trial with obsessions about character which came to the fore in late Victorian social discourse. This was an expression of the classical humanistic belief that men became virtuous by their own force of will, and by

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embracing altruism in favour of egoism.\textsuperscript{186} This ideal of character was particularly prominent in Victorian political and economic philosophy. The influential economist, Alfred Marshall, for instance justified economics as a worthwhile study because it dealt with the strongest forces shaping man's character. In his \textit{Principles}, he insisted that it was the economists' task to enquire whether prevailing human desires would help to build a strong and righteous character.\textsuperscript{187} Socialists also justified their economic programs on the grounds that they would develop and produce a higher type of character, and the Fabian Society was explicitly based on 'the cultivation of a perfect character in each and all'.\textsuperscript{188} This ideal also dominated political debates about the role of the state. And historians have more recently acknowledged the interconnected 'efficiency' and 'ethical' strands which ran through British socialism, pointing to character in their discussions of the 'moral factor' in social reform.\textsuperscript{189} José Harris, for instance, observes that the rhetoric of 'character', and moral advance through character reform, was central to social reforms of the late nineteenth and early twentieth centuries.\textsuperscript{190} She argues that invoking the virtues of character became a powerful tool for defining (and discriminating between) good and bad moral behaviour. It also formed the basis for prescribing differential treatment for the 'deserving' and 'undeserving' poor. Around the turn of the century, social commentators like Charles Booth advocated the use of 'character' as a means of selecting the 'fit' from the 'unfit' members of society, and for explaining why some people remained unemployed. Linking citizenship with moral purpose legitimised giving the franchise to some working men and excluding others. Thus the ideal citizen was one whose character was seen to be promoting the best interests of society as a whole.\textsuperscript{191}

\begin{itemize}
\item \textsuperscript{186} Harris (1993), 247-50.
\item \textsuperscript{187} Collini (1993), 61-91; Collini, Winch and Burrow (eds. 1993).
\item \textsuperscript{188} Pease (1916), 32; Bliss (ed. 1989), 1271.
\item \textsuperscript{189} By 'efficiency' strand I mean those who saw efficiency and scientific administration as the key to social reform. By 'ethical' strand I mean those who advocated moral regeneration and fulfilment of the individual as the way towards moral progress. See Kidd (1996).
\item \textsuperscript{190} Harris (1993). See also Britain (1982); McBriar (1987).
\item \textsuperscript{191} Harris (1993), 247-50; Collini (1993), 91-120.
\end{itemize}
Character undoubtedly served as an ideological device for maintaining societal order, one which, it might be argued, middle-class Victorians used to impose their values on the disruptive working class. But Wells' novel *Tono-Bungay* and the Stevens case both demonstrate that for many élites and intellectuals during the first decades of the twentieth century, the ubiquity of patent medicines and the prominence of their unscrupulous proprietors (Stevens and Ponderevo) were symbolic of the disruption in the order of class and society. Wells' *Tono-Bungay*, about the rise and fall of a patent medicine manufacturer and his secret remedy, was a social commentary on the disruption of the changing class structure. As I noted in Chapter 1, the Ponderevos were able to use the cash from the Tono-Bungay they sold to buy social credit, allowed them to slip in and out of character and across class boundaries. Their social mobility was not only facilitated by cash but by the fact that people from all walks of life bought Tono-Bungay. Stevens' Umckaloabo brought him into contact with aristocrats like Lady Malcolm, and parliamentarians like Captain Elliston. That people from all walks of life bought this remedy also symbolised a change in order. Only credulous mass men were supposed to purchase secret remedies. Intelligent men and aristocrats were not supposed to be taken in by the likes of Ponderevo and Stevens.

From around the turn of the century and throughout the inter-war period, intellectuals associated the demise of character, and the disruption of social order, with the rise of mass culture. They strongly disapproved of advertising and displaying unbridled commercial interests because such behaviour was identified with mass culture. Again, the Stevens case exemplified this. Stevens, like Wells' Ponderevo, was unrepentantly commercially driven. If the eloquent exposition of his behaviour at the Select Committee hearings was not ample evidence of this, his confession to Dr Deas certainly was. Recall how Stevens was said to have told Deas that 'since he was making a good thing out the Umckaloabo treatment as a secret remedy, he had no intention of disclosing its nature'.

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192 Stedman Jones (1971).
193 Carey (1992); Bradshaw (1994).
The Victorians' focus on 'character' presupposed an agreed moral code of Englishness where the cores of qualities were self-reliance, deliberate free choice and rational thought, and in which it was essential that these virtues be publicly demonstrated. The Stevens case and Wells' *Tono-Bungay* show that these characters were unified in ways which made elites, social commentators and public figures like Fletcher uncomfortable.\(^{194}\) Stevens and Ponderevo tried to pass as gentlemen of character, while advertising commodities to the masses, because men of character were supposed to be publicly virtuous and to promote fair dealing.

III. 2. *Standards, fairness and modernity*

Character was not the only issue concerning MRC officials. The MRC standardised drugs as a means of providing objective values and measures fairness drugs (Chapter 3). Seen as a state institution promoting standards as national values, the MRC was not unique.\(^{195}\) From the eighteenth century onwards bureaucratic officials have imposed uniform standards and measures, and established standard units of natural phenomena on citizens.\(^{196}\) The demand for a fixed calendar created by administrative needs of church and state (for applying taxes), like the institution of pocket watches and factory clocks, shows how standard time-keeping became one of the principal agencies of social discipline in daily life in industrial England.\(^{197}\) The nineteenth-century railway system distributed standard values of fuel, screws, gauges, reading matter, and station-hotel which disciplined nature, not to mention passengers.\(^{198}\) The dehumanising drive for objectivity which was facilitated by the 'metre' provides another example of the role of standards in organising social life.\(^{199}\) Establishing physical standards in particular has allowed public officials and scientists to manage nature in ways which were not

\(^{194}\) Colls and Dodds (eds. 1986).

\(^{195}\) Porter (1995), 3-33.

\(^{196}\) Porter (1995).

\(^{197}\) Landes (1983); Thompson (1967), 56-97; and O'Malley (1990).

\(^{198}\) Schivelbusch (1986). See also Sibum (1994).

\(^{199}\) Kula (1986).
unlikely other centralising forces and large-scale economic institutions within the state. The increasing shift towards standardisation and interconvertibility which historians of metrology and quantification have accounted for has transformed (and continues to transform) local skills into scientific knowledge that is valid everywhere. These historians show how standards were generated through the circulation of immutable particulars; and consensus about whether, what and how to take measurements, and which procedures to follow. However, it also seems that many of the scientists who led or were at the centre of campaigns to establish these standards, were themselves government officials and industrial scientists.

III. 2. i. Standards and fair trading

Accounts of how Europeans moved from traditional, embodied measures to an abstracted, universal metric system, as in other examples of the imposition of standards by the state, show that the role of commerce and juridical equality have been patent. So that standardisation is not only the key to generating technology and making it work, it also facilitates the objectification of expertise, and allows the expert to satisfy the moral demand for impartiality and fairness in public affairs. Whatever the procedure for setting standards, honesty, and the distribution of justice are primary objectives for policing those standards regardless of where in the world they may be produced. But fairness means different things in different countries. And the question of how people in any particular country bring standard measures and

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201 Sir William Thompson, a central figure in establishing standard electrical units, was a theorist of electromagnetism, and at the same time inventor and marketer of telegraphic instruments. Lord Rayleigh, physicist, inventor of electrodynamic devices, and guru of late Victorian precision measurements, was an entrepreneur, and also inaugurated the British Association and Cambridge electrical standards project in the late nineteenth century with influential government allies which resulted in him becoming one of the founders of the first National Physical Laboratory in Britain around 1900. Schaffer (1995); Norton Wise (ed. 1995), 136-62, 225-32, 242-64; Hammond and Egan (1992), 2-32; Hoppitt (1993).


standard procedures together with other values to demonstrate fair play has not received much scholarly attention.

The Stevens case points to how important it was for state authorities in Britain (like the MRC) to demonstrate that as a layman, Stevens was being treated fairly, and that should his remedy have met the entry criteria, it would have been given a standard trial. Stevens' credible allies were able to use the argument that he was being unfairly treated to try and force medical authorities to test the Umckaloabo treatment in a clinical trial. Here again the link between fairness and commerce was clear and direct. Therapeutic standards were not only a scientific ideal, these biological standards were important for fair dealing and fair trading as the standard units of tea or coffee or spirits (Chapter 3). MRC officials also wanted to be seen to be acting fairly and in the best interest of the public by initially withholding new and unstandardised drugs from MRC clinical trials from the public until they had been properly standardised (Chapter 4).

One of the primary virtues of standard quantities is that they allow mobility. It is for this reason that the production of standard measures matters to governments and states. It helped techniques to work outside of their immediate settings and beyond medical boundaries.\textsuperscript{204} The new discipline of biological standardisation which emerged as an emphatically international field this century was a striking example of this and one in which the MRC were heavily involved.\textsuperscript{205}

As I discussed in Chapter 1, part of the reason the 'ethical' pharmaceutical industry began to invest in methods of standardising drugs (by these chemical means) was to be able to market their drugs as reliable and unadulterated.\textsuperscript{206} But with therapies like insulin, diphtheria anti-toxin and pituitary extract, it was not possible to simply isolate the active ingredient and standardise it by chemical means. These drugs were therefore subject to biological standardisation in which they were tested on animals and their effects and dosages calibrated.

\textsuperscript{204} Norton Wise (1995).

\textsuperscript{205} Liebenau (1981), 6-41.

\textsuperscript{206} Abraham (1995), 37-86.
But which animals should be used in the biological standardisation of these drugs? And how could the 'dog unit', 'mouse unit', 'rabbit unit' or 'rat unit' used in local standardising tests be translated into calibrated therapeutic effect in humans? Researchers tried to test large numbers of animals, construct highly sterile laboratory environments for quality control, and breed standardised laboratory animals. But with no national or international agreements about which species of animal should be sacrificed for the biological standardisation a drug, and how 'animal units' for standardised drugs should be defined, these approached to being tortured ways of creating biologic standards. Setting solid dry crystalline standards which were agreed to by the consensus of national representatives at international conferences, and then distributed to centres all over the world for safe keeping, proved the most successful approach to biological standardisation of therapeutic agents (Chapter 3).

Standardisation might well be upheld as the *sine qua non* of modernity, but it brings with it a dialectic of integration and autonomy. For all the internationalism that standardisation and interconvertibility facilitates there nevertheless appear to be national styles of generating standards. For instance, there may be a British style for establishing standards, one rooted in a social order based on consensus and class rather than on a society of legal uniformity. Disagreements over the production of national standards were tainted with national pride. Some historians of metrology lean on the side of particular networks of people, rather than national characteristics, as the cause of observed differences in how standards are generated in different countries. Others stress the significance of national styles of standardising. I show the networks of physicians established through bonds of trust to test therapies (Chapter 4) in what might be a British style of conflict and consensus for establishing standard procedures of conducting clinical trials (Chapter 5). I point again and again to how the MRC’s 'noble scientists', who promoted biological standardisation and managed clinical trials, stressed the

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207 Porter (1995), 29-32; Burn (1928) and (1930); Stechl (1969), ch. 9, 132-49; Stieb (1966) and (1970).
Britishness of their own actions. They were suspicious of foreign doctors whose interest and evidence about therapeutic efficacy could not be easily traced (Chapters 4 and 5). Recall in the Stevens case how MRC officials used their international connections to find out the identity of the Swiss doctor Sechehaye (who had testified on Stevens' behalf), before attending to the foreign doctor's evidence. I propose these as more subtle ways in which the management of clinical trials and the way in which biological standardisation was pursued might inform us about national character.

III. 2. ii. Standards in modern Britain

Perhaps more than any other historical period, standardising initiatives in which the objects of standardisation have been more obviously human, and the purposes administrative and political, have been associated with the late nineteenth and twentieth century. In seeking the meaning of the term 'standard' and 'standardisation', Raymond Williams suggests that the term evolved from the mid to late nineteenth century through to the twentieth with increasingly multiple meanings. I propose two important reasons for why standardisation became a prominent issue and word during the first half of this century in Britain. First, standardisation, standards and standard-setting were directly associated with the important national concerns of efficiency, rationalisation and scientific management. Second, standards were indexed to moral values, so that standardisation and standard-setting became moral activities which would benefit the nation and the public.

Standardisation was linked to public concerns about 'national efficiency'. Geoffrey Searle has written a convincing account of how 'national efficiency' emerged as the diagnosis for what was wrong with Britain in the first decades of the twentieth century. In The Quest for National Efficiency (1971), Searle disaggregates the term 'national efficiency', showing how, during the late nineteenth and early twentieth century, a number of social and political reforms were pursued under this umbrella: compulsory education, labour exchanges, the minimum wage, the eight-hour day, National Insurance, the spread of civic universities. In some cases

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211 Searle (1971).
the aim to 'set a standard' in order to improve efficiency was explicit. In education, the steady development and increasing refinement of intelligence-testing methods to measure 'general intelligence' encouraged debates about which 'standardised' intelligence tests should be used in selecting children for further education, and how they should be used to predict natural ability and to define normality and subnormality. Debates within the growing fields of psychology and industrial psychology over how these tests should be 'standardised' also spilled into the wider public. The use of standardised tests was a part of issues linked with the expansion of state education and the extension of social services. This standardised intelligence testing was promoted by prominent figures who were driven by their commitments to national efficiency, social mobility and eugenic reform.212 The campaign for a minimum wage is another example of direct links between 'standards' and national efficiency agendas. It had a precise sense: a standard would be set, and wages could be judged by reference (back) to it. With such national minimum standards for society as a whole, the poorer members of society would be able to afford nutritious foods and housing and medical attention necessary to improve their fitness, thus making them more productive workers.213

'Standardising' was also a term explicitly associated with the vogue for Taylorism and scientific management. On the factory floor this meant accurate time studies and the planning and dispatching of operations on the basis of a pre-arranged time schedule. This facilitated the introduction of systematic procedures for the standardisation, layout and design of machines and people.214 Siegfried Giedion, in his social commentary of this period (in which he himself

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212 Sutherland (1984); Wooldridge (1994), 73-110, 203-305: Sutherland and Sharp (1980), 181-208. See also Gould (1981) and Rose (1985). Gould suggests important connections between craniometry and mental testing. Rose explains how psycho-eugenicists like Burt and Spearman came to think as they did focusing on intellectual movements such as the rise of the idea of population as a national resource, and the spread of notions of efficiency and inefficiency. The eugenic dimension to this and a wide range of inter-war activities are explored in Pick (1989), 155-7; Harwood (1989), 261; Mazumdar (1992). See also Searle (1971); and Brennan (1975).

213 Williams (1985), 298; Searle (1971), 90, 205-6, 236, 244, 248. The Webbs were particularly associated with this idea. Sidney Webb, in The Necessary Basis of Society, argued for a minimum standard of life, suggesting that setting such standards would involve 'expanding' Factory Acts into systematic all-embracing code, prescribing for every manual worker employed a minimum of education, sanitation, leisure, and wages as the viable starting-point of industrial competition'. See Gilbert (1966), 77.
lived), pointed to how these principles of scientific management, in which the protagonists called directly for standardisation of procedures, were being taken beyond their industrial contexts. Giedion noted, for example, how for influential women like Lillian Gilbreth (wife of Frank Gilbreth, one of the founding fathers of scientific management), Catherine Beecher, and Christine Frederick, work processes in the household had to be rationalised in the interest of efficiency. Making the kitchen more efficient would help middle-class women cope with fewer servants. More specifically, they argued for the 'standardisation' of kitchen equipment. Pointing to the institutional hotel kitchen as an example of how this worked, Christine Frederick, an early advocate of scientific housekeeping, said that hotels did not purchase

a kitchen table here and a stove there. Similarly, the home kitchen will have to be made efficient in the future with labour saving equipment, standardized and related by a definite system of work.  

Schemes for industrial rationalisation -- loosely conceived as 'the method(s) or technique(s) and organisation designed to secure the minimum waste of either effort or material' -- promoted in the interest of economic efficiency also explicitly invoked 'standardisation of both materials and products'. Medical concerns were central to this movement as is exemplified by the numerous committees and programs aimed at setting national nutritional standards. Not only

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214 For an informative discussion with a rich bibliography on Taylorism and the spread, practice and meaning of scientific management in Britain during the inter-war years, see Whitston (1996). See also Nelson (1974) and (1980); Frederick Taylor's famous principles of scientific management in Taylor (1913), and Edward Cadbury's response to Taylor's book, Cadbury (1913).

215 Giedion (1948), 612, see also 613-20. See also Ryan (1995); and Rowe (1993), ch. 2.

216 Urwick (1929), 20. This definition of rationalisation constructed at the League of Nations World Economic Conference, which assembled representatives of employers, employees, economists and industrialists in 1927, was arguably the way in which the term was most commonly understood. Within this economic conception however, these representatives argued for amalgamation, creating cartels, redistribution and reorganisation of capital or even welfare. For more about the meaning of rationalisation, debates about and arguments for and against it during the inter-war period and evocations of standardisation in this regard, see Urwick (1929) and (1930); Melchett (1932); Mond (1927), vii, 210-22; Gregory (1930), 106-18; Hobson (1930); Skidelsky (1970), 129-31; Fine (1990); and Fitzgerald (1988). The TUC involvement in debates over rationalisation and the social implications of the standardisation in the famous Mond-Turner talks between 1927 and 1933 are discussed in Gospel (1973) and (1979).

217 Sturdy and Cooter, Cunningham and Kamminga (eds. 1995); Smith (1995), and Smith and Nicolson (1989), and (1995).
was the medicalisation of the industrial masses in the interest of efficiency everywhere apparent, but the rationalisation of medical work was an abiding concern in hospitals as a part of the redefinition of their philanthropic purpose. Rationalising (hospital out-patients departments in particular) in the interest of managerial efficiency involved standardising hospital medical practice at a number of levels.\textsuperscript{218}

More often, and perhaps more important than the instances where explicit links were made between standardisation and the associated themes of efficiency and rationalisation, were the analogies and uniquely implicit links which inter-war Britons made with dehumanising images of assembly lines, machinery and conveyor belts. The human body was configured as an efficient motor, human power was viewed as labour power and fatigue, 'wastage' of labour and the maintaining and reproducing a 'fit' labour force became major concerns. The emergence of terms like 'hand' and 'operative' being generally used to refer to factory workers and labourers reflected the symbolic significance of efficiency.\textsuperscript{219} Oral evidence of the spread of 'assembly-line methods', for instance, also shows how female workers in factories producing biscuits, and electrical goods, saw their work as highly 'mechanised' and 'fragmented'.\textsuperscript{220}

Thus, the pursuit of standards in different public spheres helps to explain why this word and subject were prominent at the time. The many examples of its use suggests that the multiple meanings of standardisation oscillated between three senses. The first sense was of a 'standard' as a fixed point, such as a particular weight of tea or coffee. The second sense was normative, such as in intelligence testing. The third application of the term was in a moral sense, the idea of a preparation being or not being 'up to standard'. However, it is the literature of the period that produced and popularised stories, films and plays fusing images of standardisation with machines which takes me to the second reason for why standardisation became an important cultural theme during the inter-war period: namely, that it was

\begin{itemize}
\item \textsuperscript{218} Sturdy and Cooter (unpublished paper).
\item \textsuperscript{219} Rabinbach (1992).
\item \textsuperscript{220} Glucksmann (1990).
\end{itemize}
deliberately indexed with moral values. This I propose was the second reason for why these issues became prominent, particularly during the inter-war years.

John Carey has shown how other intellectuals (like Aldous Huxley, H. G. Wells and James Joyce) saw the masses as standardised in some sense: uniform subjects living empty lives in equidistant match-box houses, 'each not bad in itself, but all precisely alike in their difference from the ordinary.' Huxley, for instance, raised the question of 'standardisation' as a political tool. 'There is', he said:

> an obvious tendency, all over the Western World, to follow the lead of Russia -- not through any desire to imitate the Soviets, but because circumstances are rendering it increasingly necessary for all States to guard against the dangers of insurgent individualism. Human standardisation will become a political necessity.

However, Carey and others continue to show that writers often made standardisation a morally and politically charged issue 'by themes' of monstrosity and machinery with standards and modernity.

Consider Fritz Lang's *Metropolis*: images of assembly-lines of machine-like workers, people in an ordered state were divided into groups who use only brain and others who use only muscle. But it is Maria, a poor woman, the embodiment of the goodness and purity of humanity, who emerges as the hero. Aldous Huxley's *Brave New World*, in which humans of types Alpha-Plus down to Gamma are scientifically engineered and mass-produced like automobiles, speaks directly of standardisation. Huxley himself said that a fool-proof system of eugenics was:

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221 Graves and Hodges (1940), 169. See also Carey (1992), 3-92; Cunningham (1988), 267-340; Leavis (1930); Mulhern (1981).

222 Bradshaw (1994), 49.


designed to standardise the human product and so to facilitate the task of the managers (of the state). In Brave New World, this standardisation of the human product has been pushed to fantastic though not perhaps impossible extremes.\textsuperscript{225}

But here again, while standardisation is an effective means of controlling the \textit{Brave New World} for the lower types of human, Bernard Marx and his friend Helmholtz (two alpha-plus beings) emerge as individuals. Thus, despite the optimism of human engineering with efficient state control, the prevention of wars, and achieving happiness as its goals the novel is in many ways a triumph of intellectual individualism over standardisation.

References to products (and people) as 'standardised' and 'mass produced' during the 1930s often assumed nationalistic overtones. In such cases the issue of moral value is pitched at a national level, often with the implication that mechanisation and standardisation were not strictly British values but American invasions. The social commentators, Robert Graves and Alan Hodges, proved striking examples of this. In their popular, impressionistic account of the inter-war years, informed by contemporary newspapers, memoirs, and radio, they provided striking examples of how mechanisation was taking command of Britain. They unified images of mechanical objects with images and ideas of standardisation in reading inter-war Britain.

According to Graves and Hodges:

Mechanisation was spreading to all varieties of everyday things: there were stairs and ticket-and-change machines on the London Underground, and self-propelling luggage trucks for porters at terminal railway station and in the streets cigarette-machines, lunch and fruit-machines.\textsuperscript{226}

They referred to the 'American cafeterias' increasingly installed in the 'big shops and multiple shops, such as Woolworth's as 'mechanised restaurants' because:

one queued up with a tray and passed between a rail and a chromium-plated counter to choose from an assortment of ready-to-eat \textit{standardised} foods... Milk bars had an equally mechanised appearance with bright expanses of glass and chromium, high

\textsuperscript{225} Huxley (1955), 13.

\textsuperscript{226} Graves and Hodges (1940), 291.
counters, high stools and machines for mixing tasty milk drinks with snappy American names.227

Lamenting that even sports had become ‘mechanical’ to draw larger crowds, they highlighted cricket, a quintessentially English sport, as one of the few largely attended sports that had remained unmechanised.228

To Summarise. The Stevens case points to what was at stake in defining the therapeutic efficacy of medicines during the first half of this century. I have shown how, in this test case, discriminations of character and testimony and issues of standardisation opened into wider issues beyond this particular case and therapeutic testing. I develop the themes of expertise and efficacy in Part II, Standards, Moral Management and the State. I show how arguments for the moral and commercial values of standards were used to give the MRC legal powers in the area of biological standardisation. The way in which character judgments and bonds of trust featured in this process will also be further examined in Part II.

227 Graves and Hodges (1940), 291.
228 Graves and Hodges (1940), 289.
In a discussion between myself, a retired MRC official, and the archivist of the NIMR, the two men remembered Sir Landsborough Thomson, a high-ranking MRC official from the Council’s early years. Thomson, the records show, joined the MRC in 1919 and retired in 1957. Sir Landsborough, the two men recalled, was a senior administrator of the Council who had sat down and written the MRC’s history when he retired. And he was an interesting character at that. One of the men remembered a story of how Thomson had interviewed a new MRC recruit in full morning dress. Another recalled that an MI5 officer had interrogated Sir Landsborough at the MRC about the number of 'Reds' working there. He was impressed by the fact that Sir Landsborough, so the story goes, had told the secret services agent that those 'Reds' worked harder than the rest. Reaching for Thomson’s two-volume history of the MRC, the archivist remarked that this extraordinary man was not just an administrator, but had also been an accomplished ornithologist.

Similar words have been written about another senior officer of the MRC, Sir Walter Morley Fletcher. Fletcher, the first Secretary of the MRC, is presented as a Fellow of Trinity College, Cambridge, who had broad 'intellectual interests and a flair for organisation' and an administrator, but was also 'medically qualified', a 'brilliant scientist' -- an accomplished biochemist -- and a Fellow of the Royal Society. This century the point has been precisely that scientists and physicians like Sir Landsborough and Sir Walter claimed the right to speak for medical research, medicine and science by assuming the administrative parts of the state. In the first decades of this century, particularly during the inter-war period, these men were effectively civil servants: bureaucrats who appear more as scientists or as statesmen depending on the circumstances.
If Major Chas Stevens was the villain who exposed what was at stake in establishing rules of best conduct, and how and why certain elements were excluded from this system to assure the safety of genuine therapies, then Sir Walter Morley Fletcher shows us the moral management of pharmaceutical companies, professions and the public required to create this system and make it work. Principally, Fletcher the civil servant tried to shape the MRC as a unique department of the state. And so Fletcher is the character in focus in Part II of this thesis. The links between trials and the state were neither linear nor sequential. Neither was a system for testing and standardising the efficacy of genuine therapies the sole focus of biological standardisation during his first decade or so in office at the MRC. Following Fletcher's self-fashioning, his early MRC strategies and machinations show how clinical trials came to be connected to the state and to nation-building, and how they were linked to standardization generally, and biological standardisation in particular. I examine the way in which he claimed an authoritative role for the MRC within the state, and how this claim was justified by publicly demonstrating the moral and practical value of medical research and MRC researchers for the nation. Two rhetorical devices which Fletcher used were character, and public interest. Medical research could only be done by the right sort of character.

In Part I, I pointed to how the MRC established its authority by governing space, how this was predicated on rhetoric of character in determining who was capable of generating and disclosing genuine knowledge, and how it involved vilifying and excluding characters like Stevens from systems of genuine knowledge. I also argued that there were two forms of disclosure: disclosure as enclosure, i.e. that which occurred in Committee rooms of the MRC, between MRC allies and Committee-men, in MRC laboratories and clinics; and disclosure as a public act. In Part II, I show how Fletcher managed these two types of disclosure and the way in which he used the rhetorical devices of 'character' on the one hand, and of 'public interest' on the other to achieve this end. Medical research could only be done by the right sort of character, and it was being done in the public interest and for the public good. Managing disclosure was critical in organising the insulin trials in 1923 which set the precedent for clinical trials, as was cultivating the right sort of people to do
this MRC research. The law which secured authority for the MRC to control therapeutic standards was the product of a similar kind of management.

Chapter 3 establishes Walter Fletcher as a civil servant, examining his vision of medical research and the moral and civilising agendas of this research. I also show how these attempts to define a place for the MRC within the state through this medical research led to the MRC’s biological standardisation initiatives and eventually the establishment of the Therapeutic Substances Act. The highly publicised biological standardisation of insulin during this period assisted the passage of this law. Chapter 4 shows how the introduction of insulin into Britain and its biological standardisation which involved clinical trials was made into a public event. The moral management of physicians, patients and pharmaceutical companies which made clinical trials possible is also the subject of this chapter.

* Personal communication between myself Robert Moore, archivist at the National Institute for Medical Research (NIMR), and Philip D’Arcy Hart, 26/8/97 at a meeting concerning some archives about the Patulin trials which is the subject of Chapter 6 of this thesis.
CHAPTER 3

Bringing the State back in: Characters, Standards, and the MRC

In 1900, soon after his inauguration as a Fellow of Trinity College, Cambridge, Walter Fletcher was interviewed by a reporter from The Granta (a University newspaper).

Caricaturing the image of a scientist, the reporter insisted that Fletcher was the picture of a civil servant.

Walter Morley Fletcher, MA, MB, fellow of Trinity College, Walsingham Medalist in 1897, BA in 1894, Class I... Now [from] these particulars ... I should myself be led by them to picture a shortish, thin stooping man, with portions of black moustache, wearing gold spectacles and what is described as a 'cloven hat' who might frequently be seen bicycling rather rapidly in the direction of the laboratory... Mr Fletcher is not marked by some at least of these characteristics. He is a large man, devoid of spectacles. I do not recollect that he stoops particularly, nor is he noticeably thin. His hat is hard, and he has never encouraged a moustache. I am unable to conjecture what colour it would be if he did.²²⁹

The reporter then took the Civil Service Application form as a guide to reading his interviewee.

He asked:

Is he strictly honest, sober, truthful? Strictly....
Would you give him employment yourself, and recommend him to your personal friends? Unhesitantly.
Has he a good French accent? He is convinced of it.²³⁰

The Granta's reporter concluded that Walter Fletcher was the ideal civil servant: an intellectual, a hurdler, and a man of physical vigour. He wrily projected a world in which all future civil servants would be measured against his standard. Little more than a decade later Fletcher was formally appointed in that role.


²³⁰ See Note 1.
I begin this chapter with Fletcher's early manoeuvres as Secretary of the Medical Research Committee, the predecessor of the MRC. In depicting Fletcher as a civil servant, I set his background and pre-MRC years against the career of Robert Morant, a high-ranking civil servant who was also Fletcher's friend and ally in Fletcher's campaign for the establishment of the MRC. Fletcher the civil servant also comes into view as I show how he gave medical research a civilising agenda and a moral purpose; how he realised the ideal of medical research by invoking a rhetoric of character to shape that research, and by employing medical research to address practical concerns of his day. Fletcher did this to create a tradition for the MRC as a unique department of the state which successfully protected the public's interest through medical research. While efficiency concerned him before the war, he indexed medical research to standard setting after the war. I examine Fletcher's biological standardisation initiatives in order to show where therapeutic standard setting featured in this general scheme. The practical value of therapeutic standard setting was demonstrated through therapeutic trials of insulin which were part of the highly publicised biological standardisation of that drug. I show how this public event was used to assist the passage of the Therapeutic Substances Act which gave the MRC more secure authority to set biological standards, a step that amounted to state legitimation of a system of therapeutic trials of certain drugs.

1. **Characters: Fletcher, Morant and the Medical Research Committee**

Fletcher was appointed to the post of Secretary of the Medical Research Committee in 1913. The Committee had been established that year with a fund from Part 1 of Lloyd George's 1911 National Insurance Act. The quest for 'national efficiency' gripping the country at the time caused that law to come into being. The National Insurance Act singled out tuberculosis as a primary cause of physical and economic inefficiency and the most important cause of absence from work, and a serious drain on the sickness and disability benefits, not to mention a major cause of death in young men and women.\(^2\) Eliminating this disease, and controlling and reducing its effects on health as a way of improving productivity and economic efficiency, was

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\(^2\) Searle (1971) and Gilbert (1966).
supposed to be the object of research from the funds that established the Committee. Fletcher did initiate a few studies into problems of tuberculosis and efficiency when he began as Secretary. But when war broke out he asked the financial Secretary of the Treasury (C. Masterman) for permission to direct research into war wounds. Using the contacts he made in government, industry, academic, medical and scientific circles, he organised scientific biomedical research into war injuries and their treatment.\textsuperscript{232}

When the war was over, and the future of the Medical Research Committee seemed unclear, Fletcher made decisive moves to define and defend the Committee's territory within the state against government departments, such as the newly-established Ministry of Health, the Board of Control, and Board of Education.\textsuperscript{233} He cited the pre-war investigations he had initiated into efficiency and tuberculosis research. But Fletcher focused principally on the Committee's war-time research as evidence that the Medical Research Committee addressed issues of national concern, that 'medical research' (predominantly, but not exclusively laboratory based) was its domain, and that the Committee's unique focus warranted it being inaugurated as a separate department of the state. He particularly drew government officials' attention to the Committee's national service which had taken the form of scientific investigations on war injuries, pointing to the benefits of its work for soldiers on the battlefield as well as for hospitalised civilians.\textsuperscript{234} Fletcher told parliamentarians and government officials:

One of the important arguments in favour of a centralised State Department for research, whether in medicine or in other branches of science, is provided by the experience which has shown how often scientific research work arising out of practical problems of one administrative Government Department has yielded accessory results of value quite outside the province of the administrative Department first concerned, and yet of such a kind as to be useful either to other Government Departments or to


\textsuperscript{233} Austoker (1989), 23-33.

\textsuperscript{234} Bryder (1989), 62-7. See also \textit{MRC Annual Reports} (1914-1920); W. Fletcher (1920), \textit{The work of the Medical Research Committee. An address delivered at the House of Commons on March 19th 1920, to the members of parliament} (London: Research Defence Society).
the advance of science in general... Everybody knows now, of course, that the practical fruits of enquiry commonly spring unexpectedly from work undertaken with quite other objects in view.²³⁵

Fletcher recalled how the Medical Research Committee had responded to the War Office's request to design apparatus to supply oxygen to soldiers suffering from the effects of poison gases, and how this same apparatus had in turn saved the lives of civilian patients with pneumonia.²³⁶ And the Dakin solution, widely used in British, French, American and German armies, was a splendid example of the Committee's collaborative approach with industry to make this invaluable antiseptic.²³⁷ Again, the the Dakin solution was the product of some investigations the Committee had commissioned into chlorine compounds.²³⁸ This Medical Research Committee could also deal with national crises that might arise when there were problems with these industrially produced drugs and medicines. Here again, Fletcher pointed to an example, namely, the salvarsan crisis. The Committee's handling of the crisis over the release of toxic salvarsan had been nothing short of prompt and impressive.²³⁹ 'Salvarsan poisoning', Fletcher wrote, 'though rare, is a problem of importance at the present time to the Admiralty, the War Office, and to the Local Government Board'. In 1919, he told government officials and parliamentarians whom he sought to persuade of the Committee's exceptional value that the same men who had undertaken 'the biological testing of all salvarsan and allied

²³⁵ PRO: FDS/2, 'Appendix to Memorandum of the Future Organisation of Medical Research by Sir W. M. Fletcher' (1919), 5-6.
²³⁶ See Note 7.
²³⁷ PRO: FDS/2, 'Appendix to Memorandum of the Future Organisation of Medical Research by Sir W. M. Fletcher' (1919), 5-6. In his memoranda to the government arguing the case for the MRC, Fletcher also noted that the introduction of the highly effective Chloramine-T treatment for the disinfection of carriers of spotted fever and other diseases were also spin-offs from this work, as were the 'Halazone' tablets used to disinfect the water-bottles and small local water supplies of troops on the move.
²³⁸ Notably these investigations were conducted by his friend, Thomas Dakin, during the war. Fletcher placed such trust in these antiseptics that he personally tried Chloramine in England during the war years on a wound which was suppurating and causing him to be feverish. He decided to experiment on himself with Chloramine, known to him through being Secretary of the Medical Research Committee, but not to his doctors. See Fletcher (1957), p. 132.
²³⁹ PRO: FDS/2, 'Appendix to Memorandum of the Future Organisation of Medical Research by Sir W. M. Fletcher' (1919), 5-6.
products sold in this country' during the Great War, were continuing to ensure that this drug was safe for public consumption.  

Robert Morant was one of Fletcher's close allies. Morant was a powerful civil servant with a direct ear to influential parliamentarians. When he took over as Permanent Secretary of the Ministry of Health he appealed directly to Arthur Balfour on Fletcher's behalf, arguing for a separate research body, with Walter Fletcher at the helm. Fletcher already knew Balfour socially (they had met while Fletcher was coaching Balfour's nephew for his Cambridge exams). And, by this stage, he (Fletcher) had been given a privileged place in English society, having been knighted (in 1918) for his 'eminent services during the war'. In a letter to Balfour on Fletcher's behalf, Morant said:

The Medical Research Committee has done magnificent work, particularly during the war... The credit for the smooth working and for the effective achievement in this field has been mainly due to Sir Walter Morley Fletcher, the Secretary, who has most tactfully directed its efforts. He is a Fellow of Trinity and I think you have met him personally in former days. He is a particularly agreeable personality and has done some very fine work himself before we immersed him in the more directly administrative side of research. You will find him very delightful to deal with and the work which the Committee has done to be of high value and great interest.

The decisive words were 'magnificent', 'smooth working', 'most tactful', 'Fellow of Trinity', 'particularly agreeable personality', 'very fine work', 'delightful to deal with'. In short, Morant's letter to Balfour was intended to convey that he, Balfour, already knew Fletcher to be the right kind of person for the job.

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240 See Note 11.

241 Support for a Medical Research Committee, quite apart from other medical bodies, also came from the Haldane Committee and, reluctantly it would seem, from the Ministry of Health (Christopher Addison). Austoker and Bryder (1989).

242 Fletcher (1957),40-2,122-3,125-6,131,133,136,149-50. Balfour had been appointed Lord President of the Privy Council with direct responsibility for research in science, industry and medicine.

243 Fletcher (1957), 137-8.

244 The italics are mine. Fletcher (1957),40,122-3,125-6,131,133,136,149-50,151.
It may seem from these manoeuvres at the Medical Research Committee that Fletcher became a civil servant at the Medical Research Committee and then later at MRC, but in fact he arrived at that government Committee already cased in this mould and with a history not unlike Victorian civil servants of a muscular Christian ilk. One need only hold Fletcher alongside his friend Robert Morant to see the type of civil servant that he was. Holding the two men side by side also places Fletcher's character in perspective. Sir George Newman, the first Chief Medical Officer of the Ministry of Health, might also be added to this list, but a comparison of these three bed-fellows (interesting though it may be) is beyond the scope of this thesis.

Walter Fletcher had not gone to public school. Neither was he from a lineage of Oxbridge men. Born in Liverpool in 1873, Walter was the youngest and sixth son of ten children. His mother, Sarah Morley, the daughter of a clothing manufacturer in Leeds, took care of the children at home; his father, Alfred Evans Fletcher, originally a chemist, ended up being employed as an inspector for the Local Government Board (LGB) for most of his working life. When the family moved to London in 1884, on account of Alfred being promoted to Chief Inspector of the London area, Walter became a day boy at the University College School.

He spent his formative boyhood years in London at that school. He fancied himself as a 'naturalist': he collected facts about anthropological differences and kept a growing collection of natural specimens on display in a special room in the family home -- known as 'the Museum' -- until he went to University. He wanted native stories, legends, and photographic images to boot.

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245 Austoker (1989), 23; Elliott (1935); Kohler (1978); Hopkins (1937), 13-26. His eldest brother Herbert was the first in his immediate family to go to Cambridge. Herbert then went on to St Bartholomew's, where he qualified as a physician. It was Fletcher's Cambridge friend, T. R. Elliott (also a member of the Foster school), who suggested that Gowland Hopkins propose Fletcher for the job as Secretary of the MRC because of his combination of talents. Fletcher (1957), 17-35.

246 Walter's father originally began his career as a research chemist, but when the business he worked for failed, he joined the Local Government Board (LGB) as an Inspector for the Liverpool district, confining his research exploits to experiments in the private laboratory he had built in his home. Fletcher (1957) ; Elliott (1935).

247 Fletcher (1957), 20-1; Elliott (1935).
Morant, on the other hand, was a Winchester boy. Ten years Fletcher's senior, he was born in 1863. The sudden death of his father before the son reached the age of ten influenced young Morant profoundly. The death left the family in straitened circumstances, but despite this, funds were raised for Morant to go to public school and then on to New College, Oxford, where he read theology. He was a religious man, and had even considered taking holy orders before coming up to Oxford, seeing Oxford as preparation for the Church. He received a first class degree in 1885.  

Fletcher, by comparison, decided to pursue his naturalist interest at Cambridge. He came up to Trinity College in October 1891, and took up the Natural Science Tripos (studying Physiology, Zoology and Chemistry). He won the Coutts Trotter Studentship in 1896, and became a research fellow at Trinity the following year. While in his position as Fellow of Trinity, Fletcher also qualified as a physician at St Bartholomew's Hospital. After passing his medical finals in December 1899, Fletcher spent the remainder of his research fellowship focusing on research in muscle respiration. Determined to stay at Cambridge, he held a

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248 This room was known as the 'Museum'. Each exhibit had a place in his catalogue of Museum acquisitions referred to as the Museum's Half-Yearly Report. Walter cherished these exhibits; he preserved and polished them, and locked them in special cases, and each visitor to the house was taken for a tour around this collection of ideal types. Walter's Museum held a baby's skull, some African moths and spiders, a stuffed bat, a polecat's skull, a gull's skull, hedgehog's skin, fossils of various kinds and adult human skull and bones. Walter's naturalist interests also led him to inquire about the anthropological differences between different races. In his letters to his eldest sister Gertrude, who served as a missionary in Africa and India (and with whom Walter had a close relationship), he asked: 'Did young Africans speak English?... Can you tell me about the natives?. Do you know if any of the natives about you are especially gifted with a sense of smell?... Is their hearing keener?... Could she steal some photos of natives for him, 'showing faces etc.', and 'different types of expression in different races'... Tell me any sort of legends or old stories you hear circulated among the natives'. See Fletcher (1957), 20, 22, 24-5, 33.

249 Fletcher (1957), 22-3.

250 Allen (1934), 3-39; Markham (1950); DNB, 1921-22, 'Robert Morant', p. 386.

251 Fletcher (1957), 33-4.

252 Fletcher (1957), 40-2.

253 Fletcher was a member of the Foster Physiological School. His own research area in muscle respiration brought together physiological and chemical strands of thought. In his early works he had analysed the progressive exchange of CO\textsubscript{2} from exercised frog's muscle in air (survival respiration) under various conditions of rest and contraction. He conducted some experiments in cooperation with F. Gowland Hopkins, after Hopkins came to Cambridge, which they published in 1907. In their experiments Fletcher and Hopkins proved that resting and uninjured muscle contains very little lactic
series of short-term University positions which allowed him to continue his research. In 1905, Fletcher received a tutorship at Trinity, which he held until 1913 when he went to the MRC. While a tutor of Trinity, he conducted some experiments in cooperation with F. Gowland Hopkins. These experiments were published in 1907, and eventually resulted in him becoming a fellow of the Royal Society in 1915.

Morant did not make Oxford his home. By 1885, at the end of his undergraduate degree, he had abandoned his plans to enter the church and decided to try his hand at schoolmastering, having learned about a post for an English graduate to be a tutor to the sons of Prince Nares of Siam. In early 1887, he arrived in Bangkok, where he spent some seven years employed by the king of Siam (King Chulalongkorn (1853–1910)). Morant was taken on at a time when the king wanted to modernise and develop the education system of the country, which he believed would produce more efficient civil servants for government. Morant, who became tutor to the Crown Prince, enjoyed considerable and continuous patronage and self-consciously influenced the country’s educational service as a result. Morant's patronage ultimately diminished, and the paranoid behaviour he exhibited based on rumours that he was about to be replaced, undoubtedly contributed to him being dismissed by his royal employers. He left Siam under a cloud in 1894. When he returned to Britain he took a job as censor of studies briefly at Toynbee Hall, while waiting for the outcome of his application to the civil

acid; that exercised muscle when fatigued by contraction forms lactic acid up to a definite maximal percentage at which irritability is lost. They also showed that a free oxygen supply of oxygen can then cause the lactic acid to disappear with restoration of irritability and a coincident evolution of CO₂. Fletcher then returned to a more detailed experimental analysis of his earlier curves on the progressive discharge of CO₂ from exercised muscle. See Fletcher (1957); and Elliott (1935).

254 In June 1899, he was appointed on the staff of the college as assistant lecturer and Director of Medical Students, then Director of Students for the Natural Science Tripos. He received a lecturership in Natural Science in 1900, was Director of Natural Science in 1901, Director of all medical students in 1902, and was senior demonstrator in physiology in 1903 and remained so until 1905 when he received his a Tutorship at Trinity. See Fletcher (1957), 61.

255 Elliott (1935). See also Fletcher (1902a), (1902b), (1902c), and Fletcher and Hopkins (1907).

256 The situation seems to have changed when Morant went on leave for eight months to England. When he returned the political context had changed somewhat. France was attempting to claim Thai territory, which made education less of a priority. His patronage diminished because of lack of royal attention to education. Morant reduced his patronage further when he exerted humiliating and unnecessary control over the Crown Prince in the interest of ‘moulding his character’. See Daglish (1983).
service, before joining the Education Department in 1895. But Morant used the enigma of his Siamese experience as a focus for defining himself as a visionary who was not afraid to speak his mind -- an image which may have assisted his rapid rise through the civil service. Those around him were under the impression that 'independent influence' and 'jealousy' caused his dismissal. The Prince Devowongse's polite but yet pertinent remarks to Morant (with the King's assent) during the events surrounding his dismissal suggests otherwise. The Siamese prince wrote:

Your statements of facts show that you entirely misunderstand your situation, the conditions of your appointment, your rights and your duties. Your situation is not so exalted, it is not so exclusive, it is not so absorbing or so painful as you think it fit to describe it.

The Prince's remarks suggest that Morant perhaps promoted a one-sided and self-serving account of why he was dismissed for his own benefit.

Just as Morant used the Siam affair in his self-fashioning in the civil service, so Fletcher defined himself and his place at Trinity by finding a family history for himself which he made coherent with Cambridge traditions. Rarely does a biography, obituary, or general comment about Fletcher pass without it underlining Trinity men as his foster brethren and his loyal service to the college until his death in 1933. From the time he arrived at Trinity he said that he felt that Trinity was where he belonged. He had been preoccupied with his family -- the Fletcher--Morley heritage -- the year before he came up to Cambridge, and became convinced that he had descended from a lineage of independent-spirited, non-conformist Puritans. He was from a staunch Liberal background, and when he went to witness the House of Commons in action the year before he went up to Cambridge, he penned a diary entry of how his cousin Arnold Morley was at the debate over the Irish Land Purchase Bill. When he went to Trinity,

259 Fletcher (1957), 18, 28.
260 Fletcher (1957), 30.
Fletcher took to researching the history of his college, and of Cambridge, and while there he became a Trinity man whose family heritage of independent spirits complemented his association with a Cambridge tradition of giants like Newton and Whewell.\textsuperscript{261} Winning the Trinity College Fellowship for research helped him complete the picture.

While a Fellow of Trinity, Fletcher was recognised as someone who adored antique furniture, had exquisite taste in wines, and moved in some aristocratic circles. George Trevelyan was a friend with whom he shared an interest in poetry, literature, history and cross-country walking.\textsuperscript{262} Lord and Lady Knutsford (later his uncle-in-law and aunt-in-law, after he married Maisie) and the Pembertons were also his friends.\textsuperscript{263} And Trinity accepted him as one of their own by electing him to the College Council, the College Wine Committee and the Trinity Garden Committee -- bodies reserved for the privileged few.\textsuperscript{264} But perhaps two of the most striking examples of how Fletcher invented a Cambridge history in which he would have a place, are one involving some Elizabethan playing cards, and the other, his reinvention of the Pitt Club.

First, the playing card story. While Fletcher was a research fellow, commuting between Cambridge and London, the college had undertaken some restoration work on his staircase. Fletcher asked the workmen to keep an eye out for any relics they found and to bring them to his attention. The workmen unearthed some old playing cards under the oak threads but, believing these cards to be rubbish, tossed them in the nearby tip. Fletcher found out about this when he returned to his rooms and made the workmen rescue these cards, which he identified as Elizabethan playing cards. Fletcher then researched into the history of playing cards during his spare time and published two papers in the Cambridge Antiquarian Society's journal, an act that linked him spiritually to an Elizabethan heritage of Trinity men.\textsuperscript{265}

\footnotesize
\begin{itemize}
\item \textsuperscript{261} Fletcher (1957), 35.
\item \textsuperscript{262} Hopkins and Trevelyan (1937), 8.
\item \textsuperscript{263} Fletcher (1957), 79.
\item \textsuperscript{264} Fletcher (1957), 74, 108.
\item \textsuperscript{265} Fletcher (1957), 45. See also Fletcher (1906), 454-64; Fletcher (1915), 14-25.
\end{itemize}
As a Trinity Fellow, Fletcher served as president of the Pitt Club for almost fifteen years (between 1899 and 1914).\textsuperscript{266} This was an undergraduate club that Fletcher revitalised as a social club whose 'entry principles were emphatically not proletarian'.\textsuperscript{267} Referring to Walter Fletcher as the 'greater William Pitt', Greenwood echoed the opinion of many of his friends, that although Fletcher may have been a Liberal politically, his disposition was decidedly conservative (with a small 'c'). T. R. Elliott said that 'Fletcher's social philosophy was hardly of the left-wing'.\textsuperscript{268} Although a social club in Fletcher's time, the Pitt Club was historically associated with the Conservative party. It had originated as a Tory dining club, designed to keep warm the memory of Mr William Pitt, during the early nineteenth century. But it had gradually lost its politics.\textsuperscript{269} Walter Fletcher was not only aware of this association, but he took it upon himself to write the club's history. This, and his intense involvement in developing the club's aesthetic surroundings, social comforts and privileges at its new location on Jesus Lane, led to him being donned the club’s second founding father.\textsuperscript{270}

The intriguing traditions of court culture of Siam may be far apart from the halls of Trinity College, but Morant claimed the Saimese affair and his experience at the Education Department to fashion his character. Trinity did similar work for Fletcher. Both men were atypical civil servants in terms of lack of experience in civil service rules and norms. Morant was 32 when he joined the civil service, ten years older than the average age of fellow entrants, but within seven years he had ascended to the height of assistant secretary (one of the department's senior officials). Fletcher joined the Medical Research Committee at aged 40 as Secretary (a position which was equivalent to assistant secretaries and permanent secretaries of other government departments) having spent most of his adult life at Trinity. Both civil servants were notorious for being outspoken. Fletcher's friend, Trevelyan, marked Fletcher's

\textsuperscript{266} Fletcher (1957), 22, 79, 70, 85, 100, 106, 108, 110, 272, 282.
\textsuperscript{267} Elliott (1935), 155.
\textsuperscript{268} Greenwood (1943), 28.
\textsuperscript{269} Fletcher (1935), xi.
\textsuperscript{270} Fletcher (1935), ix, xi, 35-6.
tongue as a serious character flaw. He 'never ceased to say "That is right, That is wrong." Morant's colleague, Beatrice Webb, commented on his 'malicious tongue', and the two (as is evident throughout this thesis) were often unforgiving in labelling people as the right or the wrong sort; or further, as Greenwood believed of Fletcher, that 'emotionally [he] perhaps dichotomised mankind into Cambridge men and others'.

I leave Morant for the moment and return to Fletcher and the MRC. I turn to the role of character and practical value in his attempts to invent an MRC tradition. I examine his vision of medical research, its place within the state, and its national value to Britain. I take up the Morant–Fletcher partnership later on in this chapter, as we see them plotting to set up the right kind of committee to produce a government machine that would drive a Therapeutic Substances Bill and legalise the biological standardisation of drugs.

II. The MRC tradition: character, standards and practical values

The Medical Research Committee formally became the Medical Research Council (MRC) on 1 April 1920. It was granted an unusual degree of freedom, direct access to the Treasury, and full executive powers to choose its own Secretary, control its own administration, and determine its own policy. Just as Fletcher had fashioned himself as a Trinity man, so he drew on the historic events of the Great War and the words of great men of the past in order to invent an MRC tradition. He employed the rhetoric of 'medical research' as an unmistakably moral cause. Fletcher did this by developing the arguments he had used to parliamentarians (in his campaign which resulted in the institutionalisation of the Committee) in three ways. He displaced the 'practical man' from the seat of knowledge. He argued that medical research would literally define what was practical and what was not. And he framed the medical

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271 See Hopkins and Trevelyan (1937), 8.

272 Cole (ed. 1952), p 98.

273 Greenwood (1943), 28. Greenwood came to know Fletcher during his time at the MRC.

researcher as a special kind of citizen with certain virtues and duties to the state, which he conceived of as an organic body.

Fletcher claimed that although professionals -- physicians, engineers, and so forth -- trusted their experience, their knowledge was often misconceived. And yet these people were being allowed to determine the fate of the nation. Why were scientific methods of research still 'commonly regarded in this country as having little part to play in the guidance of the practical affairs of familiar life'²⁷⁵ Venting his frustrations about the power which these practical men had to influence affairs, in a speech on 'Medical research and daily life' (at the opening of the Field Laboratories and Pharmacology Department at Sheffield University) in 1922, he told the following story:

When I went from Cambridge to London to begin my present work in 1914, shortly before the war, I met the Minister of the department which is duty bound to take chief interest in the results of medical research work, and he was good enough to have a long talk with me on the terrace of the House of Commons. And, I remember he cheerfully and frankly said to me, 'Well, doctor' (I have never pretended, then or since, to be a doctor) -- 'well, doctor, I don't hold with research. If we want to stop disease we must give the people better grub and less dirt'. Now that was the considered opinion of a responsible Minister. There is, of course, much truth in what he said, that given 'better grub' and given 'less dirt' disease would be incalculably lessened in this country; and my reply of course was that I entirely agreed -- if he could tell me what better grub was and what less dirt was, for I know of no way of finding out those two things except by persistent scientific research work'²⁷⁶

And there were countless examples of this in industrial affairs where matters were 'decided by the common sense' of 'practical men', and not by anything as academic as scientific research.²⁷⁷ Fletcher thought that Disraeli had described the situation best when he said that 'the definition of a practical man is the man who is content to practise the mistakes of his ancestors'.²⁷⁸

'Aeroplanes ... wireless telegraphy ... the method which secures the sinking of submarines, the

²⁷⁵ See Note 46, 2.

²⁷⁶ Sir W. M. Fletcher, 'The field laboratories and pharmacological department: medical research and daily life', BMJ (1922), 2: 942. This was an address at the Field Laboratories at Sheffield University on 11/11/22.


²⁷⁸ See Note 46, 2.
efficiency of the detective force, the prosperity of insurance companies, and the success of our food rationing: all of these *practical* benefits were the benefits of scientific research.  

Medical research which addressed issues of practical import to ordinary citizens and daily life would do moral work for the state, not least because it would undo the damage practical men did. The MRC’s approach to research defined the *kind* of moral work it did, and the people who did this work -- the right kind of scientists, the men of character -- should be specially suited to MRC work. The moral imperative of Fletcher’s medical research followed directly from his views about the ideal state. He connected moral duty with labour through his organicist conception of the state. The state was analogous to a cell, or a biological organism: a community of cells was analogous to ‘a community of men joined together to form a nation’.  

Concepts of the state as a cell or organism originated from the rise of cell biology in imperial Germany, was common currency at the time. Fletcher saw ‘the animal’, as a ‘republic of individually active citizens’, ‘the new result of all their separate lives ... make up the action of the polity as a whole’. Just as each cell had ‘its individual set of properties and its individual daily life’, so each individual, by virtue of his special capacities, had a contribution to make to the state. Individuals were in a state of harmony when their attributes were suited to the community to which they belonged, and the nation-state was harmonious when its citizens were grouped in communities like these. Over time, the individuals would become ‘peculiarly well-adapted’ to groups to which they belonged for ‘the performance of special work’:

\[\text{279} \] See Note 46, 2.


\[\text{281} \] Weindling (1981). Virchow was perhaps most famous amongst the German professors of anatomy who promoted the organism as a social arrangement of parts. These theories of the cell state during the late nineteenth and early twentieth century were partially a response to the German state’s institutional control of the universities.

\[\text{282} \] This lecture, entitled ‘Animal-cells and their citizenship’, Fletcher seems to have prepared to deliver to scientists. The nature of the lecture and the notes at the end suggest that it was written for scientists and that Fletcher planned to list four central properties of the protoplasmic amoeba, cell uptake mechanisms, classification of types of animal cells. WIHM: CMAC/PP/WMF/4. W. M. Fletcher, ‘Animal-cells and their citizenship’, n. d.
the community as a whole will prosper exactly in proportion as each citizen finds that work to do of which he is most capable, and guides his powers, not as his personal inclination directs, but solely with a view to the good of the whole body of his fellows. And in this way each man, while he is loyally and unselfishly doing his own share, will profit in his turn by the result of the varied labours of his fellow-citizens.\textsuperscript{283}

Division of labour was a sign of civilisation: the more civilised the nation, the more sophisticated the division of duties amongst its citizens.

\[\text{Those] nations which at present we call the most civilized, those nations which have succeeded best in the struggle for existence, are those in which this great principle of the division of labour has been carried to its furthest limit... [The] duties which make up the functions of the whole organism are divided out among the individual cells.\textsuperscript{284}\]

Thus, the MRC was a cell within the British imperial body. It specialised in scientific 'research' to improve the physical and emotional well-being of Britons, embracing those scientists and scientific physicians who were particularly well suited to perform its special work. If the committed scientific physicians, recognised to be the right sort of people, were cultivated, they would over time become more and more peculiarly suited to MRC medical research. If the research workers were loyal and unflinchingly patriotic in their commitment to the corporate unity which Fletcher wanted the MRC to embody, the MRC, like the citizen cell of the national body, would make Britain and its empire more civilised.

The moral and civilising roles of Fletcher's medical research also had a religious face when he championed it as a form of worship which brought beauty and dignity to British society.\textsuperscript{285} He allied himself with the renaissance humanist, physic, writer and poet Sir Thomas Browne, and so lent weight to this claim.

This kind of work [medical research work] in any civilized nation is needed not only for utility, though Heaven knows that is justification enough, but for its interest and for the dignity of man, and I would add, for our worship. After all, the second great commandment about loving our neighbour cannot be more than an empty sentiment


\textsuperscript{284} See Note 55, pp. 11-12.

\textsuperscript{285} See Note 48.
nowadays unless the love takes a practical form, and unless it is free, so far as possible, from ignorance. This scientific work is necessary for the fulfilment of that commandment. It is necessary too for the fulfilment of another commandment. That consideration has, I think, never been better expressed than by a physician, Sir Thomas Browne [quoted from Religio Medici] 'The wisdom of God receives small honour from those vulgar heads that rudely stare about and with a gross rusticity admire His works. Those highly magnify Him who by deliberate research into His creatures and judicious inquiry into His acts return the duty of a devout and learned admiration'.

The burden of this important work lay with the medical research worker, someone who, Fletcher claimed, should be given national credit for their vital contribution to society; a symbolic figure to be revered and studied by other citizens. The MRC research workers' role was so critical in society, that 'it ought to be a proper part of citizenship' for members of the general public labouring in other communities of society, 'to understand something of the difficult and lonely path the pioneer investigator has to follow, and to see something of the processes by which a new fundamental discovery comes.' I propose this idealised image of the MRC medical research worker as the 'noble scientist', and in Chapter 4, I show Fletcher cultivating these characters in practice during the biological standardisation of insulin which shaped the first MRC clinical trials.

Despite the rhetoric for medical research which was aimed at removing the demand for the MRC's research to give instant answers to national problems, 'practical value' haunted the justification of medical research at every stage and in every way. Even the beauty and worship which the images of Thomas Browne were supposed to invoke was given 'practical' purpose. While defending the authority of the MRC to define medical research, Fletcher seemed determined that the institution should not be marginalised as unimportant, rarefied and impractical, by those 'practical men' -- the doctors, engineers, and even parliamentarians -- who controlled affairs. Fletcher, after all, was a man who had justified a practical training in medicine as a valuable offset to the pure research work that held his interest: a scientist who had spent two and a half years between Bart's and Trinity. For two or three days a week

286 See Note 48.

during term time, after working at Bart's, he would rush for the train from Liverpool Street to Cambridge, arrive in Cambridge too late to dine in College (i.e. after 7.15 pm), then prepare his lectures for most of the night; deliver them at nine the next morning, and then catch the train immediately afterwards in order to be back on duty at Bart's by noon.\footnote{Fletcher (1957), 44.} Fletcher seemed convinced that nothing could compete with hard evidence of how and why MRC research was valuable to Britain.

III. \textit{Making biological standards}

During this period, standards and standard setting were subjects which drew considerable interest in a number of spheres of society. And, as I argued in Chapter 2, standards and standardisation had acquired multiple meanings and associations with efficiency, scientific management and rationalisation. In the context of an increasing focus and national interest in standard setting more generally, and in the then recent crisis over toxic unstandardised salvarsan in the medical world (which I showed was featured in Fletcher's list of Medical Research Committee successes), the issue of biological standardisation was brought into sharp focus.

Briefly, salvarsan was the first effective drug against syphilis. It had been produced in Frankfurt in 1909, clinically tested there, and had a growing international market. When the war broke out, trade with Germany was suspended, leaving British pharmaceutical companies unprepared to manufacture the drug. The salvarsan they released onto the market during the war was toxic and there were problems with its quality throughout the war. Given past experience of high rates of venereal diseases amongst new army recruits the issue of toxic salvarsan became a matter of national concern and security. As I touched on briefly at an earlier point in this chapter, the Board of Trade (which had granted pharmaceutical companies their licences to produce the drug under these special circumstances) took control of the situation by forcing these companies to submit all samples to biological tests by the MRC. The

\footnote{Fletcher (1957), 40-2.}
MRC, in turn, gave companies official certificates for safe and non-toxic batches.\textsuperscript{290} The way in which this crisis embarrassed legitimate drug companies like Burroughs Wellcome and May and Baker, to name just two, should not be underestimated. As I mentioned in Chapter 1, and discussed in Chapter 2, these were precisely the companies that set themselves apart from patent medicine manufacturers by marketing their products as high quality, standardised drugs.

Fletcher seized upon this public crisis of salvarsan as evidence of a need and demand for biological standardisation, but standardising drugs was only one part of his scheme: tissue cultures should also be standardised. When the Asquith Reconstruction Committee sent around a questionnaire to medical bodies up and down the country, asking them to submit their best strategies for 'promoting the conservation of health of the population', Fletcher's response was a Memorandum 'upon a National Laboratory for Biological Standardisation'. His memo proposed a government laboratory for biological standards analogous to the National Physical Laboratory.\textsuperscript{291} Fletcher imagined a collection of specially preserved standard culture types, all housed under one roof; he imagined this laboratory supplying bacteriological, serological and therapeutic 'standards of measurements, to furnish a common basis of comparison for the results obtained by different observers'.\textsuperscript{292} And, 'in the course of time', he hoped that there would be 'international recognition for such standards, so that the statement of an agglutination titre in a scientific paper would have the same worldwide validity, if not the same accuracy of measurement, as a record of temperature or weight.'\textsuperscript{293}

Between 1919 and 1925, Fletcher conducted three separate biological standardisation projects simultaneously: one, the National Collection of Type Cultures, and its complementary Standards Laboratory of bacteriological and serological types at Oxford; two, an anthropometric standard; and three, a campaign for laws giving the MRC authority to control

\textsuperscript{290} Liebenau (1989).

\textsuperscript{291} PRO: FD1/996, 'Memorandum submitted to Mr Asquith's Reconstruction Committee by the Medical Research Committee upon a National Laboratory for Biological Standardisation', December 1916.

\textsuperscript{292} See Note 63.

\textsuperscript{293} See Note 63.
the biological standardisation of therapeutic substances. Fletcher indexed these standard-setting agendas to the moral advance that he predicted would come through medical research carried out by the right sort of characters. He selected people to make these standards, and so he expected each of these projects to produce a biological standard, which he would then be able to demonstrate (to those practical men in power, and to the British people) was both scientifically and commercially valuable for the country. The gallery of standard cultures materialised, and the Standards Laboratory was very productive, but Fletcher's characters failed to produce an anthropometric standard. Fletcher, who (as I have shown earlier) seemed possessed by a need to produce hard evidence of the MRC's natural value, was deeply disappointed with the Anthropometric Standards Committee. I propose that this failure made it all the more imperative for the other biological standards to succeed.

Fletcher could not have predicted that insulin would have been 'discovered' in Toronto around this time, or that the University of Toronto would have given the MRC the gift of the insulin patent. But given the public commitment he had now made to biological standardisation, and the problems with the anthropometric standard project he was simultaneously managing, Fletcher seized this gift and, as I shall show in Chapter 4, made the biological standardisation of insulin a public event. The clinical trials of insulin, also made public, were managed as a part of this drug's biological standardisation. However, Fletcher's simultaneous management of three different biological standardisation initiatives, particularly the anthropometric standard, was proving that the institution's national value was indexed to standard setting in a piecemeal fashion. The MRC's authority, and ultimately the value of its standards would come under constant scrutiny and attack by experts in other fields. I shall now turn to the issues of why making standards of demonstrable national value in the way Fletcher tried to make the anthropometric standard was problematic; and why controlling therapeutic standards by law appeared to offer a more secure authority. I shall show how Fletcher used what he now claimed as the MRC's insulin success story of biological standards in the public interest to assist the Therapeutic Substances Act in parliament. The details of how Fletcher managed the insulin affair, and the pivotal role of clinical trials in this process, will follow in Chapter 4.
III. 1. Under pressure: giving three biological standards national values

The National Collection of Type of Cultures, a gallery of standards, was the realisation of Fletcher's museological vision for a National Laboratory of Biological Standards. The initial impetus for this particular gallery of bacteriological and serological cultures seems to have come from pathologists, who, perhaps after learning of his interest in the subject, approached Fletcher about establishing such a collection. But Fletcher's naturalist interests, dating back to his younger years when he kept a 'Museum' of standard types, may have given this project personal significance. The museum of standard types, which started in 1919, became a collaborative effort between the MRC and the Lister Institute. Its acquisitions came from renowned and eminent experts (especially those who specialised in particular strains) who were asked to select the best 'authentic' samples of a type of culture and send them to the Lister Institute. A director was appointed along with a full-time curator. Fletcher saw the 'Museum' as a statement of national pride. These standards embodied a civilising agenda for Fletcher. He fully intended for this 'herbarium' to stand as a 'nucleus for samples from all over the world', a collection of ideal types and immutable particulars, to be copied and dispatched to bacteriologists, pathologists and physicians everywhere. He also wanted it to be a collection of organisms of 'economic importance in the widest sense'.

The following year, 1920, Fletcher appointed the Anthropometric Standards Committee

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294 PRO: FD1/985, A. E. Boycott to C. J. Martin, 26/7/19; C. J. Martin to W. M. Fletcher, 29/10/19; C. J. Martin, 3/12/19.

295 Fletcher (1957), 20, 22, 24-5, 33.

296 PRO: FD1/985, 'National Collection of Tube Cultures (MRC) Provisional Constitution and Regulations of Approval'.

297 PRO: FD1/985, 'National Collection of Tube Cultures (MRC) Provisional Constitution and Regulations of Approval'; Fletcher to Martin, 20/11/19. Quotations that refer to this collection as a herbarium can also be found in this letter. See also PRO: FD1/985, Fletcher to Morant, 'Central Collection of Type Cultures of Bacteria and Protozoa', 4/1/20.
to consider and advise upon the selection and description of standard measurements of human body characters capable of easy determination and accurate record, having regard to their probable value either for practical purposes in relation to judgements of physical condition or for the purposes of scientific anthropometric survey.²⁹⁸

The advantage of this MRC standard was that it would take account of static measurements of structure, as well as of dynamic measures of function, of specific physical efficiency and of general capacity (often described as 'physique').²⁹⁹ Fletcher imagined that these MRC standards would provide better knowledge of the capacity and strength of the British population.³⁰⁰

Physicians, employers, government officials, health inspectors and the like might be able to use this MRC standard to measure individuals against values of 'normal' health, and compare their efficiency for both sexes, for all ages, and perhaps for different races.³⁰¹ Quite apart from the possibility of using it in a national anthropometric survey of the kind many had been calling for since the Boer war, and were calling for again during the Great War, I propose that an effective anthropometric standard might also have been valued by eugenicists by offering a normative scale against which 'unfit' as well as superior stocks could be measured. Evidence from these studies might subsequently prove or disprove various biological theories of class and race.³⁰²

²⁹⁸ PRO: FD1/3762: Fletcher, Anthropometric standards, 12/1/20; Fletcher to Dreyer, 23/12/19.

²⁹⁹ PRO: FD1/3762, Fletcher to Dreyer, 23/12/19; Fletcher to Sir John Goodwin, 24/12/19.

³⁰⁰ The Interdepartmental Committee, appointed after the Boer War in 1903, had called for anthropometric surveys. At the time, the introduction of compulsory military service in 1915 had forced a national survey of men called to arms. Later, in 1917, the Medical Boards, set up by the newly-formed Ministry of National Service, had initiated another systematic survey. However, this 1917 survey only involved men under 51 who had not already been called to arms. At the time when Walter Fletcher tabled his plan for making anthropometric standards, these Medical Boards had, in Sir Arthur Keith's words, 'become grading machines, working according to definite standards, sorting men who came before them -- men varying in age from 18-51 -- drawn from known districts into four groups or Grades I, II, III, IV, according to their degree of 'physical fitness'. While the 1917 survey was of a more practical and physiological nature than the comprehensive anthropometric survey initially proposed some (like Arthur Keith) believed that practical 'grading' was not enough. A. Keith, 'Anthropometry and National Health', Journal of State Medicine (1919), 27: 33-42; Mazumdar (1992), 58-96.

³⁰¹ PRO: FD1/3762, Fletcher to Dreyer, 23/12/19.

As in the case of the collection of standard cultures, where only eminent pathologists had been asked to produce standard types, Fletcher hand-picked scientists who would produce a reliable standard, one that would be accepted by medical, scientific and statistical experts, and that was likely to be widely used. The Committee comprised Arthur Keith, Professor of Anatomy at the Royal College of Surgeons and a powerful advocate of anthropometry (Chairman); George Dreyer, Professor of Pathology at Oxford; John Brownlee, statistician at the MRC; Colonel Lelean, Professor of Hygiene at the Royal Army Medical College; Lieutenant-Colonel Martin Flack, Director of Medical Research in the RAF; and F. G. Hobson (Secretary), a recently qualified medical student who had earned military distinction during the war. Fletcher was particularly impressed by George Dreyer. Dreyer, a graduate of Copenhagen University, had become the first Professor of Pathology at Oxford University in 1907 when he was only 34 years of age. Fletcher saw him as a man of ’extraordinary skill in technique’. He went so far as to claim that ’pathology would be a different science if other pathologists had his mathematical knowledge’. Dreyer was also a friend and well-known supporter of the idea of producing and applying biological standards in medicine and beyond. Dreyer’s 1919 memorandum on his method of measuring physical fitness had encouraged Fletcher to set up this Anthropometric Standards Committee. Dreyer was also a supporter of Fletcher’s biological standardisation initiatives and had devoted his prestigious Harvey Society Lecture that year to ’Biological Standards and their application in medicine’.

303 I am grateful to David Smith and Sally Horrocks for allowing me to see their presently unpublished paper on the history of anthropometry and historical anthropometry. More specifically, F. G. Hobson had studied physiology during the war, but had interrupted his studies to become a dispatch rider in 1914. In 1917, he was awarded a DSO. He returned to England that year and completed his medical training at St Thomas’ Hospital. See F. G. Hobson (obituary), BMJ (1961), 2: 115-16.

304 See Note 75.


306 Dreyer (1920). See also PRO: FD1/3756, G. Dreyer, ’The Normal Vital Capacity in Man in its relation to the size of the body. The importance of this measurement as a guide to physical fitness under different conditions and in different classes of individuals’. Sir Arthur Keith, who had served as President of the Royal Anthropometric Institute, would have given the standard credibility and use in a national survey. For more about Keith’s influence, see ’Sir Arthur Keith (1866-1955), The Lancet
Around this same time, between 1919 and 1920, Fletcher met with his close ally Morant about the laws controlling therapeutic standards.\textsuperscript{307} Recall the Select Committee for Patent Medicines from the Stevens case in Chapter 1. Not two years before the war, this Committee had also argued for a complete reassessment of the laws regulating quality control of therapeutic agents, and related legal issues. Morant, who was known to be machining at dead of night,\textsuperscript{308} joined with Fletcher and together they convinced Christopher Addison, the Minister of Health to set up a government committee to examine this question of biological standardisation with the view to establishing legislation to controlling therapeutic standards. Addison agreed to the Departmental Committee on Control of Certain Therapeutic Substances. Fletcher and Morant selected the reforming committee.

When it came to selecting committee men, Fletcher had met his match in Morant. Morant was known to make a virtue out of choosing the right sort of character, to produce the right sort of government machinery. We left him at this point earlier on in this chapter. In sparring for the right sort of character, the two men gave reasons for proposing and rejecting certain characters so that here, more than ever, the image of the right sort of character (for individuals and committee machines) working for the MRC and the state becomes patent.

Fletcher told Morant that he wanted his friend Henry Dale, who was on the staff at the MRC, to sit on the Committee,\textsuperscript{309} because, as he put it, 'Dale will bring, I feel sure, all the

\textsuperscript{307} PRO: FD1/996, 'Memorandum submitted to Mr Asquith's Reconstruction Committee by the Medical Research Committee upon a National Laboratory for Biological Standardisation', December 1916. See also Memorandum by the Medical Research Committee upon use of Registered Trade Marks for Therapeutics Substances (1917) (London: HMSO); Liebenau (1989).

\textsuperscript{308} Stacey (1984), 70. Stacey draws attention to a letter Morant wrote to Addison about the setting up of the Medical Research Committee on 'Thursday midnight', the letter signed 'goodnight, yours ever'. A close colleague of his, Zoe Puxley, also claimed to have received a letter from him dated 'Monday midnight'. Stacey analyses this as a lack of self-consciousness on Morant's part. But it seems utterly self-conscious and designed either to send a clear message of his dedication, or to leave a record for the office files, or perhaps a bit of both.

necessary technical scientific knowledge'.\textsuperscript{310} Dale will become a more important figure in Chapter 4, and I shall add details about him there. For the moment, it will suffice to say that Dale had first-hand knowledge of the practical problems of standardising sera, and of the problems of organising, preparing and testing standards of drugs from his years working for Burroughs Wellcome pharmaceutical company before he joined the MRC. Since the Minister had decided that Sir Mackenzie Chalmers would chair the committee, Fletcher and Dale thought that if the scientific representation of the Committee was not controlled from the MRC's side, MacKenzie Chalmers might:

press again for Wilcox [who] is quite maddening on a Committee, because he speaks at the rate of 5 words a minute. He has no first-hand expert knowledge of the parts of the subject that will be difficult.\textsuperscript{311}

Morant wanted another scientific representative to join Dale on the committee. Fletcher and Dale suggested that Charles J. Martin would be 'the best man' for the job. Martin was Director of the Lister Institute and a strong supporter of Fletcher's National Collection of Type Cultures. Fletcher recognised Martin as a man with:

first-hand knowledge ... of the details of manufacture of such sera as the Lister Institute supplies... Technically, Martin can be truthfully described as a Director of an Institute which makes a profit on sales of sera, which it applies for research purposes... If the Government imposes controls or tests, the Lister Institute must be among the firms whose products will be controlled or tested. I see arguments both ways; you may say that, e.g. Burroughs Wellcome might grumble if the Lister be represented in the Committee, but again, it might be regarded as a fair thing that a representative of the future victims of control should be on the Committee especially as he is a distinguished man of science... Martin, by the way has [also] got administrative notions and a good deal of 'horse sense'.\textsuperscript{312}

Dr G. F. McCleary was chosen as the token doctor who would be seen to represent the practitioners' angle on matters, though as Fletcher put it in an off-hand remark, this was 'pretty

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obvious'. But there was certainly no need for two physicians (in that capacity, because Dale and Fletcher were also both qualified physicians) on the Committee. So, when Sir William Hale White's name was put forward (perhaps by Mackenzie Chalmers), Fletcher rejected it out of hand. He told Morant:

Hale White, nice as he is, would be quite useless; he has only the practical physician's knowledge of how to use things when he is provided with them. If, for political reasons unknown to me, you want a Consultant physician for window-dressing, he would be better perhaps than any other.  

Morant made one final addition to the list, namely Mr A. B. MacLachlan, because he thought that a Committee such as this, intended as it was to make recommendations to push a bill through parliament, needed a proper administrator. Morant saw MacLachlan as the right sort of man, because he was 'a clever man from [my] administrative staff [at the Ministry of Health]'. In any event, he reasoned, MacLachlan 'would probably also be the one to handle the matter administratively, if and when it [came] to fruition'. And so the Committee to investigate the biological standardisation of therapeutic agents stood thus: Dr Henry H. Dale, F.R.S., Dr C. J. Martin, F.R.S., Dr G. F. Mc Cleary, and Mr A. B. MacLachlan.

The events of the years that followed made this Committee and its specially selected men seem insignificant in creating a law regulating therapeutic standards. In March 1920, before the Mackenzie Chalmers Committee (as the Interdepartment Committee became known), Morant suddenly died. Fletcher still got the committee men that he and Morant had handpicked (when the Committee was finally appointed later that year), but he now had to work with Arthur Robinson, Morant's successor as Permanent Secretary of the Ministry. If Morant was one of the 'zealots' and 'storm-troopers' of the Victorian civil service; Robinson was a 'mandarin'. Robinson was a member of that emerging generation of servant who had climbed steadily up the service ladder, becoming more steeped in the accepted canons of  

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313 See Note 81.
314 See Note 81.
official behaviour with each level of ascent, so that when he reached the dizzy height of Permanent Secretary, he could (as indeed Robinson did) use this knowledge as a powerful resource. The Mackenzie Chalmers Committee (chosen by Fletcher and Morant) held fifteen sittings and examined twenty witnesses from all spheres of science, medicine and industry, that year. While the Committee were meeting, Fletcher contacted Arthur Balfour (who had been in favour of standardisation in certain areas of industry) to ‘squeeze the Treasury for money’ for biological standardisation.

Meanwhile, that same year (1920), the Anthropometric Standards Committee made a promising start. They met three times between January and May of that year, and decided on how to measure head, face and body dimensions, hair-type, eye colour, lung function and pulse rate. The Collection of Culture Types flourished. The Oxford Standards Laboratory dispatched a large volume of cultures and sera to British and foreign institutions. And there were moves to print a catalogue of the types held in this national collection.

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316 Stacey (1984), 59, 63, 64-104, 123-44.

317 These witnesses and representatives included: the Ministry of Health (Drs T. Carnwath and A. Eastwood), the War Office (Col. D. Harvey), the Admiralty (Surgeon-Captain Bassett-Smith), His Majesty's Customs and Excise (Mr J. L. Mackie), the Government Lymph Laboratory, Hendon (Dr F. R. Blaxall), the Medical Research Council (Sir Walter M. Fletcher), the General Medical Council (Sir Donald MacAlister), the Royal College of Physicians of London (Sir William Hale-White), the British Medical Association (Prof. W. E. Dixon), the Society of Medical Officers of Health (Dr Duncan Forbes), the Society of Apothecaries of London (Sir Shirley Murphy and Mr F. W. Gamble), Messrs Burroughs Wellcome and Co. (Mr G. E. Pearson), Messrs. Evans Sons Lescher and Webb, Ltd. (Dr H. E. Annett), Messrs Parke, Davis and Co (Messrs H. J. Fisk, and T. Maben), and Messrs May and Baker, Ltd. (Mr P. Blenkinson). Report of Departmental Committee on Control of Certain Therapeutic Substances, Ministry of Health (1921) (London: HMSO).


319 PRO: FD1/5332: 'Meeting of the Anthropometric Standards Committee', 12/1/20. See also PRO: FD1/5332, 'Anthropometric Standards Committee', 10/2/20. It was decided that the eyes and hair of individual schoolchildren would be held up against these standards. Standing height and sitting height of each person (deciding on the best method to use in each case). They decided on the following measurements: gabella, occipital protuberance, upper border of the meatus, vertex, nasion, mentum, subnasal point, the greatest breadth of the head, the greatest width of face, the jaw width.

320 Curators were willing to duplicate for a nominal fee of one shilling. The charge of one shilling per culture was chosen not only to help maintain the collection but because it was believed that it would ensure that the laboratory kept their cultures alive, thus saving the Bureau the trouble of unnecessary duplication of the same standards. 'National Collection of Tube Cultures (MRC) Provisional Constitution and Regulations of Approval'. See also MRC Annual Report, 1925-26, 49; MRC Special Report Number 64: Catalogue of the National Collection of Type Cultures Maintained at the Listed
Fletcher compiled the MRC's Annual Reports around October and November of each year. When he took stock of his biological standardisation initiatives in October 1921, however, the situation looked less promising. He could write in the section of the report headed, 'The Determination of Biological Standards and the Methods of Biological Assay and Measurement', that the National Collection of Types now had 300 cultures, and that the Standards Laboratory in Oxford had answered requests for cultures and sera from some 120 workers and had shipped consignments of standards from Rhodesia to Australia. But there had been no word from the Anthropometric Standards Committee since the previous May (1920), and the chances of this standard having an immediate and widespread national impact now seemed increasingly unlikely. The large-scale anthropometric survey that Keith and the MRC hoped might be established had not materialised. Worse, that March (1921), Dr Major Greenwood alerted Fletcher that the entire basis of Dreyer's approach of making such a standard might be fatally flawed. Greenwood, the physician who had been trained in statistics by Karl Pearson, was now becoming an eminent statistician in his own right. He will reappear in Chapters 5 and 6 of this thesis and I shall have more to say about him in these chapters.

Greenwood wrote to Fletcher because he had seen a book of tables Dreyer had published in 1920 which gave the expected vital capacity of three different classes of people, of perfect, medium and poor physical fitness, based on measurements of weight, stem length and chest circumference. Dreyer had also published an article in *The Lancet* on this subject that same year. It is unclear whether Greenwood knew of Dreyer's central role in creating an MRC anthropometric standard directly (from Fletcher) or indirectly (from the MRC’s Annual Report).
What we do know is that Greenwood found Dreyer's statistical analysis to be 'very brief and rather crude', and that Greenwood also showed Dreyer's work to Pearson, who concluded that the statistics were 'grossly inaccurate', and that 'all the conclusions were nonsense'. With the Committee falling silent, and no hard evidence -- in the form of final results or conclusions -- emerging from Dreyer's and Hobson's investigations, Fletcher was, as it were, caught between a rock and a hard place. He respected Greenwood as a statistician, and trusted him as a friend. Greenwood kept him informed about what was going on at the Ministry of Health (where Greenwood was employed at the time) and the two would, on occasion, plan how to manoeuvre physicians whom they believed were scientifically minded into vacant chairs of medicine. But Fletcher (as I mentioned earlier) was also impressed by Dreyer, and regarded him as a friend. With the infant disciplines of biological standardisation on the one hand, and medical statistics on the other, Fletcher saw character and expertise in these areas embodied in Greenwood and Dreyer respectively. And with Pearson opposed to the statistics, it looked as if the standard was in trouble. The anthropometric results would have to be examined before decisions could be made about the value of this standard, and as to how it could, and whether it should, be released into the public domain. So, where were the results? This was the question Fletcher began to ask Dreyer and Hobson.

Matters did not look better for the campaign for a therapeutic substance law in late 1921. The Ministry of Health's MacKenzie Chalmers Committee had produced their final report in February of that year. The Committee had recommended that therapeutic substances which could not be tested adequately by chemical means -- 'biologica...
would be prepared and maintained. The Committee also recommended that the MRC (which, they noted, was already doing this work) should be the authority legally responsible for discharging these functions, and for scheduling the substances which needed such control. It recommended that legislation should refer to three classes of substances, (A), (B) and (C):

(A): A group comprising the bodies conveniently described in the United States Regulations of 1919 as 'biologic products' i.e. vaccines, sera, toxins, antibodies and analogous products.

(B): A group of patent synthetic remedies such as salvarsan and its analogues.

(C): A group corresponding more nearly with the popularly received definition of ordinary 'drugs', e.g. preparations of Digitalis, Strophanthus, Squill, Ergot, Cannabis Indica, Pituitary Gland, etc. 326

The Committee recommended that manufacturers would retain responsibility for ensuring that their products were standardised in accordance with these MRC standards. The system would involve minimal inspection of their premises to ensure that standards were being faithfully and properly applied. 327 But the Committee's report had received mixed reviews in the public press. While The Lancet praised the Mackenzie Chalmers Committee for 'this useful and business-like piece of work', The Times was severely critical.

According to The Lancet, the Committee had been efficient and impressive: efficient because it had operated 'at minimal expense to the public' (a mere £182 in their estimation), and impressive because it had achieved the favour of manufacturers for its fairness in protecting their commercial interests as well as public interests. 328 Establishing biological standards for producing safe drugs for patients was a strictly medical matter. The journal made this point clear. This interpretation was echoed in other medical responses to the Mackenzie Chalmers Report. But The Times wrote the investigative committee off as a group of eminent


men whose aim to draft a Parliamentary Bill to standardise and control biologicals was 'excessive and meddlesome'. According to The Times leader, this epitomised what the paper saw as an increasing tendency towards unnecessary government interference, through the inspection and control of the finest details. Crucially, the paper presented the very appointment of such a committee as an appalling indictment of an authority that was out of touch with what the country really needed, and what was genuinely in the public interest. It seemed to them that, at a time of rising unemployment, controlling biological standards could not be considered to be in the public interest. Furthermore, The Times suggested that legislating for the standardisation of therapeutics would encourage an inflated bureaucracy around 'standards', and would impose unnecessary controls on everyone, from manufacturing companies to the local housewives. In short, controlling biologicals in the public interest could not be treated as a strictly medical matter to be dealt with by scientists and doctors because, in the end, the whole country would be asked to pay dearly for these oppressive measures in the form of high taxes.\textsuperscript{329}

Is there no way of shielding the unfortunate taxpayer from Dr Addison's incessant attempts to heap up the cost of public services? ... In a perfect world which is the ideal of the Ministry of Health we have no doubt that excellent reasons could be produced for the inspection, testing, and analysis of every separate mutton chop sold to the public. Death may lurk even in the mutton chop, and the time may come when the Mutton Chop Department, controlled by a swarm of Dr Addison's myrmidons, will supervise the sale of each tiny cutlet sought by the innocent housewife. But we are living in times when there are a million people out of work partly because the money which ought to go to the revival of industry is being commandeered for the payment of extravagant and inflated bureaucracies... These 'therapeutic substances' the government proposed to standardise are manufactured with great care by firms of high repute, and their standard has broadly satisfied the medical faculty ... [Dr Addison] is now armed afresh with material for another elaborate and costly scheme. In order to 'standardise' and 'control' various vaccines, sera, and other drugs, a whole series of expensive measures are to be devised.\textsuperscript{330}

By October 1922, the situation stood thus. The National Collection of Cultures increased its numbers and the Standards Laboratory was similarly productive. The Anthropometric

\textsuperscript{329} \textit{PRO: FD1/999, 'Dr Addison's activities', The Times, 25/2/21.}

\textsuperscript{330} See Note 101.
Standards Committee had convened a fourth meeting the previous December for Dreyer and Hobson to report on their progress. They had negotiated with trade unions and employers to gain access to miners, cotton and wool spinners and weavers, and arranged for elementary schoolchildren, and female medical students to be measured. The London policemen and firemen had also volunteered themselves for the investigation. Over 6,000 people had been examined, over 6,500 measurements had been taken, but Hobson (as Secretary of the Committee) had still not produced the final report complete with statistically analysed results.331 By this stage A. V. Hill (a former student and protégé of Fletcher's) had complained to Fletcher about the discrepancy between the results they had collected in Manchester and the outcome predicted by Dreyer.332 Pearson had made his feelings clear about the results, and Greenwood had warned Fletcher that Pearson or his students would think nothing of attacking a standard based on these results in their journal Biometrica or of making a public controversy of this standard which might embarrass the MRC.333 Fletcher withdrew his support from the Anthropometric Committee by refusing to support a request to arrange large-scale measurements. Perhaps reading this as a sign of real and considerable doubt in Dreyer's methods, the Committee convened a final meeting in April 1922. At that meeting it was concluded that the Committee could not recommend Professor Dreyer's method as an anthropometric standard, but Committee still had yet to produce a set of statistically analysed results.334

331 PRO: FD1/3756, Dreyer to A. L. Thomson, 26/7/20; Hobson to Thomson, 28/10/19; Hobson to Thomson, 4/11/19; Hobson to Thomson, 22/11/19; Hobson to Fletcher, 23/2/20; Hobson to Thomson, 3/3/20; Hobson to Fletcher, 4/7/20. PRO: FD1/3764, Mumford to MRC, 17/7/20; Hill to Fletcher, 17/7/20.

332 Fletcher (1957), 66-7, 122, 123, 136, 147, 164, 200. See also Elliott (1937). He had tutored A. V. Hill and Keith Lucas at Cambridge. Fletcher and Hill became close friends discussing food, and holidays and their emotions as well as science in their communications with each other. See Churchill: AVHL/II/4/27; Fletcher to Francis, 2/10/05; Fletcher to Hill, 2/6/08; Hill to Fletcher, 10/10/10; Hill to Fletcher, 27/3/11; Hill to Fletcher, 8/2/11; Fletcher to Hill, 18/3/11; Fletcher to Hill, 14/11/12; Hill to Fletcher, 20/3/16.


334 PRO: FD1/3762, Fletcher to Keith, 1/4/22; Hobson to Fletcher, 4/1/22.
Fletcher was disappointed with this outcome. The details of the problems with the anthropometric standards are beyond the scope of this thesis. But he could not bring himself to blame Dreyer. He blamed Brownlee, for whom he did not care much, for not attending to statistical matters. He blamed Hobson who, as the most junior of the Committee, had collected the bulk of the results, for not producing a full report with analysed results. But Dreyer, who designed and named the method, and published papers justifying it with measurements collected during this investigation, seemed blameless in Fletcher's eyes. Years later, when Fletcher was still to be found asking his Cambridge statistician friend G. U. Yule if he could do anything with these anthropometric results, and after Dreyer's reputation had been further tarnished by the diaplyte vaccine results, Fletcher still refused to make Dreyer a scapegoat in this affair.335

II. 2. Therapeutic standards: public interest, practical value and the civil servants

The year 1923 marked a turning-point in Fletcher's campaign for a therapeutic standards law. Insulin had been isolated in 1922, the MRC had been given the patent rights for the drug, and it had made a public event of the introduction of insulin into Britain in late 1922 and early 1923 (Chapter 4). Fletcher and Dale had managed and controlled this public event which had undoubtedly raised the MRC's profile, and which had positive effects on Fletcher's campaign for the Therapeutic Substances Act.

The medical press came out in favour of both therapeutic laws to protect the public and the MRC. But The Times had spoken for the Treasury. So, when the Ministry of Health officials submitted the draft Therapeutics Substances Bill to the Treasury, they went to great lengths to assure the Treasury that the MRC's 'highly qualified scientific staff' could control therapeutic standards, at minimum costs: travel expenses and a small subsistence allowance for

335 Smith and Horrocks (1996). In 1923, Dreyer published a report of some research, for which Fletcher had granted MRC funds, which related to the preparation of a vaccine for the treatment of tuberculosis. The product was based on the assumption that if the tubercle bacillus was treated with formalin, followed by repeated extraction with acetone, it would enhance the antigenic properties of the bacillus. After animal experiments small quantities of the substances were released to a number of centres for clinical trial but the results were disappointing. See MRC Annual Report, 1922-23, pp 33-4, 46-6, and MRC Annual Report, 1923-24, pp 41. See also Bryder (1988).
MRC inspecting officials would be required.\textsuperscript{336} Even this was too expensive for the Treasury. Their response was that the measure should be completely self-supporting: since commercial firms would benefit from this government stamp of approval, they should pay an annual licence fee to cover inspection costs.\textsuperscript{337}

Preparing to do their usual battle with the Treasury, Ministry of Health officials asked Fletcher to submit an estimate of the cost of making and policing standards.\textsuperscript{338} Fletcher consulted Dale (since Dale would be in charge of organising these inspections), who reasoned that £2000 per annum would cover the cost.\textsuperscript{339} This figure alarmed the Minister's Assistant Secretary (L. G. Brock) who told Fletcher plainly:

I cannot understand how Dale arrives at this estimate of additional expenditure in respect of the duties imposed by the Bill... The point is important because if the Bill really imposes new duties which are outside your present province and which will entail an annual expenditure of anything like 2000 [pounds] a year, the Treasury will not improbably object to its being introduced at all. Even if it is introduced we shall have to show that cost in the White Paper, which has to be circulated before the financial resolution is taken, and the opponents of the Bill will say (as \textit{The Times} did when the Chalmers Report first appeared) that it is merely another scheme for the State endowment of more doctors. If Dale's estimate is right, I am afraid it wrecks the bill.\textsuperscript{340}

Just as a national scheme to standardise and control biologicals in the public interest could not be separated from the government acting in the public interest as a whole, financing a measure to standardise biologicals and inspect these standards depended on government officials' interpretation of standards. As far as the Ministry of Health was concerned, inspection merely involved casting an eye on factory production. As the Ministry's Brock wrote to Fletcher:

When we discussed the matter here I gather that you contemplated that Dale personally would visit the five or six firms concerned and that once the layout of their

\textsuperscript{336} PRO: FD1/999, Brock to the Secretary of the Treasury, 10/3/23.

\textsuperscript{337} PRO: FD1/999.

\textsuperscript{338} See Note 109.

\textsuperscript{339} PRO: FD1/999, Fletcher to Barker, 19/4/23.

\textsuperscript{340} PRO: FD1/999, Brock to Fletcher, 1923.
buildings and their methods had been found to be satisfactory, very little more would be needed except an occasional test of samples. My impression certainly was that Dale or a deputy could do the visits without interfering with other duties and that there would be no occasion for additional staff... It is solely the work of seeing that the producing firms comply with the standards, laid down in the regulations made by the Joint Committee on the recommendations of the MRC and the work of advising standards, where no accepted standards at present exist, which is surely within the province of the MRC already? As I understand it the Bill does not impose either on us or you any obligation to incur expenditure in devising of standards; merely provides machinery for the practical enforcement of such standards when in the ordinary course of research they have been advised and accepted by the scientific world....I cannot see that the effect of the Bill is to require you to do any more in this direction than you have already been doing for some time past.\footnote{PRO: FD1/999, Brock to Fletcher, 1923.}

For the MRC's Dale, biological standardisation was not analogous to factory inspection, it involved more than casting an eye on the manufacturing process of drugs in a factory. Managing the biological standardisation of drugs and controlling therapeutic standards was medical research.\footnote{See Note 113.} In the end Fletcher was forced to concede.

We recognise that this falls properly within the sphere of work of the Council. The Treasury could therefore be told that the work would be done by the Council at once with their existing resources... the Treasury can fairly be told now that the work can be done with our existing resources.\footnote{PRO: FD1/999, Record note from Fletcher, 30/4/23.}

If he wanted the Bill to have a chance in parliament, the proposed £2000 administrative cost would have to be withdrawn. Even so, getting the Bill through parliament seemed fraught with difficulties. The Therapeutic Substances Bill was introduced successively by the Lloyd George Coalition government, the Bonar Law Conservative government and the Ramsay MacDonald Labour government. It had its second reading three times, but failed in each case because of rapid successive dissolutions. In 1923 Brock told Fletcher that if he wanted this Bill to have a safe passage, he would have to show parliamentarians a) that it was a practicable measure, b) that it was urgently needed to protect the public good.
I agree that the scientific case for the Bill is very strong, but the Parliamentary case is not, because of the difficulties of producing concrete cases to prove that the dangers we seek to guard against are anything more than theoretical dangers.\textsuperscript{344}

Fletcher, as we have seen earlier, had been arguing for standards on the basis that it was travesty for a civilised nation like Britain not to have laws to provide such assurances. As Brock put it:

The House of Commons is \textit{not} moved by the argument that practically every other civilised country has realised the necessity for some precautions to secure reasonable standards of purity and strength in sera and vaccines.\textsuperscript{345}

If they pursued this line, they would be 'met by a demand for evidence of fatal cases'.\textsuperscript{346} The seasoned civil servant remarked that:

From the House of Commons point of view a single case of a popular actress poisoned by some toxic salvarsan or impure vaccine would be worth all the scientific arguments in the world.\textsuperscript{347}

Fletcher sensationalised his approach. He suggested that Robinson might advise those on the Ministry's side to take one or two of the following 'perfectly clear examples of detail'.\textsuperscript{348} They were examples which Fletcher presumably thought would focus the meaning of 'standards', show what was at issue in the biological standardisation of therapies, and show these matters to be urgent, and practical. The variable standards of pituitary extract preparations on the market showed how the Bill would save the lives of mothers and babies; the successful introduction and biological standardisation of insulin, which had been marketed (as we shall see in Chapter 4) as a public event, demonstrated how valuable biological standardisation could be in practice, when managed by the MRC. First, the pituitary extract.

\textsuperscript{344} PRO: FD1/999, Brock to Fletcher, April 1923.

\textsuperscript{345} See Note 116.

\textsuperscript{346} See Note 116.

\textsuperscript{347} See Note 116.

\textsuperscript{348} See Note 116.
In the case of pituitary extract used increasingly all over the country in childbirth, five firms willingly submitted samples of their products for standardisation in the National Institute. Though all purported to be equivalent in potency, one preparation was found to be eighty times as potent as the other, the samples of the remaining firms being graded between these extremes. A doctor, by using one sample instead of another, might cause a ruptured womb, with certain death of the child and the possible death of the mother.\footnote{349}

Fletcher argued that manufacturers exposing the public and the profession to such common and proven risks did not desire the 'maintenance of this evil'.\footnote{350}

It springs not from any desire on the part of firms to supply cheap goods, it has nothing to do with questions of 'quality'. It is the result of the absence of a declared 'standard' of reference and the expression of the unitage of each sample sold in terms of the common standard.\footnote{351}

As for insulin, this story, and the MRC's management of it had already been disclosed to the public. Fletcher told Robinson:

\textit{Doctors will not use secret remedies}.\footnote{352} No remedy will be used of which the therapeutic effects are not capable of experimental demonstration and of accurate standardisation. Insulin is still quite 'unknown, scientific product'. No-one knows its composition, or is likely to know it for some years. Various firms have various ways of making it. But a standard reference has been set up, and no doctor would venture to give a dose of Insulin without knowing the number of 'units' by reference to the common arbitrary standard, in the dose administered. All the firms have welcomed the Insulin standard and the compulsory testing of their products for accurate unitage. The present control of Insulin unitage which the profession and the public now enjoy has only been obtained by means of special agreement with the Medical Research Council. It is exactly this system, to be applied generally, which, under proper authorities, the Bill will set up.\footnote{353}
These two cases along with the received view of the MRC’s management of the salvarsan crisis, were often used by members who stood in favour of the Bill in parliament.

The Bill came up again for consideration in parliament in 1925. This time Fletcher approached Lord Balfour in an attempt to persuade him of the urgency of this measure by presenting a dramatic account of the history of events. Arguing that the medical profession, scientific community and pharmaceutical communities supported the Bill he implied that all of the parties demanded it.

The profession is calling for it; there was a strongly worded leading article in The Lancet last month, complaining of the repeated delay.\textsuperscript{354}

Fletcher also suggested that this standardisation of therapies was essentially apolitical since it had been put forward and supported by parties in government on both sides of the House.\textsuperscript{355} He pointed out to Balfour that even in June 1925, at the point of its Second Reading in that session of the House, 'Mr Neville Chamberlain is extremely anxious to get it'. Fletcher could not understand what the problem might be:

> A month ago Mr William Graham wrote to me to say: "Unfortunately the Government have delayed the Second Reading for more days but (i.e. the Opposition) are telling them that there is no opposition to the measure, and that they can take it after 11 o'clock at night if they please, without the slightest chance of protest. I do hope we shall get them to stand up to this arrangement." Week after week, since then the Bill has been in the Parliament but has been postponed, and I am told the Government Whips postpone it only because they think the Ministry of Health in general is taking up too much time.\textsuperscript{356}

Adopting the moral high ground, he argued that the Bill not only saved lives but that its absence killed mothers and babies, and that a government which killed mothers and babies by failing to protect a public from the evils of unstandardised drugs would be held accountable to laymen for not acting in their best interest:

\textsuperscript{354} PRO: FD1/999, Fletcher to Lord Balfour, 23/6/25.

\textsuperscript{355} See Note 126.

\textsuperscript{356} See Note 126.
lives are being steadily lost all over the country for want of [the bill]. It is impossible to measure the suffering and mortality due to the lack of control over the potency of any single weapon in the hands of a doctor, like diphtheria antitoxin, for instance... If the public knew that this necessary protection was being withheld from them without a shadow of Parliamentary justification I think they would be rightly angry.357

Fletcher suggested that the sticking point might have been members' failure to recognise the urgency of the matter, implying for these purposes that the average House of Commons member was no different from, and indeed represented, the average layman in this case. He told Balfour:

I think part of the difficulty lies in its unattractive name. The ordinary layman can see nothing urgent about it.358

He therefore outlined the five main virtues of the Bill to Arthur Balfour. At its most important level, the Bill was about fairness. The first virtue he cited was that the Bill protected the public (both patients and doctors alike) through a 'principle of fair dealing', which assured that the purchasers got what they paid for. In so doing, Fletcher argued, it merely extended to certain therapeutic substances a principle already in common use with other commodities.359 This could only be done by fixing standards for strength and purity of therapeutic substances which, because they could not be 'weighed, like tea and coffee, or chemically analysed, like gold or petrol', had to have their potency and purity measured by indirect methods.360

Second, 'the Bill provided safeguards for life and health'. 'A doctor, betrayed by the absence of potency tests, may quite inadvertently give an overdose having serious or fatal results; or again, betrayed by lack of purity tests, he may expose the patient to other dangers'.361 The third virtue of the Bill was that it closely followed the current working

357 See Note 126.
358 See Note 126.
360 See Note 131.
arrangements which had been set up in Britain in previous years, in the instances of salvarsan and insulin:

Obvious benefit has come [in these cases] from this to the public and to the profession, and the arrangements [had] worked smoothly without any resentment from the manufacturers or any other interests concerned. The Manufacturers, indeed, have warmly welcomed the control for which accident alone in these two cases has given opportunity.\textsuperscript{362}

Fourth, the Bill would bring Britain up to date with civilised countries. Finally, if Britain did not introduce legislation for official standards, it would find its pharmaceutical products being excluded from the international market in the very near future:

The question may shortly have new and urgent importance for them in view of a proposed international convention under which many countries will prohibit the importation of therapeutic substances which are not subject to official control in the country of origin. It will be humiliating indeed if other countries exclude British products on the ground that Great Britain, unlike other civilised countries, has no effective control over standards of value for these important and dangerous substances.\textsuperscript{363}

The Bill was passed through this session of the Parliament and became the Therapeutic Substances Act in 1925. A number of factors were crucial in assuring its passage.

Fletcher's petition to Balfour in 1925 and Brock earlier influenced the parliamentary debate. One by one members who stood in favour of the bill cited the insulin success story and the fatal pituitary extract case. Some added the salvarsan crisis to their list, others substituted the pituitary case of salvarsan, but insulin was always there. As for the terms of the debate. Members' primary concerns were about whether the list of drugs included in the bill was comprehensive and whether foreign drugs subject to other standards subject to other standards would be allowed into the country. They seemed to be pacified by ministerial assurances that certain drugs could be added to the list should the need arise in the future, and the MRC, rather than the bureaucrats at Customs and Excise, would determine whether drugs from foreign countries subject to other standardising procedures would be

\textsuperscript{362} See Note 131.

\textsuperscript{363} See Note 131.
subject to MRC standardising criteria. What is striking is the way in which parliamentarians understood standard setting. Parliamentarians connected the terms 'standardisation', or 'standardising', with other national concerns, this giving them multiple meanings. The point here is that these meanings and connections suggest that use of this term may have given Fletcher's calls for biological 'standards' wider meaning. It may also have given parliamentarians and government officials the impression that it seemed directly relevant given that the term was in common parlance at the time. This fluidity of meanings of 'standardising', which Fletcher complained about as a conflation of meanings, may have helped to make biological standardising of therapeutic agenda seem apolitical, and may thus have assisted in the eventual passage of the Therapeutic Substances Act in 1925. For, even those with reservations about the Bill in particular, or legislation to control therapeutic substances in general, praised its aims to standardise. The Medical Press, for instance, in a critical article registering various objections to the Bill, said:

first let it be again conceded that [the Bill] has one redeeming feature. It aims at standardising the various substances mentioned. This is not likely to meet with opposition and there is no harm in it.

Similarly with the famous *Times* response. The disagreement was not with standardising drugs in principle, but with Dr Addison's attempts to control therapeutic standards with the taxpayer’s money at a time when national priorities should have directed elsewhere. Thus, although Fletcher gave focus to the meaning of 'standards' and urgency of legislation on the matter, this fluidity, which he saw as a frustrating conflation of meanings of 'standards' and 'standardising', may have assisted in the passage of the Bill by giving it a wider cultural meaning.

**To Summarise:** Fletcher, in his part as the civil servant gave medical research a civilising agenda and a moral purpose. He tried to create an ideal of medical research by invoking a rhetoric of character to shape that research, and by employing medical research to address

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364 PRO: FD1/999, Fletcher to Robinson, 16/10/23.
366 See Note 137.
practical concerns of his day. Fletcher did this to invent a tradition for the MRC as a unique department of the state which successfully protected the public's interest through medical research. In the context of public concern about standards, Fletcher indexed medical research to standard setting after the war. Fletcher's biological standardisation initiatives included therapeutic standard setting featured in this general scheme. The practical value of therapeutic standard setting was demonstrated through therapeutic trials of insulin which were part of the highly publicised biological standardisation of that drug. This public event was used to assist the passage of the Therapeutic Substances Act which gave the MRC more secure authority to set biological standards, a step that amounted to state legitimation of a system of therapeutic trials of certain drugs. I now turn to how Fletcher and Dale made the introduction of insulin a public event.
The introduction of insulin into Britain was something Henry Dale did not forget. In May 1966, an interview with Dale about his role in the 'exciting history of insulin', decades after biological standardisation had been firmly established as a laboratory-based discipline, the 91 year old Dale focused on two details. First, he spoke about his role in recognising 'the discovery to be genuine', and second, he remembered his part in making a dry international insulin standard. Dale described the events of the 1923 conference which led to the dry insulin crystals he and Harold Dudley had made at the National Institute for Medical Research (NIMR) in Britain being established as the international standard. Dale recounted the following:

Towards about 4 pm it became obvious that everybody was tired, and in despair of any agreement [about how the standard unit of insulin should be defined] ... and ready to adjourn sine die, unless something further could be done... The time was thus ripe for me to make my positive intervention. Madsen [head of the States Serum Institute in Copenhagen] and I had both, to different degrees, been temporarily pupils of Paul Ehrlich ... I could therefore quote with some effect Ehrlich's authority ... that the only safe basis for the definition of insulin, or of any other potent remedy, would be in terms of a precise weight of a standard, stable sample of the remedy in question, in the form of a completely dry powder, which could be preserved and distributed with all necessary precautions...MacLeod replied to this proposal in a manner which played directly into my hands. 'I should entirely agree with you in theory, Dale', he said, 'but I am bound to regard your suggestion as impracticable for the reason that it has so far not been possible, and that I doubt whether it will ever become possible to prepare a standard for insulin in the form of a dry, stable solid.' I was accordingly able to take a little sealed tube out of my waistcoat pocket and roll it across the table to Macleod, and just say, 'There it is.'

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367 The quotation is from the opening line of the article which transcribes the interview with Dale. See Murnaghan and Talalay (1992), 440.

368 See Note 1.

Henry Hallett Dale (1875-1968) was one of Fletcher's 'noble scientists'. He was a Trinity man who had come up in 1894 (three years after Fletcher), read Physiology and Zoology and he was a contemporary of Fletcher's at Trinity, in that they were both members of the Cambridge University Natural Science Club (a group of specially elected scientifically-minded students who met weekly during term-time and read each others' papers), but they were not close friends at Cambridge. Although Dale also went on to qualify as a physician at St Bartholomew's Hospital directly after completing his Natural Science degree at Cambridge, the two men had very different career paths before ending up at the MRC. The same Coutts-Trotter studentship that led Fletcher to believe he could have a career in science, led Dale to think that he could not continue in scientific research. He went to Barts' reluctantly, hoping for an opportunity to do research and missing the Cambridge College he had left behind. Still wanting to research in physiology after receiving his medical degree in 1902, he pursued this independently in the physiology laboratories of J. N. Langley, E. H. Starling and Paul Ehrlich (see Chapter 2) before being offered a post as a pharmacologist at the Wellcome Physiological Research Laboratories (WPRL) in 1904. Dale took the job because he thought it would offer him the freedom to do his own research. And it did. Some of the research he conducted there led to him winning a Nobel Prize (in 1936), but the company also employed Dale to use his science to improve the quality of their drugs, and crucially, to standardise these products. Drug standardisation and quality control was one of his primary responsibilities at the WPRL. So when Dale was recruited as a permanent member of the Medical Research Committee in 1913, around the same time as Fletcher, he brought experience in drug standardisation, and an ability to produce and recognise drugs with therapeutic effects. In short, Dale could recognise a genuinely effective drug, and a genuine therapeutic effect.

I began by noting that Dale's ability to recognise authenticity made him proud of his involvement in the insulin affair. His story about producing the insulin crystals from his pocket shows that he was also proud of how he had produced a dry standard. While Dale was reaping the benefit of months of research to produce a dry insulin standard for international approval at

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that international conference, the MRC was introducing insulin into Britain. The details of the conference, how it came to be called, and the definition of the Toronto Unit which Dale's standard replaced are not important for the moment; these matters will be discussed later on in this chapter. What is significant here is that Dale represented the MRC and Britain in this international context, and that he claimed his association with authoritative figures to assert the value of the standard he had made at the MRC. He produced the standard crystals into the public domain from the private pocket of his waistcoat as if it were a single event. Dale's public demonstration helped to make it the international standard in subsequent months. It epitomises the way in which he and Fletcher framed the long-term introduction of insulin to Britain between 1922 and 1924 as a single public event. How this was done, how the introduction of insulin was used to enhance the reputation of the MRC, and how MRC officials recruited arguments for conducting insulin trials in the clinic are the subjects of this chapter.

I. Controlling public knowledge about the insulin trials

Insulin was discovered in Professor John Macleod's laboratory at the University of Toronto by Macleod, Frederick Banting, Charles Best, and James Collip, between 1921 and 1922.\(^\text{371}\) At the time, diabetes (generally viewed as a deficiency of the internal secretion of the pancreas which resulted in the body's inability to assimilate food) was treated by various starvation diets.\(^\text{372}\) Insulin appeared to be a miracle cure that would save diabetics from death by starvation, from coma, and from secondary infections. The MRC brought insulin to Britain, releasing details of the steps it had taken to manage the commercial manufacture, laboratory research and clinical trials of the drug to The Times (and other national papers such as The Daily Telegraph), regional papers (like The Morning Post, The Manchester Guardian, The

\(^{371}\) An account of the discovery of insulin can be found in Bliss (1983) and (1993).

\(^{372}\) See Bliss (1983); Allen (1916); Allen, Stillman and Fitz (1919). There were also a number of patent medicines and idiosyncratic diets that were promoted as 'cures' for the disease or comfort to the patient. The animal diet of the Edinburgh physician, John Rollo, was famous amongst these. Rollo's diet included items such as 'fat and rancid old meats' which were designed to make the patient reduce his calorific intake. See Diabetes, (1956) 5: 325-7.
In November 1922, Fletcher informed the newspapers that the University of Toronto had offered the MRC a gift of the British patent rights to control the preparation of insulin. The press was also told that Drs. Henry Dale and Harold Dudley (representing the MRC) had visited Canada and America to examine the claims being made about the efficacy of insulin, and that on the advice of these eminent scientists, the MRC had accepted the patent rights for Britain. That same November, The Times announced that the MRC would be unable to protect the public without testing the potency of each sample, prior to its actual use for a patient in the hospital ward, and that these tests required a well-equipped physiological and biochemical laboratory. In February 1923, several progress reports later, Fletcher informed The Times that 'insulin was being used to treat diabetic patients selected for the purpose of research at St Bartholomew's Hospital, Guy's Hospital, St Thomas', The London, and University College Hospital, the University Department of Pharmacology and Physiology, and the Royal Infirmary in Edinburgh. Finally, in April of that year, the national papers informed the general public that the MRC had released insulin onto the market, and that the drug was available from The British Drug Houses Limited, Allen and Hanbury's Limited, and the Wellcome Pharmaceutical Company, at a fixed price of 2s 6d per dose to hospital doctors and general practitioners who could make accurate blood-sugar measurements.

373 PRO: FD1/902, D. Williams to W. Fletcher, 28/8/22; PRO: FD1/902, Fletcher to Williams, 30/8/22; and Liebenau (1989), 167; Bliss (1983). The Times alone published some forty articles about insulin between October 1922 and the passage of the 1925 Therapeutic Substances Act. The drug was discussed within a number of spheres in Britain, as was evident in the regional papers. I am grateful to Robert Tattersall for drawing my attention to newspaper articles from Nottingham. See Nottingham Evening Post, 20/4/23 and 15/5/23; The Scotsman 7/11/22; The Glasgow Herald, 17/11/22; The Yorkshire Post, 17/11/22.


377 ‘The supply of insulin: new diabetic cure in use at hospitals’, The Times, 21/2/23. Glasgow was later added to this list. See Liebenau (1989).
The MRC raised its prestige by framing the introduction of insulin to Britain as a national event. By claiming to manage the affair for the public good in its reports to the press, Fletcher sought to promote the moral value of this national institution. It also made these clinical trials possible at a practical level. For instance, Fletcher was able to convince slaughterhouses in London to donate pancreases (one of the primary sources of insulin) to the operation. The London Metropolitan Cattle Market Committee placed a room at the MRC’s disposal. It was to be used for ‘collecting and preliminary treatment of pancreatic material from freshly killed oxen to be used in the treatment of hospital patients suffering from diabetes’.

These bodies said that they were making these donations ‘in view of the importance to the public work’ the MRC was carrying out in this area. The government's Commissioners of Custom and Exercise also exempted specially denatured alcohol (another important ingredient) from duty.

Newspapers were not the only means of shaping public opinion. Inter-war Britons visited fairs and exhibitions of the products of modern science in droves. So, when the Burroughs Wellcome Pharmaceutical Company asked Fletcher for permission to ‘make a small exhibit of ‘just a few grammes [of insulin] in a suitable container’ at the British Industries Fair, Fletcher reflected on how this might affect the public perception of both insulin and the MRC.


380 PRO: FD1/902, Fletcher to the Towns Clerk Market Committee, 21/11/22; Cattle Market Clerk to Fletcher, 21/11/22.

381 PRO: FD1/902, Fletcher to the Towns Clerk Market Committee, 21/11/22; Cattle Market Clerk to Fletcher, 21/11/22.

382 PRO: FD1/902, Fletcher to the Towns Clerk Market Committee, 21/11/22; Cattle Market Clerk to Fletcher, 21/11/22.

383 PRO: FD1/919, Burroughs Wellcome Pharmaceutical Company to Fletcher, 5/2/23.
The fair was to be held at White City in Shepherd's Bush between 19 February and 2 March 1923, and members of the Association of British Chemical Manufacturers were preparing exhibits to 'indicate the progress of the chemical industry in this country'. Participating in it would generate sales for pharmaceutical companies. It would also set them apart from proprietary medicine manufacturers (the significance of which has been discussed in Part I). Furthermore, in 1923, after the Salvarsan crisis of the Great War exposed the weakness of the British pharmaceutical industry, exhibiting therapeutic successes of insulin would have made a powerful national statement. In the words of the representative of Burroughs Wellcome Pharmaceutical Company, making an exhibit of insulin:

could create much interest as the new therapeutic substance and would serve the very useful purpose of indicating that its production on a commercial scale is in progress. We would of course make it clear that it is not at present available for issue, but we are making every effort to produce it in sufficient quantities as soon as possible.

Fletcher refused to allow it, arguing that 'it would be against the public interest for such a public exhibition to be held until the manufacturer has sufficiently advanced to provide a supply with some guarantee as to efficiency, sterility and regularity.'

Here, in his response to the Burroughs Wellcome Company, as in his press releases, Fletcher implied that the MRC's goal was to accelerate the proper production of insulin while dutifully safeguarding 'the public'. 'The public', the MRC kept referring to in this case was 'the diabetic'. Moreover, the particular interests of diabetics were taken to represent the general interests of the lay consumer because for Fletcher, the average layman was a consumer above all else. He was a consumer because he took drugs. He was also a consumer because he purchased them. These were the arguments Fletcher was using to convince parliamentarians to

384 PRO: FD1/919, Burroughs Wellcome Pharmaceutical Company to Fletcher, 5/2/23.
386 PRO: FD1/919, Burroughs Wellcome Pharmaceutical Company to Fletcher, 5/2/23.
387 PRO: FD1/919, MRC to the Burroughs Wellcome Pharmaceutical Company, 7/2/23.
regulate therapeutic standards by law while he and Dale were engaged in the insulin affair. The same arguments also applied to the specific case of insulin, so that standardising the price of insulin was as important as producing a fixed, immutable solid crystal in the laboratory for defining a standard commodity for the purposes of fair trade.

One of Fletcher's main arguments for the virtue of a law regulating standards of therapeutic substances was that it would create the conditions for fair dealing. I demonstrated this in Chapter 3 where I showed how Fletcher placed the weight of his arguments for bringing therapeutics in line with other consumer commodities such as tea, coffee, and so forth, on fair dealing. Certainly, the mood with regard to consumer rights in England during the inter-war years was best summarised by the phrase: bargainer beware. Consumers were unlikely to obtain legal compensation for sub-standard commodities they had purchased.389 When the MRC disclosed the details of the price restrictions it had imposed on commercial companies in this now special case of insulin, and when it published the instructions issued to doctors on how to use the drug carefully and economically, it provided the bargaining public with invaluable facts about the contents, nature and application of this commodity in the interest of fair dealing.390

MRC press releases presented insulin testing as both a natural and necessary part of public protection. Although the testimonies of the efficacy of the drug labelled it as being effective, MRC officials implied that insulin could only be safely administered to helpless lay people with diabetes by the scientific physicians working for that state body. Marketing the drug in this way was successful in the sense that the MRC was not criticised because it was testing a drug it claimed was still in the experimental stages on innocent patients. Instead the MRC was accused of over-regulating the introduction of this efficacious drug into the public domain. But Fletcher turned this situation on its head. He used the fact that the MRC had

389 The 1932 legal case of Donaghue versus Stevenson has become a classic case which demonstrates this point. Farrar and Dugdale (1990), 116-119.

390 'Insulin. Conditions of its distribution', The Times, 20/4/23, p. 16. The MRC noted that additional supplies from the American firm, Eli Lilly and Co. would be used to supplement the insulin supplies of those British firms already producing the drug, and that the MRC would allow firms to release American insulin in proportion to the volume and of insulin they were already able to produce. See also 'Insulin and diabetes', The Times, 7/6/23, p. 16.
announced and initiated clinical trials of the drug while it was still in its experimental stages to argue that the drug was not being withheld from the public. Nowhere was this more evident than in his response to Mr. Vivian Gabriel, a layman who criticised the MRC in *The Times*, and to Henry H. Armstrong, a fellow of the Royal Society, who complained to the same newspaper about MRC controls.

Henry Armstrong accused the MRC of being a 'scientific bureaucracy'. He contended that this new 'class of a-moral scientific workers' was 'interfering with and checking' the 'progress of discovery and invention by imposing rules', and that their restrictions could not 'be countenanced by public opinion'. Responding to this public attack in private, Fletcher called Armstrong a man who was 'so notorious an ass that it seems almost unsportsman-like to take him seriously'. But, as a Fellow of the Royal Society himself, it would have been unprofessional of Fletcher to attack a member of his fraternity in the public press. Responding to Mr Vivian Gabriel, however, was an entirely different matter.

Gabriel complained in *The Times* of 18 July, 1923 that 'insulin was still not generally procurable', and that many patients had died because of this long delay in releasing the drug to the wider public. He blamed the MRC for this travesty. In particular, Gabriel accused the MRC of suppressing the efforts of a public-spirited London practitioner who had tried to make his own insulin to save diabetic lives. If anyone was a hero in the insulin affair, Gabriel suggested it was Professor Blum of Strasbourg who had been making insulin and selling it privately to English patients.

Dr. Blum had no funds at his disposal ... and he was unaware of the precise formula for insulin, the patent for which was in the hands of the MRC in London; but he worked out his own [formula] and by the end of last year had saved many lives in various parts of England... He has treated a continuous stream of patients from this

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392 PRO: FD1/902, Fletcher to Colonel Mildmay, 28/11/22.

393 Gabriel, V., 'Cost of insulin. Cheaper supplies from Strasbourg', *The Times*, 18/7/23. It seems that Vivian Gabriel was Lieutenant-Colonel Edmund Vivian Gabriel, another colonial soldier living abroad but writing from his London club.
country, and has taught them, after complete restoration of health, to continue the
treatment themselves. 394

Arguing that the MRC had been given the power to restrict the drug from the public because of
the patent they had been given by the University of Toronto, the layman Gabriel asked:

Did Jenner, Lister or Pasteur patent their free gifts to mankind? Did they advance the
bureaucratic argument of our MRC that mistakes might have been made in the
application of the remedy, or that it was necessary to standardise it and to have a
sufficient quantity for every one before allowing some to the public? 395

Fletcher responded to these criticisms and rhetorical questions with a personal letter to the
Editor of *The Times*. In it, he defended the achievements of the MRC's scientific staff
researching into insulin, insisting that MRC regulations were similar to those operating in
Canada and the USA, and that Gabriel was quite wrong about Professor Blum. According to
Fletcher, Blum had visited the USA and Canada the previous summer, just as MRC
representatives (Dale and Dudley) had, and his progress had paralleled that of the MRC. He
also suggested that Blum's insulin was inferior to that of the MRC, having been made 'without
the same control of sterility'. Taking the moral high ground, Fletcher told the public that unlike
Blum, who had effectively been making insulin for personal use, 'the MRC had responsibilities
not only to one clinic but to the whole country'. It was because the MRC had taken its national
responsibilities seriously, that it had arranged laboratory experiments and *clinical trials* at
several centres simultaneously.

During the months preceding the successful large scale manufacture which began in
April insulin was produced on a laboratory scale in 9 different labs in England and
Scotland under arrangements of the Council. Of these 8 served hospital wards, where
patients received the treatment and where the necessary studies were made to guard the
knowledge of the profession towards its most effective use. 396

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394 Gabriel, V., 'Cost of insulin. Cheaper supplies from Strasbourg', *The Times*, 18/7/23.

395 See Note 27.

396 Fletcher, W., 'Large supplies in Great Britain' (letter to The Editor), *The Times*, 19/7/23, p. 8.
Fletcher branded Gabriel's utterances as 'almost shameful'. 'Instead of honouring the high skill which British men of Science have brought to the solution of these problems and the energy with which the manufacturers have done their work', this layman made unpatriotic allegations against the MRC. At the same time, he told the public that not only was British-made insulin being used on the continent and in the Dominions, there was 'probably no laboratory or factory in the world now engaged in making insulin which has no reason to be indebted to the results of scientific work in England.' In short, Britain had set the standard for the rest of the world.

Between October 1922 and early 1925, the MRC managed to reframe the initial public statement of insulin as a single miracle cure for diabetes, as a statement of a different kind of public event: namely, that insulin was a treatment which needed to be standardised and carefully controlled by the MRC in order for it to become public property. Fletcher wanted the property the MRC had defined to be associated with safety and standards. He was promoting this as a moral virtue of the MRC’s standardising agendas. Like Dale's dramatic presentation of the crystals that he had made in private (from his waistcoat pocket) in the public domain of an international conference, and his later tale of it as an act that settled the crisis, the MRC’s virtue had to be publicly performed for it to be moral. This publicly performed moral act was a vector for launching the MRC’s moral role of standardising insulin in particular, and standardisation in general within the state. However, in this section, by pointing to ways in which this state body released public facts in increments, I show that standardising insulin was not a single event. I shall now demonstrate how these incremental steps translated into a management system behind the scenes. I shall show how insulin became more than a single drug. Indeed, it became a management system through which social contracts were agreed with certain scientific physicians to further the MRC’s research agenda. It also became the management system through which moral control was exerted on the pharmaceutical industry, which wanted the chance to mass produce and sell this successful drug, and the patients who

397 See Note 27.
398 See Note 27.
wanted the new life this 'wonder drug' promised. It was through these forms of moral control and negotiated social contracts that fair trading acquired meaning.

II. Management and moral control: the making of standard insulin

The MRC claimed insulin by virtue of its patent over the drug. MRC officials adopted a nationalistic tone, especially when they spoke about this claim to the newspapers. In reality British insulin was made by viewing North American evidence, and with the benefit of American experiences of making and testing the drug. Dale and Dudley visited Macleod's laboratory and the Eli Lilly Company. Historical accounts of the discovery of insulin and its introduction into medical practice in Britain tend to focus on these two ports of call. But the pair travelled all over America to examine evidence of insulin's efficacy, and to observe the conduct of clinical trials of the drug and various 'commercial aspects' of its production all over North America. They watched Woodyatt's clinical trials at the Otto Sprague Institute in Chicago, saw Drs Geyelin, Harrap and Loab conducting insulin trials in Dr Palmer's clinic at the Presbyterian Hospital in New York City, and observed insulin trials in progress at the Johns Hopkins University in Baltimore. Their view of American evidence informed the way they initially produced the drug and steered the MRC's organisation of clinical trials.

MRC officials like Dale sought to avoid alleged American mis-management of making and testing insulin. In so doing they cultivated an internal management ideology, one with a

399 See Bliss (1983), 165-7, 175. For more on this visit to Toronto, see WIHM: CMAC/GC/67/10, note by Henry H. Dale, on the additional documents submitted by C. Best, 29/5/59.

400 Woodyatt had been researching insulin since June 1922. Geyelin, Harrap and Loab, and Joslin had begun in August of that year. See Journal of Metabolic Research, April 1923. This special edition of the journal is devoted to their first experiences with insulin. I am grateful to Robert Tattersall for drawing my attention to this source. For more about the details of the North American clinical trials, see Geyelin, Harrap, Murray and Curvin (1922); Banting, Best, Collip, Campbell, and Fletcher (1922); Banting, Campbell and Fletcher (1923). For more about the clinical trials of Joslin, see Bliss (1983), 150, 156, 160-4. Allen's reaction to insulin and his trials, and the clinical trials of Williams are also discussed in Bliss (1983), 150-64. For more on Sansum, see Bliss (1983), 140-1, 149, 156, 190. The only clinical trials which Dale and Dudley did not observe at first hand were Dr Elliott P. Joslin's trial in Boston, Dr John R. Williams' clinical trials in Rochester, Dr Frederick M. Allen's clinical trials in New Jersey, and Dr W. D. Sansum's trials in California. It is likely that they learned about the progress of these trials from their American colleagues in Philadelphia, Boston, Chicago, New York City and Baltimore. See PRO: FD1/902, H. H. Dale and H. W. Dudley, Report to the Medical Research Council on our visit to Canada and the United States to examine the 'Insulin' treatment of Diabetes, 30/10/22, pp. 2-3.
distinctly British face, and one that was particularly associated with this institution. Dale and Fletcher did this partially by feeding specially treated facts about the British insulin experience to the public through the press, some of which were discussed in Section I of this chapter. In the private quarters of the MRC, Dale and Dudley argued that the American approach to standardising insulin and clinically testing the drug demonstrated the importance of 'prudence in presenting the treatment to the medical profession and the public'.

In Dale's view, it was 'quite clear that a serious error of judgment has been made in [North America] by permitting clinical trials at a very early stage of the investigation.' The problem was not one of 'untoward results'. It was with the 'brilliant promise' of the insulin trials, because insulin had created:

a premature demand for the treatment from an excited public, so that workers, who ought to be devoting their energies to the urgently needed experiments, are obliged to give practically their whole time to the care of patients already under treatment, and to the preparation of the constant supplies [of insulin] which this treatment demands.

Managing the insulin affair the American way (as conceived by Dale) would have made the MRC's 'noble scientists' appear to be little more than general practitioners. Dale, who, like Fletcher, had trained as a doctor but decided not to practise medicine in the interest of pursuing a career in scientific research, would have wanted to avoid this fate. Moreover, Dale told Fletcher that managing the trials by this inefficient American approach was cruel, because once a patient has been put under the treatment, and has experienced the extraordinary pleasure of augmented diet and freedom from symptoms, stoppage or even suspension of treatment, involving relapse into the previous condition of misery and deprivation, inflicts a cruel hardship.

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401 PRO: FD1/902, H. H. Dale and H. W. Dudley, 'Report to the Medical Research Council on our visit to Canada and the United States to examine the 'Insulin' treatment of Diabetes, 30/10/22', pp. 5-6.

402 See Note 34.

403 See Note 34.

404 PRO: FD1/902, H. H. Dale and H. W. Dudley, Report to the Medical Research Council on our visit to Canada and the United States to examine the 'Insulin' treatment of Diabetes, 30/10/22, pp. 5-6.
Fletcher, who had emphasised the MRC's benevolence in feeding facts to the press, believed that Englishmen were particularly moved by accusations of cruelty and pain. 'The Englishman', he reflected:

is in some ways paradoxical. He is characteristically kind-hearted; he hated pain, and if pain were presented to him he desired to help... But the Englishman was not so imaginative as the instructed public of those other nations. If pain was stopped, or at least if it were out of his sight, he forgot it, and did not think so deeply of the importance of preventing it for the future. 405

Fletcher and Dale believed that the MRC could avoid the cruelty of the American trials and run efficient, well-coordinated British insulin trials by a) inviting only a few physicians from reputable and well-equipped hospitals to test insulin on a small select group of patients in the initial stages; b) bringing these men together to MRC headquarters to coordinate these trials; and c) negotiating specific terms under which the drug should be mass produced.

II. 1. Trust and obligation: making the Noble scientists

In Chapter 1, I demonstrated that Fletcher had an organicist picture of the ideal state as one in which the citizen and the citizen's duty to the state were defined in terms of the work he did. Here I argue that Fletcher used the insulin trials to cultivate physicians he trusted to judge the efficacy of medicines in their clinics for the MRC as a part of the new kind of work that he was defining for the MRC. This work, as I showed in Chapter 2, was medical research. As a result, those scientific doctors who were being cultivated to do this work would be enacting a new kind of citizenship. Through their involvement with the MRC, they would be doing moral work for the state. I shall designate these scientific physicians 'noble scientists'. The physicians who were being recruited to test insulin were being asked to do moral work of standard setting. Fletcher defined a contractual relationship with the physician researchers he wanted to cultivate. Through his social contract, defining their work and duties, he made them 'noble scientists'. The way Fletcher negotiated and enforced these social contracts was akin to the

405 Fletcher (1922), 941.
'moral control' he and Dale tried to impose on the pharmaceutical companies manufacturing insulin.

Fletcher invited Professor T. R. Elliott from University College London, Dr Hugh MacLean at St Thomas's Hospital, Professor Francis Fraser from St Bartholomew's, Dr Poulton at Guy's Hospital, Professor Mellanby at Sheffield, Professor Meakins at Edinburgh and later, Professor D. Noel Paton at Glasgow, to conduct clinical trials of the drug. The physicians were expected to give priority to acquiring the 'full-time services of a biochemist to make insulin and carry out blood-glucose and urine glucose analysis'. They were also encouraged to employ an assistant physician to 'deal with the time demands of this research work'. In turn, these physicians and biochemists would 'have the freedom to pursue research on interesting collateral inquiries which presented themselves', and would be able to publish academic papers which might give them professional credit. In their unique positions as physicians testing insulin for the MRC, they would be given access to unpublished information about the nature of the drug and its administration to patients. They would also have access to Henry Dale's expertise in preparing and using insulin and would therefore be better informed than most physicians and scientists in England. Finally, Fletcher assured them that the MRC would arrange for physicians to have raw materials such as free pancreas, some 'ordinary laboratory resources and equipment for their wards and dispensary'.

In return, the Council demanded certain assurances from these physicians. They could only give insulin to 'pedigree' patients they had selected for treatment within their own wards. The physicians were told that it was imperative that demand for insulin should never outweigh the manufacturing capacity of their laboratories. Under no circumstances were these

406 PRO: FD1/910, Fletcher to Elliott, 10/10/22. Letters of this form were sent to all of the other team members trying insulin at other centres.

407 PRO: FD1/910, Fletcher to Elliott, 10/10/22.

408 See Note 40.

409 A small grant of £200 was offered in some cases to defray the cost. PRO: FD1/910, Fletcher to Elliott, 10/10/22.

410 PRO: FD1/910, Fletcher to Elliott, 10/10/22.
physicians to supply insulin to anyone other than the patients they had selected for clinical trials, 'without the express sanction of the Council'. Any requests for insulin, or questions about how to make it, were to be directed to the MRC's head office. Fletcher and Dale would deal with correspondence from the public.

Fletcher adopted a custodial role in these matters. Acting as a spokesman for the MRC’s institutional interests, he suggested that these duties, which were framed as rules, were designed to protect these noble scientists 'from loss of time and energy that might become serious'. He also implied that the justice of these guidelines was embedded in the fact that the Council had both a legal and moral right to make such demands. This social contract protected the 'noble scientists' while promoting their individual professional progress. In Fletcher's scheme, if biochemists and physicians kept the MRC fully informed about their research, 'through immediate private communication without the delay that even prompt publication entails', the individual rights of research workers would be protected. In the event of a dispute over intellectual property, he and Dale would be able to act as independent authorities to 'secure a fair solution' because they possessed all of the facts.

Fletcher and Dale invited physicians and biochemists they knew to try the drug, thereby connecting a network of close colleagues and personal acquaintances as 'experts' whose abilities and integrity they could vouch for. These networks of trust were established by recruiting onto trial teams physicians who were protégés of team leaders, friends (or friend's wives) and close associates of Dale's or Fletcher's. For instance, at Sheffield, Edward Mellanby, Professor of Pharmacology, a friend of Fletcher's and a prominent specialist in nutritional research, selected the physician John Cowan to assist him. Fletcher approved of Cowan, who had also been recommended by his friends T. R. Elliott and D. Noel Paton as 'a

411 See Note 43.
412 See Note 43.
413 See Note 43, p. 3.
414 See Note 43, p. 3.
good clinical man for the job. Similarly, Professor J. B. Leathes, who was to work with Mellanby, engaged a medical graduate of Sheffield University, Dr Margaret Pratt, to help him make insulin because she was a former student of his, and 'the wife of one of the demonstrators in pathology'. Leathes vouched for her to Fletcher. He said 'she was one of my students formerly, and I know her work to be good'. Similarly, the young assistant physician, Dr D. Murray Lyon, found his way onto Jonathan Meakins' team in Edinburgh because, as Meakins wrote to Fletcher, he 'has been doing very good work with me since I came on a number of clinical problems'. On this same Edinburgh team, Dr Lambie, who 'had been working for many years with Professor Cushney's laboratory', was asked to address the pharmacological and physiological side of the question and standardisation.

Indeed, trustworthiness and commitment to the research agenda were more important qualifications for belonging to the trial teams than clinical expertise in treating diabetes. This was particularly evident in the establishment of the team at St Bartholomew's. Professor F. Fraser, the recently appointed assistant director of the Clinical Medical Unit, wanted to recruit George Graham and John Trevan for his trials. Graham was a physician with a long-standing interest and a reputation in diabetic therapy. Graham ran a private practice while working with Fraser on the newly established unit. So Fraser applied to Fletcher for extra funds to compensate him for the income he would lose if he joined the trial team at Bart's. Fletcher agreed to pay Graham a salary of £200 in this special case. But he demanded

415 PRO: FD1/902, D. Noel Paton to Elliott, 19/12/22; PRO: FD1/902, Elliott to Fletcher, 21/12/22; PRO: FD1/914, Fletcher to Mellanby, 15/12/22.

416 PRO: FD1/914, Leathes to Fletcher, 17/1/23.

417 PRO: FD/1/1015, Meakins to Fletcher, 25/7/22; PRO: FD/1/913, Meakins to Fletcher, 15/11/22.

418 Francis Fraser, later Sir Francis, had been appointed as director of the new unit in 1920. Fraser (1885-1964) was already becoming a reputable clinician at St Bartholomew's, and was seen as a distinguished physician at the time. For biographical details, see obituaries in BMJ (1965), 2: 449-52; BMJ (1964), 2: 950-1, 1015; Journal of Path Bact. (1965), 9: 701-11; Lancet (1964), 2: 867-8; The Times, 8/10/64.

419 Graham (1882-1971) had worked on the protein-sparing action of carbohydrates in Munich between 1912-1914 and was known for his discovery of the principles of under-nutrition (in 1915) which had guided his treatment of diabetes since then. In 1920 he was employed in Fraser's new unit at Barts. See Obituaries: Munks Roll, vol. 4, p. 205-6, BMJ (1971), 4: 563; and Graham, G., 'The Goulstonian Lectures on glycaemia and glucosuria', The Lancet (1921), 1: 1003-7.
additional confirmation from Fraser that: 'Dr Graham will not, without previous reference to
the Council make use of insulin products obtained in (Fraser's) unit for any purposes whatever
outside the experimental treatment within the Unit.' I propose that Graham's promise to be
faithful in this regard was an important reason for him being invited onto this MRC team. This
was evident in Fraser's attempt to buy a second expert, John W. Trevan. While this full-time
pharmacologist at the Wellcome Physiological Research Laboratories was a close colleague of
Henry Dale's, Fletcher would not agree to have Trevan 'help prepare insulin'. Fletcher told
Fraser that Dale and Dudley would handle the work of standardisation. Apart from being too
expensive (on a salary of £1000 per annum), Trevan would have had a divided loyalty to the
MRC's standardisation program since he was still working at the WPRL. In short, Trevan's
personal and commercial interests with the pharmaceutical company Burroughs Wellcome
made Dale and Dudley more trustworthy allies in the standardising agenda involved in the
trials.

It was precisely these personal connections between Fletcher and his noble scientists
that allowed Fletcher's impersonal written contract to become a powerful instrument with
which to make these physicians feel obliged to uphold MRC rules. The full extent of these
obligations only emerged when Fletcher believed that the trial physicians were not living up to
their end of the bargain. He expected the physicians to borrow laboratory equipment, to 'ginger
up' maintenance men, and to grease the administrative wheels at their local centres, if

PRO: FD1/912, Fletcher to Fraser, 16/12/22.

Letter from Fraser to Fletcher, 16/11/22. John W. Trevan (1887-1956) was an physiologist and
pharmacologist who had begun his medical career at St Bartholomew's.

As a compromise Fletcher agreed to an additional sum of £300 for Graham to spend on a trained
assistant (Mr. Harris) who performed blood-sugar analysis and a laboratory attendant (Mr. Woodhill)
who measured the respiratory quotients. There seems to have been another attendant of unknown
identity who was engaged in the preparation of insulin. See PRO: FD1/902, W. Fletcher, 'Insulin
treatment of diabetes'. Minutes of the Insulin Committee meeting, 5/12/22. Trevan was receiving
£1000 per annum at the WPRL. PRO: FD1/912, Fletcher to Fraser, 16/11/22. From 1914 to 1920
Trevan worked as a demonstrator of physiology, and in 1920, he was appointed pharmacologist of the
WPRL. See J. H. Gaddam (1957), 'John W. Trevan', Biographical Memoirs of the Fellows of the
Royal Society, 3: 274. The experimenters were also instructed to reduce 'the cost as far as possible by
employing apparatus which you may be able to borrow for instance from your hospital or from
associated departments'. PRO: FD1/912, Fletcher to Fraser, 19/12/22. See also PRO: FD1/912, cover
letter of insulin report, Fraser to Fletcher, 29/3/23.
necessary, to get the trials going. Some physicians (leading trial teams) understood this without it being stated formerly. When they reported to Fletcher, they marked the progress of their insulin trials with details of how they had been 'borrowing as much as possible'. One physician even noted that he had arranged to recover alcohol from a hospital dispenser to make insulin. Fraser told Fletcher that he had borrowed a 'sausage-grinder' to mince the pancreas for the insulin in his laboratory. Borrowing a 'sausage-grinder' was no different to inviting a good physician or laboratory attendant onto a trial team, so a physician like Fraser, who seems to have understood MRC demands to extend beyond formal limits, spoke of borrowed goods and clinical expertise with the same breath.\textsuperscript{423} Professors Miller and Morris at the London Hospital seem not to have appreciated these ways.

Like the other professors, Miller and Morris had agreed to conduct clinical trials in November, but in March their insulin trials were still not underway. While Fletcher acknowledged that the slaughter-men's strike in London had delayed the proceedings, he found it inexcusable that they had still not finished building the temporary laboratory they needed for their trials (in March).\textsuperscript{424} He complained to Morris, perhaps expecting an apology and a promise that the trials would begin shortly afterwards. But when Morris suggested that they had not been 'entirely idle' at the London Hospital, Fletcher dispatched an angry response:

I know you have had difficulties but the London Hospital never allowed difficulties to triumph. I understand your contractor was very slow over the temporary laboratory and was not ginned up soon enough. You say ... that meanwhile we have not been idle, because Marrack is already doing standardising tests. You can't bluff me that way. Marrack is doing tests at your suggestion for one of the manufacturing firms, which are paying for them. The fact is that a manufacturing firm starting with our information a week or two behind your unit, have not only solved the special problems of large scale manufacture and made special machinery, but are already producing good stuff ... before the Unit has managed to make any at all even on the small scale. The fact you quote about Marrack is not a feather in your cap, but a measure of your own backwardness.\textsuperscript{425}

\textsuperscript{423} PRO: FD1/912, Fraser to Fletcher, 3/1/23.

\textsuperscript{424} PRO: FD1/917, Fletcher to Sidney, 2/3/23.

\textsuperscript{425} PRO: FD1/917, Fletcher to Morris, 8/3/23.
Morris, clearly embarrassed at being caught out in this way, wrote back saying: 'What thumps! I ached all over since I have read your letter.' Fletcher visited the London Hospital on 9 March, soon after these communications, and the trials at the London were in progress by the end of that month.

When Fletcher and Dale defined the terms for testing insulin they were also identifying the appropriate behaviour for a noble scientist. It was acceptable to seek professional credit from academic articles. Making financial profits from trials was discouraged. But physicians certainly did reap commercial benefits because (or at least in part, because) they were involved in the MRC's clinical trials. One physician, Hugh MacLean, who headed the team at St Thomas' Hospital, was able to convince Sumner and Company to market a kit he designed for measuring the blood sugar of diabetic patients after his involvement in clinical trials. MacLean argued that the attraction of this kit was that 'any medical man' with the 'minimum of medical knowledge', minimum laboratory equipment, and 'a little time at his disposal' would be able to make the necessary blood-glucose measurements. E. P. Poulton, trying insulin at Guy's Hospital, produced a book for diabetic recipes, a book that he sold to the public after clinically testing insulin for the MRC. Furthermore, physicians whose outside interests (commercial or otherwise) prevented them from meeting MRC terms of employment, were not included within this trial system, regardless of their status or suitability in other respects. Fletcher's approach to a request from Duff House to test insulin on their in-patients provides a striking example of the creative ways in which he promoted himself and his noble scientists as disinterested and therefore fair-dealing parties acting in a wider national interest, while keeping elite expert physicians on side.

Duff House was a private sanatorium in North Wales. Opened in 1916, the sanatorium specialised in patients with disorders requiring chemical investigations and dietetic treatment. A number of these patients were diabetics. Dr. Edward Spriggs was the senior

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426 PRO: FD1/917, Morris to Fletcher, 9/3/23.

427 H. MacLean (1922). The method is described in this monograph. See advertisement for kit in Medical Annual 1924. A book of these recipes was published by J. A. Churchill around 1924. Although this book is mentioned in W. W. Payne, 'Insulin treatment of diabetes mellitus', Guy's Hospital Reports, 1924, 308-28, see p. 310. However, I have not been able to locate a copy of it.
physician at the House. Spriggs, previously assistant physician at St. George's Hospital, was a respected elite physician, not unlike those Fletcher had invited to test insulin. He also had special expertise in treating diabetic patients. So when Spriggs wrote to Fletcher asking if he could try insulin at the House as a part of the MRC's clinical trials, Spriggs reassured Fletcher that he had the facilities, clinical materials and expertise to make and clinically test insulin on the premises. More specifically, he told Fletcher:

We have arrangements here for the daily accurate dieting of a considerable number of people, and the necessary scientific staff for the laboratory control of cases of diabetes. I can undertake that the administration of Insulin would be controlled carefully and suitable records made.\footnote{429}

Spriggs certainly could not be refused insulin on the grounds that his critical judgement was untrustworthy, or that his laboratory facilities for preparing insulin, or his hospital facilities for treating patients, were not up to scratch.\footnote{430} In Fletcher's own words:

If a supply of active extract were now available, you may be sure we should realise that there are few places which could compete with your establishment for the purposes of obtaining accurate records of the results of administration.\footnote{431}

But before taking Spriggs' application any further, Fletcher interrogated him on a number of points. Fletcher asked:

\begin{quote}
I understand that you are a whole-time salaried officer at Duff House. Would it be true to say that you have no personal interest whatever in the financial success of Duff House, except in so far as it might affect your security of tenure? Patients at Duff House, unlike those at other hospitals where the Council may get research work in this subject done, pay for their treatment. Am I right in thinking that these payments could easily be made to cover the cost of the laboratory work and other expenses necessary for making preparations of Insulin under licence from us, within Duff House?\footnote{432}
\end{quote}

\footnote{428} Edward Spriggs (later Sir Edward Spriggs) became assistant physician at St George's in 1903, but his career was interrupted in 1910 when he developed pleurisy. See Munks Roll, vol. 4, pp. 468-9.

\footnote{429} PRO: FD1/916, Spriggs to Fletcher, 7/11/22.

\footnote{430} See Note 63.

\footnote{431} PRO: FD1/916, Fletcher to Spriggs, 11/11/22.

\footnote{432} PRO: FD1/916, Fletcher to Spriggs, 11/11/22.
Spriggs assured Fletcher 'in confidence',\(^{433}\) that Duff House was run 'to help doctors and medicine', that it was 'conducted as a consulting physicians' practice should be conducted' and, that because patients paid fees which he admitted 'were naturally high', the hospital would be able to afford to prepare insulin.\(^{434}\) He insisted that Duff House was *not*, however, a commercial outfit and that the institution rested on the broad basis of the approval of the medical profession rather than to make money. 'No one', Spriggs remarked, 'has made a fortune here'.\(^{435}\)

Despite this defense, Spriggs was forced to admit to having personal interests in Duff House.

It is not true that I have no personal interest in the financial success of Duff House because I am one of the Directors of the Company and that involves by law being a shareholder. When I accepted this post, I made a Directorship a condition with the knowledge and concurrence of the then President of the College of Physicians, on the ground that if a physician is working for a Limited Company and is not a Director he is unable to exercise effective control over the policy of the Company. The advantage of such a controlling influence being exerted by men having a knowledge of what professional standards should be is great.\(^{436}\)

After gathering these facts about the case, Fletcher decided that, although Duff House had the facilities for testing and standardising insulin on animals and patients, they would not be allowed to try insulin for the MRC.\(^ {437}\) As director of Duff House, Spriggs might have been able to influence the conduct of their trials, but he would have other interests of the House (and its

\(^{433}\) See Note 66.

\(^{434}\) PRO: FD1/916, Spriggs to Fletcher, 14/11/22. According to Spriggs, the patients at Duff House were all charged the same rate for the reasons that 1) the patient knows what he has to pay; and 2) the doctors are free to make or repeat any investigations they think necessary without involving the patient in extra expenses.

\(^{435}\) *We do not stint any reasonable expenses for the treatment or comfort of the patients, and the fees, which are naturally high, are fixed by the Auditors from year to year according to the expenses.* PRO: FD1/916, Spriggs to Fletcher, 14/11/22.

\(^{436}\) PRO: FD1/916, Spriggs to Fletcher, 14/11/22.

\(^{437}\) PRO: FD1/916, Fletcher to the Under-Secretary of State, Home Office, 26/1/23.
patients) to consider. In short, Spriggs would not have ultimate control over how the trials there were run and there might be occasions in which Spriggs' decisions were overturned by the other directors.

Since including Duff House in these MRC insulin trials would mean relinquishing control over the clinical testing and insulin standardisation, Fletcher decided to arrange for Spriggs to make a separate application for a laboratory license for Duff House. This would allow Spriggs to have a laboratory for making insulin, for standardising it on laboratory animals and testing the home-made product on patients at Duff House. Fletcher wrote to the Under-Secretary of State at the Home Office on Spriggs' behalf, arguing that it was in the 'public interest' to allow Spriggs' parallel research on patients 'drawn from classes of the community different from those represented at [the MRC] centres of research', in other words, aristocratic patients. These separate trials, on a better class of patients, would enrich the MRC's research which drew patients from the masses for study.

II. 2. 'Moral control' over manufacturers in the making of standard insulin

When Dale began making the arrangements for the commercial management of insulin in 1922, he had just returned from his American tour with Dudley, and he was still dealing with the aftermath of the salvarsan crisis. In addition, Dale and Fletcher were campaigning

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Spriggs' attitude towards diabetes and diabetic patients, and the way he aimed to deal with them at the Duff Hospital, are in many ways reflected in his article on educating the patient. Here he talked about how he had decidedly introduced a course of instruction including a class by the diet sister and in the laboratory, urine testing, and argued that every hospital should have something similar for both in- and out-patients with diabetes because the benefits would far outweigh the expense. See E. I. Spriggs, 'The education of the patient', The Lancet (1921), 2: 959-60.

PRO: FD1/916, Fletcher to the Under-Secretary of State, Home Office, 26/1/23.

PRO: FD1/902, H. H. Dale and H. W. Dudley, 'Report to the Medical Research Council on our visit to Canada and the United States to examine the 'Insulin' treatment of Diabetes', 30/10/22, p. 9. In particular, Dale put it to the MRC that 'if the affair was handled firmly and wisely, and with an obvious desire to help and not merely restrict manufacture', the manufacturers would 'submit to control' in the same way they had done in the case of Salvarsan products. Manufacturing companies such as Burroughs Wellcome also had the case of Salvarsan in mind when they were defining their relationship with the Medical Research Council. When the MRC suggested that the arrangements should involve setting a 'maximum selling price', representatives of the Wellcome Company argued that since 'the principle of a fixed selling price' had been adopted in the new licences for salvarsan and neosalvarsan, it should also be applied to insulin manufacture. See PRO: FD1/902, Messrs
vigorously for the Therapeutic Substances Act (to regulate the biological standardisation of medicines) to be passed. Insulin was a gift. To be sure, Dale and Fletcher intended to use these experimental trials to strengthen their arguments to parliamentarians for legal control of biological standardisation through the Therapeutic Substances Act (Chapter 3). In his report to the MRC, Dale stressed that the situation with insulin gave:

an added urgency to the long contemplated legislation, on the lines of the report (about state control of 'Biological Standardisation') to the Ministry of Health by the MacKenzie Chalmers Committee. With the powers that such an Act would give, preparations purporting to contain the active hormone of the pancreas would be simply scheduled for control.  

Regardless of their struggle to make this bill law, Fletcher and Dale were convinced that moral control over therapeutic standards was more important than legal control. Dale believed that the American experience particularly demonstrated that legislative Acts, on their own, had limited authority. He argued that the MRC should use its patent rights of insulin to gain moral control of the production and standardisation of insulin specifically in Britain, by controlling information about the drug to manufacturers.

Nobody in England can make or test insulin satisfactorily without information which the patent does not give, but which we can supply. Under such conditions it seems not unlikely that the holding of the Patent by the Council would enable them to exercise a moral control over manufacturers, and would induce the latter to submit to a system of supervision, as regard this product, which the law does not enable the Council at present to enforce.

Burroughs Wellcome and Co. to the Secretary of the MRC, 22/12/22. The details of how setting a fixed price would affect their commercial interests are set out later in this chapter.


442 Dale made this point to Fletcher and the Insulin Committee. He reflected on the fact that the Hygienic Laboratory in Washington D.C., which controlled the quality of all curative sera and vaccines, apparently had difficulty in adding insulin to its schedule, on account of the unfortunately limited definition of substances subject to control, given by the Act from which the authority was derived. PRO: FD1/902, H. H. Dale and H. W. Dudley, Report to the Medical Research Council on our visit to Canada and the United States to examine the 'Insulin' treatment of Diabetes, 30/10/22, p. 8.

443 The emphasis is mine. See PRO: FD1/902, H. H. Dale and H. W. Dudley, Report to the Medical Research Council on our visit to Canada and the United States to examine the 'Insulin' treatment of Diabetes 30/10/22, p. 8.
Fletcher and Dale acted with the conviction that the authority to exercise such control belonged to the MRC's department of the state, and that these powers had been vested in the MRC by the public. In Dale's words, it was 'apparently generally admitted that control from this Government Department (the MRC) of Biological Standards would be the ideal method, if it could be applied.'

Dale and Fletcher defined the nature of the manufacturing equipment, laboratory conditions, and the skills required to produce insulin as a means of exerting moral control over manufacturers. They also assumed the authority to control the production and quality of the final product. Pharmaceutical companies were responsible for producing safe, potent insulin and for employing effective methods of checking the standard of the product. They were also expected to bear the cost of this cross-checking at the fixed rate of two guineas for each test.

Dale and Fletcher gave formal expression to these ideas through the terms they negotiated with representatives of the major pharmaceutical companies. In November 1922, the companies were invited to send one representative each to meet with Dale and Fletcher at MRC headquarters to discuss the terms of manufacturing insulin. These companies agreed to the terms: Burroughs Wellcome and Company, Allen and Hanbury's Ltd, Park, Davis and Company, May and Baker Ltd., the British Drug Houses Ltd., Evans Sons Lescher and Webb Ltd., Duncan, Flockhart and Company and Boots Pure Drug Company. The terms were as follows:

1. Manufacturers had to determine that they had appropriate equipment and staff for proper biological and other testing.
2. The NIMR would test every batch and issue certificates.

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444 See Note 77. The italics are mine.

445 PRO: FD1/902, Dale to the pharmaceutical companies, February 1923, p. 2. This was subject to modification if experience proved the cost of the test to be more or less than this sum.

446 PRO: FD1/919, A. L. Thomson to Burroughs Wellcome and Company, 29/11/22. The same letter was sent to Allen and Hanbury's Ltd., Park, Davis and Company, May and Baker Ltd., the British Drug Houses Ltd., Evans Sons Lescher and Webb Ltd., Duncan, Flockhart and Company and Boots Pure Drug Company. Not all of the companies sent their representatives to this meeting. The Evans Sons, Lescher and Webb Company sent their apologies at not being able to send representatives to the meeting since their chemist was away in Liverpool. See PRO: FD1/932, Evans Sons Lescher and Webb Ltd. to Secretary of the MRC, 30/11/22.
3. All initial sales would be handled by the MRC.
4. Costs to manufacturers had to be supplied, and although these data would be confidential, a fixed maximum selling price would be imposed.
5. 'Insulin' would be the only name under which the product could trade.
6. The MRC reserved the right to review all published statements.
7. A standard MRC statement on the use of insulin was to be supplied to consumers by the producer.
8. Batch numbers and a measure of the level of activity would be included on all labels.
9. A nominal royalty was payable to the MRC. 447

After the November meeting, Dale circulated a document of the terms of licenses to these companies in January of 1923, and telephoned them to discuss these terms and secure their acceptances. Dale then visited the scientific representatives of the companies who had agreed to the terms, promising Fletcher that he would 'give them what information we have, so that they may get on with their experiments and place orders, if necessary, for the plant which they require.' 448 Dale was well known to the representatives of the company, having himself headed the Wellcome Physiological Research Laboratories (WPRL) before joining the MRC, and having moved within the small group of research scientists who worked for the major drug companies in Britain. E. M. Tansey shows how he worked with a network of chemists and physiologists in establishing the quality control of Wellcome drugs. 449

This agreement also benefited the drug companies. At the end of the day, they would have a certificate of government approval on every bottle of the insulin they had produced and would be set apart from proprietary medicine manufacturers in this respect. Their credibility


448 PRO: FD1/902, Dale to Fletcher, 1/1/23. In this letter Dale refers to a telephoned acceptance from BDH and Allen and Hanbury. 'I hear over the phone', wrote Dale, 'from Miss Luke, that an acceptance and application for Licence has today been received from the BDH on behalf of themselves and Allen and Hanburys.' This suggests that these two companies had conferred with each other before accepting the MRC's conditions.

and status as modern scientific manufacturers would be certified with every commercial sale of this wonder drug. Not only would this license with the MRC legitimise their product, but manufacturers knew that government certification boosted drug sales.\footnote{450} Even within the legitimate pharmaceutical industry, there was a distinction between those with MRC approval and those companies which had not been able to secure a licence to produce the drug. R. Sumner and Company, for instance, were rejected when they applied for a licence because the MRC claimed that their facilities were not up to standard.\footnote{451}

Pharmaceutical companies agreed to these terms on paper, but they disregarded them in practice. As early as January 1923, Dale discovered to his horror that O'Brien (who had succeeded Dale as head of the WPRL) had made private arrangements to produce insulin for George Graham (who was testing insulin for the MRC at St Bartholomew's). Dale told Fletcher that he had put his 'foot on this very heavily', that he had 'had a very straight talk with O'Brien' who, he said, now realised any such action would 'be regarded by us as a breach of confidence, and treated accordingly'.\footnote{452}

Managing responsibility was one of the keys to maintaining moral control. One advantage for drug companies of being under the MRC's moral control was that they could not be held fully accountable for complaints from the public about potency. Part of the responsibility for any complaints which diabetic patients made about potency, efficacy and safety could be deferred to the MRC. This was also one of the key concerns when physicians like Graham, and drug manufacturers like O'Brien, broke their social contracts with the MRC. But Graham was not alone in this respect. At one point, Hugh MacLean (testing insulin at St Thomas' for the MRC) was using insulin which he had indirectly acquired from Boots on his patients. MacLean had approached Boots, intending to make private arrangements with them to supply him with insulin, despite his promise to Fletcher that he would only use insulin which

\footnote{450} It was known that the public took government certificates on drugs as stamps of approval. The government tax duty required for proprietary drugs was often regarded by the public as government approval and this had boosted the sales of these drugs to members of the public.

\footnote{451} Liebenau (1989).

\footnote{452} PRO: FD1/902, Dale to Fletcher, 1/1/23.
he had produced in his laboratory on the patients in his clinical trials. This time, perhaps because of Dale's words with O'Brien regarding Graham having broken this same promise, Boots went straight to Dale and told him that they had been approached by the team leader at St Thomas'. The Managing Director of Boots said that he was writing to clear the matter with Dale first:

Under the terms of the proposed agreement with the MRC, we are not to supply insulin to medical men or institutions without a certification from the MRC.\textsuperscript{453}

Boots made the following proposal:

if Professor MacLean is agreeable to take our product, use it as his own insulin, accepting entire responsibility for all results of treatment, perhaps you will permit us to supply Prof. MacLean as he desires.\textsuperscript{454}

This was precisely the sort of situation Dale had been trying to avoid.

The position which has arisen is due to the slight embarrassment which we foresaw of Brett being at the same time a worker in MacLean's department and an employee of Boots. Boots have been turning out small batches of Insulin powder, and Brett has been testing these.\textsuperscript{455}

Dale decided that, in this case, the matter rested on the question of who would accept responsibility for the outcome of clinical testing, his aim being to ensure that in resolving this issue, the MRC was relieved of all responsibility for the outcome of MacLean's insulin trials. 'If MacLean liked to take material produced by Boots and use it as though prepared in his own department, making himself responsible for testing and sterilising it', then he, Henry Dale, 'could see no objection'. But, 'such material was not to be regarded as officially passed for use', and should 'not be supplied to anybody else'. While Dale found it reasonable for MacLean to tell Boots about his trial results 'in confidence', since they were supplying him with weekly

\textsuperscript{453} PRO: FD1/930, Managing Director of Boots Pharmaceutical Company to Dale, 14/3/23.

\textsuperscript{454} See Note 87.

\textsuperscript{455} PRO: FD1/930, Dale to Fletcher, 15/3/23.
consignments of insulin, Dale forbade Boots from using this concession in their advertisement of, or propaganda about, the product.\footnote{456}

It was neither prudent nor effective for Fletcher and Dale to reprimand physicians and manufacturers for such behaviour. In some cases Fletcher and Dale chose to turn a blind eye to these private arrangements between pharmaceutical companies and physicians until it suited them to do otherwise. In the case of the tardy team at the London Hospital, for instance, Fletcher knew that Marrack was working for the MRC team while conducting standardising tests for a manufacturing firm before he approached Morris and the others about their delay in starting the trials. But he only mentioned these transactions, and the conflict of interest they represented, when they could be used to enforce his position that the London team was morally obliged to start their insulin trials on time.

II. 3. The duty of the diabetic citizen: the 'moral controls' on individual patients

Physicians and manufacturers were not the only ones with moral obligations in the trial system. Some patients also felt obliged to try insulin and to join the MRC's experimental trials. Being tested in these trials meant daily insulin injections, not to mention repeated blood-glucose and urine tests, and regular weight measurements. One sceptical patient, who was treated with insulin during these early months of its introduction into Britain, talked about the moral obligation he felt to try this new drug in an article in \textit{The Times}. The patient said that he was not optimistic when he

submitted to the course of punctures and injections and blood tests. The prospect rather bored me, but I had the chance; and anyhow I would be rid of the reproach that I had let it go by.\footnote{457}

This outspoken patient was a rare case of an individual who made his feelings known to the general public. For the most part, it was physicians who imposed their definitions of appropriate behaviour and moral obligations on the patients they tested. And some physicians

\footnote{456} See also PRO: FD1/930, MRC to Boots, 16/3/23.

\footnote{457} 'Insulin. A patient's point of view', \textit{The Times}, 7/8/23, p. 12.
treating diabetics with insulin explicitly interpreted their role in conducting clinical trials in terms of citizenship. One physician testing insulin on patients at a London hospital gave voice to this in *The Daily Telegraph*. 'A man', this London practitioner proposed:

> has a right to live when his fellow-citizens consider that by his continuing to live something is gained, either directly or indirectly. If a man through his services to King and country is damaged in a way that prevents him earning a living the gratitude and sympathy of his fellow-citizens make them assume the burden of his maintenance. On the other hand if a man is rendered helpless because, while drunk, he wandered in front of a motor bus his fellow citizens are sympathetic but not grateful and they are willing to supply him with the actual necessities of life, but not with luxuries. Again, when a man is ill his fellow-citizens supply him with the necessities of life in infirmaries; but since infirmaries are supplied by citizens who are charitable, and also by citizens who are not charitable, the authorities have only the right to provide necessities. The Treasury cannot give £250 per year to 5000 people without Parliamentary sanction.

In this involved argument about the relationships between fellow-citizens, this doctor implied that the deserving diabetic on insulin was being maintained by the charity of his fellow-citizens and the taxes of others, thus suggesting that the patient's right to have the drug was inextricably linked to his place in the society.

Other physicians testing insulin for the MRC took the view that these trials would have been in vain if an individual diabetic patient's behaviour was not controlled. Citizens who refused to exercise self-restraint, and physicians who failed to control their patient's behaviour, posed problems for everybody concerned. Dr. Hetzel at University College Hospital (UCH) drew T. R. Elliott's attention to one disturbing case at that hospital. Elliott believed this case illustrated that if diabetic citizens failed to control their appetite for insulin there could be serious national consequences. He brought the case, which Hetzel published in the *BMJ*, to Fletcher's attention. This situation with insulin would have had echoes in other areas. Ministry officials had been complaining about the rising cost of medicines *per capita* for insured persons because of the extravagant prescribing habits of doctors treating patients on medical benefit. The Ministry's approach to reducing these costs was to encourage Insurance Committee Panel doctors to justify prescribing a medicine for which there was an equally

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effective and less expensive alternative. Fletcher took up the financial issue of over-prescribing in the case of insulin with the Minister of Health, arguing that such cases demonstrated that the Ministry ought to enforce treatment limits on patients in general practice in the interest of efficiency and standardisation. Ministry officials seem not to have responded to his suggestion. The way in which this case was framed for the medical press, however, speaks volumes about the moral purpose of the MRC's noble scientists and patients' duties in the progress of clinical trials.

The case was as follows. A 43-year-old bricklayer went to hospital in March 1923 and was diagnosed with diabetes. Since insulin 'was then scarce', he did not receive that 'special treatment' on this occasion, but while in hospital his diabetes nevertheless yielded to dietetic control (the standard treatment at the time). In June the bricklayer's doctor commenced the patient on insulin, 30 units daily. However, his doctor allowed the bricklayer to have a 'loosely controlled diet'. Hetzel wrote that this diet was:

a loosely controlled diet which appears to have risen to nearly 3700 calories, almost twice as much as the patient could efficiently use... In November the man came again to hospital his weight and strength much wasted and his diabetes so far advanced that he nearly passed into coma soon after admission. After three weeks of treatment in hospital his diabetes was sufficiently controlled and he was able to return to actual work, on 2,000 calories together with insulin. In the meantime, he had lost nearly six months' work at £3: 10: 0 a week; he had spent £25 on a holiday, which did him no good, and much money on extra food which was harming him, while the insulin supplied almost uselessly, because of his prodigal consumption of food, had cost the Ministry of Health over £350. The sole fault was in the neglect to control his diet.

By calculating the individual bricklayer's personal 'prodigal consumption' in terms of pounds and pence, and loss of six months' wages, the case was framed to expose the moral responsibility of individuals using experimental treatment to restrain themselves. It was also designed to show that patients were to be controlled by their doctors, and Hetzel argued that

459 Stieb (1966), 121-2.

460 Dr. Hetzel from the UCH involved in trials and research published a paper in the BMJ making a case of a particular patient. Extract from a short paper for the BMJ by Dr. Hetzel, UCH, attached to a letter from Elliott to Fletcher, 23/1/24. Fletcher took the paragraphs of the paper to the Ministry.

461 See Note 94.
the case particularly demonstrated that, contrary to popular belief, insulin emphasised the need for more, rather than less accurate control of food in diabetics. The *BMJ* article linked the need for prudence on the part of doctors with national concerns about efficiency. According to the *BMJ*, 'clinical experience had made it certain that insulin, if used with scientific intelligence, does prolong the life and increase the efficiency of diabetics'. Insulin was therefore linked to the productivity of citizens.\textsuperscript{462} Further, implicating the Ministry of Health as ultimately bearing the cost in this particular case emphasised the point that the State bore the cost of inefficient medical management. Hetzel suggested circulating a set of guidelines in which food and insulin were calibrated in terms of normal everyday experience. He specified these guidelines.

When insulin is used for chronic diabetics, doctors and patients alike must learn to measure the food. With printed tables of foodstuffs the circulation of a dietary in terms of calories can be learned almost as quickly as one learns when abroad on holiday to estimate the price of a dinner in French francs at a given rate of exchange. (It would take 2/- worth of insulin to metabolise the sugar of a penny bun (2ozs) in a completely diabetic patient.)\textsuperscript{463}

Hetzel was effectively arguing that these guidelines could be used as standards against which to interpret the behaviour of individual doctors and patients, and to give this behaviour moral meaning.

I have examined the moral economy of the relationship between MRC officials, manufacturers and physicians, and the ways in which physicians then sought to define what should stand as appropriate behaviour for patients in moral terms. I shall now turn to the management of production and standardisation of insulin in the laboratory, and the ways in which physicians tried this drug on their patients.

\textsuperscript{462} See Note 91.

\textsuperscript{463} See Note 91.
III. Standardising insulin in the laboratory and on patients

Dale believed that the best kind of standard was one embodied in a stable object: a fixed sample of solid insulin crystals in a bottle, kept under lock and key at the MRC. He said:

The standard preparation would then serve as a convenient currency, by means of which the unit could be transmitted to every country concerned, each institution being left to use, for measurement with reference to the standard, the particular species and method in which individual experience gave confidence.\footnote{See H. H. Dale, 'Introduction', The Biological Standardisation of Insulin (Publications of the League of Nations, 1926. III. 7., C. H. 398), pp. 5, 6.}

Dale was becoming one of the international figures who campaigned for biological standardisation around the time of these trials. Not a year before the insulin operation, Dale had been campaigning for biological standardisation on an international stage at the first League of Nations' International Conference on Biological Standardisation, held at the Ministry of Health in London in 1921, where he had represented Britain.\footnote{The first International Conference on biological standardisation had been held at the Ministry of Health in London on 12-14 December 1921. Dale also attended the second International Conference which was held from 20-26 November 1923 in Paris at the Pasteur Institute. See International Conference on the Standardisation of Sera and Serological Tests convened by the Health Committee of the League of Nations and held at the British Ministry of Health, London, 12-14 December 1921. Publications of the League of Nations, 1921; and Second International Conference on the Standardisation of Sera and Serological Tests convened by the Health Committee of the League of Nations held from 20-26 November 1923 at the Pasteur Institute, Paris, Publications of the League of Nations, 1923.}

Dale was himself experienced in the biological standardisation of commercial products, namely diphtheria sera, at the WPRL.\footnote{Tansey (1994).} He also spoke with the authority of a scientist who had worked with Paul Ehrlich. This famous German medical scientist, Nobel Laureate, and commercial scientist was regarded at the time as the father of the new field of biological standardisation.\footnote{Tansey (1994); Liebenau (1990).}

When they visited Toronto in October 1922, Dale and Dudley found it unsatisfactory that the Toronto group were testing and defining the standard activity of insulin in terms of the degree of hypoglycaemia in rabbits.\footnote{On his return, Dale announced that finding a method of...}
standardising and controlling potency which was 'simple, quick and quantitative' would be one of his main priorities.\textsuperscript{469} He was not able to make these dry, stable crystals when he and Fletcher began arranging the clinical trials of insulin that November. In the absence of a solid standard, he and Dudley defined a standard procedure for making insulin for the MRC trials. The recipe they concocted served as a procedural standard which could be used as an instrument of control. If biochemists and physicians at each of these experimental centres followed the recipe they would produce insulin of adequate quality and potency that would be safe to use on patients. If they were not making good quality insulin then the recipe could be brought out for examination.

Dale and Dudley produced and guaranteed the efficacy of their insulin recipe using the face-to-face evidence they gathered from the American clinical trials, and by conducting 'a number of [laboratory] trials' at the NIMR laboratories. They had been impressed by the way Dr. Woodyatt had made and tested insulin in his clinic in Chicago. Dale and Dudley's recipe was based mainly on Woodyatt's laboratory procedure, but informed in part by the semi-industrial method they had observed at Toronto, and by the commercial production at the Eli Lilly factory which they had presented to Fletcher and the MRC. Theirs was a five-stage recipe that produced a batch of insulin in five days. One batch of insulin could either serve 40 patients for one day, or one patient for 40 doses.\textsuperscript{470} The primary ingredients were 5 kilograms of pancreas, 5 litres of 95% alcohol, and approximately 400 cc of absolute alcohol. The same 95% alcohol was also required for washing filtrate and for making up the concentration of the filtrate. Other necessary equipment included large folded filters (e.g. thick Chardin papers), a 'jean' cloth, a cooling apparatus for storing alcohol, a sausage-machine or grinding-machine, a vacuum, a battery of round-bottomed flasks, a water-bath heated to 45°, a vacuum desiccator, sulphuric acid and dry ether. The MRC's recipe for making good standard insulin was as follows:

\textsuperscript{468} PRO: FD1/902, Methods of Preparation, Report from Toronto, pp. 5-7.

\textsuperscript{469} See Note 102.

\textsuperscript{470} PRO: FD1/902, Methods of Preparation, Report from Toronto, pp. 1-3.
Day 1: Five kilograms of perfectly fresh ox pancreas are minced through a sausage machine and 5 litres of 95% alcohol, previously cooled to 3°C, are added to the mince with constant stirring. It is advantageous to strain off the minced tissues on a fine sieve, squeeze out as much of the alcohol as possible by hand, mix the tissue, into the alcohol, and repeat the mincing a third time, to get the tissue as finely divided as possible. The mixture is then allowed to stand for two hours at room temperature with frequent stirring. It is then filtered through large, folded filters (thick Chardin paper). As soon as the main bulk of the liquid, which may be slightly turbid, is filtered, the thick mud on the papers is transferred to a suitable press and as much liquid as possible is squeezed out of the cake. Paper and mud are wrapped up together in cloth ('jean') and pressed. This filtration is slow, but is completed in 3 to 4 hours. Approximately 5.5 litres of filtrate are collected. 1 1/2 volumes (i.e. 8.25 litres) of 95% alcohol are now added and the liquid is placed in a cold room at -3°C overnight.

Day 2: The liquid is filtered through large folded filters in the cold room. This filtration proceeds without difficulty, giving a perfectly clear, yellow solution.

Day 3: The turbid liquid is distilled *in vacuo* in a 5-litre flask (water bath at 45°C). The fat separates in buttery lumps and distillation is continued until the volume of the aqueous residue is about 200-250 ccs. It is then filtered from fat is shaken out of the flask and squeezed as free from water as possible. The aqueous solution is then made up to 80% with absolute alcohol; that is to say, to every 100 ccs solution are added 400 ccs absolute alcohol. It is then placed in the cold room overnight. (Probably adding 400 cc of 95% alcohol to 75 cc of the solution would be as effective).

Day 4: A yellow, watery syrup and a small amount of solid matter have separated out of the 80% solution. It is decanted without difficulty and made up to 93% alcohol by the addition of two volumes of absolute alcohol. It is then placed in the cold room overnight.

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471 PRO: FD1/902, Preparation of Insulin, section of Dale and Dudley's report. See Note 86. Note that 'Methods of Preparation' and 'Preparation of insulin' are two separate documents. The Toronto experience had demonstrated that there was nothing to be gained by preserving (cooling or alcoholising) pancreas in the abattoir before bringing it to the laboratory. The yield preserved pancreas was no different to fresh starting material. Further, in Toronto it had been demonstrated that a procedure of this kind involving large amounts of alcohol could be expensive, and that slaughterers might be inclined to help themselves to alcohol.

472 See Note 102. This duplicated Dale and Dudley's record of Woodyatt's method.

473 For their own reference to Woodyatt's method, Dale and Dudley noted only that '80% alcohol is added... to bring the strength up to 90-95%. The addition of' that is to say, to every 100 ccs solution are added 400 ccs absolute alcohol' ensures that the biochemists following the recipe produced the correct concentration. See Note 113, p. 5. There is no specific mention of such a step in their report of the Lilly method.

474 This last instruction was a tip from the approach in Toronto where, after bringing the solution to 90-95%, they had left the solution to stand in the ice-chest for 24 hours so that the precipitate would settle at the bottom of the container. See Note 102, p. 2.

475 This step was informed by the Toronto method. Dale and Dudley noted that it had recently been discovered that making up this solution and decanting off more solid matter again was found 'to get
Day 5: A white granular precipitate ('insulin') has separated out of the '93% solution'. The main bulk of the alcohol is removed by siphoning, about 50 ccs being left covering the precipitate, which is then stirred up into the residual alcohol and poured into centrifuge tubes. The precipitate is centrifuges down, washed once with absolute alcohol and once with dry ether in the centrifuge. After pouring off the ether the tubes, containing the precipitate, are quickly transferred to a vacuum desiccator and dried over sulphuric acid. 476

The potency of the laboratory insulin, however, was a separate matter. Temporary laboratory tests -- using a physiological standard -- could be used to check the efficacy of the procedural standard, and quantify it for human consumption.

To make up their physiological standard, the Toronto group had drawn a direct analogy between normal laboratory animals and the human condition of diabetes mellitus. They connected laboratory animals and human beings in a physiological conversion equation designed to calibrate the therapeutic effect of insulin in humans. In principle, any animal could have been used to calculate the units on the animal side. Frogs, mice, rats, rabbits: the choice was a matter of convenience. 477 Rabbits had been selected as the physiological test animal in Toronto because in their systematic laboratory trials they had found that insulin lowered the blood sugar of normal rabbits. 478 In addition to becoming hypoglycaemic, the majority of rabbits tested developed characteristic convulsions when their blood sugar had been lowered to rid of irritating substances which give trouble when the liquid is injected with a hypodermic needle'.

See Note 102, p. 2.

476 See Note 102, p. 3. Woodyatt had followed Toronto and the Eli Lilly company in filtering the solution through a Berkefeldt candle to produce the final precipitate. However, Dale and Dudley had observed that the effect of this method of filtering it had an unpredictable effect. Indeed, just before the pair left America, both the Lilly company and the Toronto Laboratory had had problems with their products. The insulin preparations they had produced were proving to be unstable, with the potency falling off to practically nothing in a week. Dale and Dudley implied that using acid in the preparation of insulin may have been the cause of this. They noted that Woodyatt, who used no acid in his preparation of insulin, did not have these problems with stability of the final product. See Note 102, p. 8.

477 MacLeod had observed nothing characteristic when he injected insulin into the lymph sacs of frogs. Mice and rats had been tried, but not systematically, since it had been concluded that insulin did not increase their utilisation of glucose in muscles or livers in vitro.

478 Dale and Dudley referred to it as the 'rabbit test' in their report of the Toronto visit. See 'Methods of Preparation', Report from Toronto, FD1/902, pp 5-7. See The Biological Standardisation of Insulin (Publications of the League of Nations, 1926. III. 7., C. H. 398), p. 11.
approximately 0.045 per cent. The Toronto physicians therefore decided to define one unit as the amount of insulin to cause this effect.479

Thus the 'rabbit test' was born.480 The test was as follows:

a rabbit weighing approximately 2 kilos is starved for not less than 16 hours and then receives a subcutaneous injection of insulin. The fall in the blood sugar is observed hourly. When this reaches a value of about 0.045 per cent the animal goes into convulsions. The smallest amount of insulin which will bring about this result within 4 hours is called one rabbit unit.481

Dale recommended that the trial units measure the potency of the insulin produced by their recipe in terms of the amount of insulin it took to send a two-kilogram rabbit into convulsions.482 If the batch was potent, 5 to 10 milligrams of the insulin powder should reduce the blood sugar of a two-kilogram rabbit (which had been starved for 24 hours) sufficiently to cause the rabbit to convulse within about 2 hours.483 To confuse matters further, there was more than one rabbit unit. The Eli Lilly Company took a rabbit unit to be the amount of insulin required to put one, 1 kilogram rabbit (starved for 16-24 hours) into convulsions within 4 hours.484 Physicians making and trying insulin in their clinic used different versions of the test. For instance, Dale and Dudley noticed that Dr. Woodyatt used 2-kilogram rabbits, like the manufacturers at Lilly, but defined his unit in terms of 1-kilogram rabbits.485 So that 4 Toronto Units = 2 Woodyatt Units = 1 Lilly Unit.

479 MacLeod and Orr (1926), 11.
480 MacLeod and Orr (1926), 11. Although starvation for such a short time would not ensure complete removal of glycogen from the liver, they believed that it would bring the amounts to a tolerably uniform low level in the different animals. Note that in 1926, MacLeod reported that food was withheld from 18-24 hours. See PRO: FD1/902, Methods of Preparation, Report from Toronto, p. 6.
481 PRO: FD1/902, Methods of Preparation, Report from Toronto, p. 6.
482 PRO: FD1/902, Dale to the 7 MRC centres, 30/12/22.
483 See Note 101, and PRO: FD1/902.
484 See Note 101.
485 See Note 101.
Dale and Dudley informed Fletcher's 'noble scientists' about these rabbit tests. Physicians and biochemists used versions of the rabbit test to check the potency of their local insulin. But the Toronto rabbit test involved a lot of 'work, expense and waste of material', so Dale and Dudley began to conduct a systematic study of the effect of insulin in mice, and to work on finding a reliable method of estimating that effect. Mice were cheaper test animals, they were more dispensable, and Dale believed that using a standard would eliminate some of the individual variations that occurred when experimenters used rabbits to standardise insulin.

By chance Dr T. Madsen, head of the States Serum Institute in Copenhagen, telephoned Dale soon after he returned from Toronto in 1922. The States Serum Institute had been a designated centre for holding international standards. Madsen phoned to ask Dale to prepare a report listing the therapeutic substances, other than sera and vaccines, that should be subject to international standardising agreements. Dale said he immediately told Madsen that insulin was a fine example of just such a substance. Over the phone, they discussed the possibility of making a dry stable insulin standard, and about arranging an international meeting on the subject. Madsen convinced the League of Nations Health Committee to hold a special conference of the biological standardisation of drugs other than sera.


See Note 101, p. 7.


Dale also suggested a number of other drugs, including those from the digitalis series, ergot, cannabis, preparations of the pituitary, suprarenal and thyroid glands, and organic arsenicals.

In the 1966 interview, Dale spoke of how he and Dudley focused on purifying and concentrating insulin after that telephone call. For 12-25 months they researched in their laboratories at the NIMR to make and separate a solid which could be brought to the state of a sufficiently fine, dry powder, and that could be completely desiccated *in vacuo* and stored in small sealed tubes filled with dry nitrogen.\(^\text{492}\) I began this chapter with Dale's record of the events of the conference day where he presented his dry, stable insulin standard to the international community, at Edinburgh. His public demonstration convinced Madsen and the others present was given the blessing of the League of Nations to prepare a dry insulin standard.\(^\text{493}\)

### III. 2. Physicians, patients and embodied standards

Physicians tested insulin in idiosyncratic ways and used these trials in the name of biological standardisation as opportunities to express their clinical prowess and demonstrate their individuality. Significantly, however, Fletcher and Dale found these idiosyncratic trials acceptable. However, I shall show that the pair had separate opinions about how this clinical evidence should be used to create standards. Here, I shall focus on the interim reports of the trials at three different centres to demonstrate the nature of these standardising clinical experiments.

Consider T. R. Elliott's trials. Elliott and his assistant physician Charles Kellaway selected three diabetics suitable for their insulin experiments. They conducted 'routine investigations' on these patients which involved injecting the diabetics with insulin, and then testing their blood sugar to find out how much each specific dose of insulin had reduced the glucose levels. It seems that the MRC trial patients had their blood sugar measured twice daily.\(^\text{494}\) Elliott and Kellaway also gave insulin to a normal -- non-diabetic -- person to see its effect. The normal person was anonymous. Whether he or she volunteered to participate in this

\(^{492}\) Murnaghan and Talalay (1992).

\(^{493}\) See MacLeod and Orr (1926), 13.

\(^{494}\) A. Innes, 'Insulin treatment without blood sugar estimations', *BMJ* (1924), 1: 55-6.
experiment is unclear. The physicians reported that when this 'normal individual' was injected with insulin he collapsed. They also asked the 'normal individual' to account for his experience, noting that although the normal person complained of drowsiness and lethargy, but without the warning sensation of impending doom.\textsuperscript{495} When diabetic patients collapsed they complained of being sweaty and dizzy. Their fainting also caused them to experience visual disturbances, fear and a sense of doom. Elliott and Kellaway must have asked their diabetic patients to recount how insulin made them feel. In order to discover these facts, Elliott and Kellaway used this 'normal individual' as a standard against which to measure the effect of insulin on diabetics.

Elliott and his assistant also conducted a number of observations on the changes in the basal metabolism of diabetics under the influence of insulin.\textsuperscript{496} Over the months, they added selected patients who came to their clinic as test subjects for their insulin. The patients were from different age groups, and represented a range of clinical states, courses and prognoses. Most of them were tested and observed in hospital, but later Elliott and Kellaway 'watched' their progress at a distance. The doctors even allowed eight of these patients to give 'insulin to themselves as out-patients'.\textsuperscript{497} Elliott and Kellaway believed that watching these diabetics would allow them to acquire a range of facts about the therapeutic effect of insulin. In July 1923, Fletcher asked Elliott to estimate the range of insulin units required in diabetic therapy so that the MRC could prepare standard clinical guidelines for treatment. By this time Elliott could identify three categories of diabetics and the amount of insulin they required from his experiences: 'mild', 'severe' and 'exceptionally severe'.\textsuperscript{498} He reported:

\begin{quote}
I have a severe case which made very little headway for some months under 20 to 30 units, remaining in bed, thin and weak. Now she has 70 units she has gained 24 pounds in 17 days and is capable of a fair day's work... A case of diabetic coma
\end{quote}

\textsuperscript{495} PRO: FD1/910, Kellaway to Fletcher, 12/3/23.

\textsuperscript{496} PRO: FD1/910, Kellaway to Fletcher, 12/3/23; PRO: FD1/910, Elliott to Fletcher, 27/9/23. It had been arranged for these biochemical analyses, such as those to determine blood-glucose levels and basal metabolism, to be conducted by Professor Starling's and Professor Drummond's laboratory. See also PRO: FD1/902, Fletcher to Elliott, 10/11/22.

\textsuperscript{497} PRO: FD1/910, Elliott to Fletcher, 27/9/23.

\textsuperscript{498} PRO: FD1/910, Elliott to Thompson, 23/7/23.
required a day or two of very large doses, 100 to 200 units ... [And] young cases actually need as much as adults, and no smaller doses in relation to body size.\textsuperscript{499}

Thus, for this team, blood glucose served as biochemical evidence of potency of the drug in humans, while weight was the meaningful sign of efficacy of the drug: therapeutic efficacy was measured in pounds and ounces.

George Graham's trials at St Bartholomew's hospital were another case in point. Graham had devoted a good part of his career to the dietetic management of diabetes and argued that physicians could not accurately gauge the severity of the disease in each patient until that particular case had been 'under expert treatment', for some time. In his conception, this included 'persistent attempts to make the patient sugar free by starvation, and then gradually increasing the carbohydrate content in the diet without producing glycosuria.'\textsuperscript{500} Thus in March 1923, months after beginning his trials, Graham had \textit{selected} three cases for close study. His clinical experiments so impressed Dale, that Dale described them to Fletcher as an example of how, by:

\begin{quote}

care and patience, studying the effect of each dose on the blood-sugar from the time of injection until the effect has completely subsided, giving only one dose per diem to each patient, and carefully adjusting the diet, he [Graham, had] now got two severe cases with practically normal blood-sugars on a dosage of insulin which is rapidly being reduced.\textsuperscript{501}
\end{quote}

Graham \textit{selected} two cases, which after rigid dietetic management could be described as a 'very severe', and a 'mild' case (he had only proposed to try insulin on) when he submitted his progress report to Fletcher. Graham was then 'fortunate enough to have had one man who was on the verge of diabetic coma' to be admitted to the hospital during the time of the trials. The comatose patient formed the third case. It was Graham's first case of the very severe diabetic which Dale saw as a clinical experiment. This, I propose, was also a standardising experiment.

\textsuperscript{499} PRO: FD1/910, Elliott to Thompson, 23/7/23.

\textsuperscript{500} PRO: FD1/912, report on insulin investigations (untitled), 29/3/23.

\textsuperscript{501} PRO: FD1/912, Dale to Fletcher, 14/4/23.
Graham's standardising case was as follows. A man with a very severe form of diabetes was admitted to another ward practically in a coma, who, 'after treatment along the usual lines', he had been discharged, though 'still passing sugar and still very ill.' He was re-admitted to Bart's a few weeks later, but this time Graham took over the case. Graham starved the patient for two days but found that he was still passing sugar in his urine. This was followed by two egg-and-vegetable days, and then two more hunger days. Graham then stressed the patient's glucose uptake capacity to its maximum by putting him on a diet of 53 g of protein, 109 g of fat, and 16 g of sugar. On this diet, with its total calorific value of 1360, the patient passed between 25-33 g of sugar per day and as Graham put it 'was almost a complete diabetic'. He measured the diabetic's blood sugar at 0.23 to 0.25 at 9 o'clock on this diet, and he then injected the patient with increasing doses of insulin, measuring the blood glucose at 9 am the next morning. At 12 units of insulin, Graham measured the fall in blood glucose caused by insulin every two hours from 9 am. He calculated that the blood sugar fell to its lowest point of 0.14 after 6 hours and did not rise above this for another 10 hours, reaching its original level of 0.20 after 16 hours. But after 24 hours, the patient's blood-sugar levels had fallen to 0.17 and his urine was clear of sugar. Keeping the diet constant, Graham repeated this regime of titrating insulin against the patient. He observed that the blood sugar levels were decreasing steadily each day (descending to 0.135 at one point), so he reduced the patient's insulin dose from 12 to between 8 and 6 units per day. When he submitted the report, Graham identified this as a successful case: the patient had not passed glucose in his urine, he was on a reducing daily dose of insulin, and his aceto-acetic acid levels were low.

Unlike Graham, who saw his trials as clinical experiments, Hugh MacLean at St Thomas’ specifically defined his clinical tests as standardising experiments. When MacLean tried his fresh batches of insulin on rabbits he reported that 'different rabbits ... react very differently to insulin'. He decided that it was therefore impossible to 'standardise the product with any accuracy using these rabbit tests'. So MacLean performed only a 'very rough


503 See Note 135, p. 2.
standardisation' on the rabbits with fresh insulin, before trying it on patients, 'for the human patient is just as variable in response as is the rabbit.'\textsuperscript{504} MacLean tested insulin on a total of 8 serious diabetics. He said it was 'quite easy to standardise insulin directly on any particular patient without performing any rabbit or other tests', and that this could be done 'without any risk, provided moderate doses are used to begin with'.\textsuperscript{505}

MacLean believed that, 'ideally', insulin 'should be standardised on each individual patient'. He standardised insulin on each patient as a first stage of his trial, and then began by injecting patients with a low dose of insulin, working his way up to higher doses of the drug.\textsuperscript{506}

I pushed the dose to the extent of producing the usual general symptoms -- that is flushing, sweating, giddiness, faintness, etc., but whenever these effects occurred the dose was reduced. In one patient, I found it almost impossible to remove the glycosuria entirely, even when the dose was pushed so that marked symptoms were produced.\textsuperscript{507}

MacLean, it seems, put each patient on a diet and measured the total calorific value of the diet before standardising the drug on them. He measured the total calorific intake of their diet, taking particular note of the carbohydrate content in grams. MacLean also measured their weight regularly, monitored their blood sugar (twice daily on average), and examined their urine for glucose and ketone bodies at least once a day.\textsuperscript{508} His diabetics were injected with insulin twice daily, using roughly 5 to 10 mg per day, and kept just under the insulin limit he had established in his initial standardising experiments.\textsuperscript{509} Giving them a measured caloric intake of carbohydrates, he monitored their blood for glucose, their urine glucose and ketone bodies. MacLean attributed his patient's reactions to insulin either to 'normal personal reaction' or 'modified reaction dependent on the gravity of the diabetes from which he is suffering'.\textsuperscript{510} He

\textsuperscript{504} See Note 135, p. 2.
\textsuperscript{505} See Note 135, p. 7.
\textsuperscript{506} See Note 135, p. 7.
\textsuperscript{507} See Note 135, p. 7.
\textsuperscript{508} See Note 135, p. 7.
\textsuperscript{509} See Note 135, p. 7.
\textsuperscript{510} See Note 135, p. 7.
reported that all of his cases 'responded favourably' to the insulin on the grounds that 'any symptoms produced were more or less trivial even after large doses of insulin', because they 'were always quickly removed (within 10 to 20 minutes) after taking sugar by mouth.\footnote{Quote is taken from p. 3 of report. See 'Report on Use of Insulin. by H. MacLean', PRO/FD1/911, p. 3. The patient who had been pushed to marked symptoms, 'in spite of this' had done 'very well'.}

Dale was unimpressed with MacLean's insulin trials. Dale did not specify his reasons. But it is significant that MacLean described his clinical trials as an exercise in 'standardisation', and treated them as a form of biological standardisation, while Graham, whose experiments gained Dale's praise, did not. I propose that Dale wanted standardisation to be defined as a strictly laboratory activity done by scientists, not as clinical trials by doctors. These MRC insulin trials were a secondary part of the standardisation process. This was also evident in his response to Fletcher's suggestion that the testimonies of such 'intelligent' patients about the symptoms they experienced with every dose of insulin could be valuable for Dale's assessment of different standards of batches of insulin. Fletcher's attention had been drawn to a case where one of the doctors trying insulin at his centre for the MRC had asked a friend, Mr S. Sack, formerly on the staff of his department, to compare the effects of various batches of insulin on himself and to record the difference in order to see if there was any difference in these batches. The patient had concluded from his experience and record that one of the batches was ineffective. He offered to submit a bottle of the ineffective batch to Fletcher and Dale.\footnote{PRO/FD1/910, MacLean to Fletcher, 23/10/23.} Fletcher, passing the bottle on to Dale, suggested that in addition to laboratory results:

> intelligent observations by selected patients might, I suppose, be really useful to supplement the objective observation of physicians. A man like Sack would probably willingly co-operate and his subjective observations be put to service, side by side with other data he could collect and record.\footnote{PRO/FD1/910, Fletcher to Dale, 24/10/23.}

Fletcher believed that evidence from intelligent patients could have the same status and value as laboratory tests for potency. While Dale politely responded that 'it would be very useful to

\footnote{See Note 135, p. 7.}
use a man like this', he said that this patient's evidence would have to be taken 'alongside more objective records made by workers in the units'. Indeed, by October 1923, Dale was beginning to have serious doubts about the value of the whole plan of clinically testing each batch. While some patients may have demonstrated an impressive discriminatory ability to relate their symptoms to insulin, their focus on difference hindered standardising initiatives aimed at defining several batches under the same umbrella. Dale told Fletcher: 'One's faith in it [Sack's evidence] is a little dashed by the fact that Sack not only finds wide differences between the different batches of 'A and B' insulin, but equally the ones between the different batches,' which had been subjected to elaborate testing on pedigree patients at six other clinics.\textsuperscript{514}

Some patients described their experience of being involved in these early insulin trials in terms of pain, food, the pleasures of life and financial benefits of work. MRC trial physicians, however, were concerned to demonstrate in their reports that pain was not a factor in the equation. Dr. MacLean, for instance, noted that he had 'used a very fine needle to inject the drug', because 'it made a very great difference to the comfort of the patient and apparently reduces very much the chances of a local reaction ensuing'.\textsuperscript{515} He told Fletcher that the majority of patients, 'said that they felt no pain whatever after the injection'.\textsuperscript{516} Dr. Graham reported that his severe diabetic had 'no unpleasant symptoms' at low blood-glucose level. He believed that this diabetic felt better for being tried on insulin. 'The psychic effect of the insulin treatment undoubtedly contributes to his feeling of well being.' As for the injections, Graham insisted that 'practically no inconvenience' had 'been caused by the injections, except on one occasion when the patient was required to endure an 'old preparation ... used in error' producing 'great swelling of one arm'. But this, he reported, subsided in about four days.\textsuperscript{517}

While patients may have refrained from complaining to their doctors about the therapeutic ordeal, those who described their experiences to the public described them as a pain

\textsuperscript{514} PRO/FD1/910, Fletcher to Dale, 24/10/23.

\textsuperscript{515} PRO: FD1/911, H. MacLean, Report on Use of Insulin, p. 3.

\textsuperscript{516} See Note 150.

\textsuperscript{517} PRO: FD1/912, Report on Graham's insulin investigations (untitled), 29/3/23.
worth enduring, rather than 'comfortable' and 'painless' as MRC trial physicians reported. The sceptical patient who wrote to The Times about being 'submitted to the course of punctures and injections and blood tests' said:

I was so sceptical after my first injection -- they jam in a sharp tube an inch or two under the skin -- that I even felt a little virtuous. My reward was a slice of good honest bread at luncheon instead of those abominable biscuits of the taste and consistency of sawdust.518

Another of these first patients writing to The Times about being on almost 4 cc of 'the new insulin treatment' per day described 'these large injections' as 'painful at the time.'519

To Summarise: The introduction of insulin into Britain was made into a public example of biological standardisation involving clinical trials of that drug. Fletcher sought to make this a public event by carefully controlling information for public consumption. He fed the national press facts about progress of this medical research that had been conducted in private, and on a few patients, as if it were a national and public event. The MRC's actions were universally defended as being in the public interest and for the public good. Fletcher and Dale made this biological standardisation production work by establishing social contracts between pharmaceutical companies, doctors and patients, thereby defining the duties and obligations, codes of acceptable behaviour of these groups. This moral management, orchestrated and controlled by the MRC for the public good, served Fletcher's vision and interests. Standardisation gave each group a different kind of credit. Some of the doctors involved saw themselves as the standardisers. As a group of 'noble scientists', specially selected to test this drug in the private spaces of their wards, or research units, Fletcher framed them as standard-setters produced by the MRC for the medical profession. Their critical judgment, clinical acumen, and idiosyncratic method of determining therapeutic effect made them each individual standard-setters. For Dale however, standardisation was strictly a laboratory activity,


519 'Insulin', The Times, 11/9/23, p. 6. This patient also described the experience as something of a ding-dong battle.
controlled by the laboratory techniques to produce a fixed weight of dry crystals. Until a dry standard was in place the scientist could not truly stand and say that insulin had been genuinely standardised. His demonstrative act at the international conference which opened this chapter was the culmination of the private laboratory experiments he conducted. While, together, Dale's and Fletcher's managerial production was about managing commercial, professional and institutional interests to produce insulin for the public, Dale's standard, the dry crystals, was about managing the place of patient testimony in the account (be it written or orally conceived) of the events leading up to the international insulin standard.

Each of these parties needed, required and expected patients to behave in particular ways: as a group they were to be painless, to restrain their demands for the drug before it was ready (i.e. before the MRC was ready to release it) and to control their appetite for standard insulin --the fruit from the MRC's tree of knowledge. The fact that they did none of these things could not be made public except to point to the national consequences of irresponsible behaviour.
The Public. Who were they? And why did they have to be appealed to? Principally, 'the public' was a resource. Idealised and analysed into different groups of patients, they were a resource which physicians could draw from to demonstrate their critical judgement, clinical acumen and individuality. Physicians demonstrated these things when they used idiosyncratic methods to determine the therapeutic effects of drugs. 'The public' was also a unorganised collection of lay people who needed to be standardised and categorised as 'unfit' or 'efficient' by Fletcher's anthropometric standard, or 'Dreyered' (by George Dreyer's standards) in classes of 'perfect' 'medium' and 'poor' fitness. The lay people who comprised the public could also be seen as demanding consumers. Framing the public as consumers, whose behaviour needed to be controlled, justified the MRC’s moral management of insulin for the public good. On other occasions the same MRC implied that ordinary people could be grouped together as a passive and credulous mass which was easily swayed by the influences of 'new' phenomena. When Fletcher refused to allow the Wellcome Pharmaceutical Company to display 'just a few grammes of insulin in a suitable container' at the British Industries Fair in the public good, he implied that the MRC needed to protect the public against nefarious commercial influences. Thus, 'the public' was a resource from which the MRC could draw evidence for their unique role within the state.

Using 'the public' as a foil against which to shape and justify public policy was a successful MRC ploy. For instance, Fletcher's MRC promoted fair dealing, and it did so in the public's interest and for the public good. As I showed Fletcher telling Balfour in Chapter 3, it was imperative for the MRC to have legal powers to standardise therapeutics, and for a Therapeutic Substances Bill to be passed in order to ensure that consumers got what they paid for. I argued that fair trading was also a motive for defining insulin as a standard commodity,
and that printing the instructions the MRC had privately issued to doctors about this drug in the public press was also in the interest of fairness.

Some recognised the MRC (and its predecessor, the Medical Research Committee) to be doing 'magnificent' work for the state because of how it engaged with the public, and because it claimed to be protecting the public against harm and danger in ways that no other department could or would. As we saw in Chapter 3, the Medical Research Committee had produced medicines for healing soldiers during the Great War by virtue of its medical research and its collaboration with industry. The MRC also sought to protect mothers and babies from unstandardised pituitary extract preparations through the Therapeutic Substances Act, just as they were protecting diabetics from unstandardised insulin in their management of the biological standardisation and therapeutic trials of insulin.

However, 'the public' was also a resource for those challenging MRC authority. As I showed in Part II, some invoked public interest to this end. The Times attacked the very election of a MacKenzie Chalmers Committee. Recall the question the paper posed: how could spending money on therapeutic standardisation genuinely be in the public's interest when millions of people were unemployed and the country's financial circumstances were so depressed? In this case public interest was a rhetorical stick used to beat a government which had tied its colours to the mast of the people, and who claimed to be in tune with the people's needs and interests. In short, The Times was challenging the minister's and his government's ability and right to control the state. However, as we saw in Part II, 'public opinion' was another rhetorical stick which could be deployed to challenge MRC authority. A body like the MRC may have been acting in the public interest, but was public opinion really on their side? This was Henry Armstrong's approach (as shown in Chapter 4) when, as Fellow of the Royal Society, he said that the MRC's 'class of a-moral scientific workers' were 'interfering with and checking' the 'discovery and invention of insulin by imposing rules' which could not 'be countenanced by public opinion'.

Nevertheless, it would be misguided to conclude that 'the public' was a virtual entity during the inter-war years. They were quite real. Lay people like Vivian Gabriel, who blamed the MRC for causing diabetic deaths through its standardising exercises, taunted this state
body when he claimed that the foreign Professor Blum of Strasbourg had stolen their insulin show. Patients also wrote to the newspapers with their personal stories. The outspoken diabetic who wrote to *The Times* about his 'ding-dong battle' with insulin is a primary example. He made his private feelings, pain and battles with the drug public, thereby speaking for himself rather than through the testimonies of doctors. Fletcher's response to Gabriel directs us to one salient point, namely, that the MRC had to manage outbursts from lay people in the public press in order to standardise insulin for the public good. An outburst like Gabriel's, featured in *The Times*, was a challenge to Fletcher's honour and the MRC's status. Similarly, the bricklayer whose prodigious use of insulin, using it as though it was his private property, had to be made an example of in the medical press. Insulin was the property of the state and its manufacture and eventual release onto the market was part of a system the state had established. The state had allowed some diabetics to have it, but if individual members of the public abused the system others would suffer.

The way in which Fletcher and Dale moved insulin from the laboratory bench, through clinical trials, to the public, draws our attention to moral management as a way of creating expertise to run clinical trials. Fletcher and Dale established social contracts between the MRC and physicians in order to create a pool of expertise. In so doing, they appeared to be operating as if they belonged to a separate class of people with inherent abilities to recognise genuineness. This ability was conveyed to other members of the same 'class' in two different ways: 1) through character sketches, and 2) by the degree and nature of their trust in each other. Morant's description of Fletcher to Balfour, and Fletcher's unstinting trust and support of Dale exemplify these points. The incommunicable skills and knowledge Fletcher and Dale deployed to recognise the authenticity of medical therapies demonstrates one kind of expertise. The scientists and physicians they trusted to biologically standardise therapies comprised another set of expertise. Fletcher and Dale promoted the national purpose of their work and shaped the MRC as a unique institutional arm of the state with expertise and the moral purpose of nation-building. Professionals such as the average doctor (or engineer, as Fletcher cited as an example of a practical man) ranked below Fletcher's MRC experts.
Significantly, these characters and experts standardised the material world around them. While the implication, for physical standards have been marginalised by experts so that the effects of standards on these individuals' lives is more easily masked (Chapter 2), this was not easily done when it came to biological standardisation. For instance, Dreyer needed policemen, mine workers, and so forth, to make the MRC's anthropometric standards. These standards would in turn be used to 'type-cast' other lay people, thereby making them more recognisable to 'practical men', that is, professionals. Standard culture types of bacteria and sera, again originating from the public body, were then used to define the type of disease ordinary people suffered from, and thus to authenticate the validity of their symptoms for the doctor.

Most significant of all for our purposes was biological standardisation. Dale saw standardisation as strictly a laboratory activity: a process by which to produce a fixed weight of dry crystals. To make these internationally recognised crystals Dale rendered physicians' reports as testimonial evidence. The recipe for making insulin was not only a form of rules for making insulin. Fletcher, Dale and Dudley clearly knew that insulin could not be made by religiously following a recipe and a set of rules. They admitted as much by sending out the recipe along with helpful hints. The recipe was also a moral stick with which to beat physicians, as Fletcher's treatment of the late-starting London group demonstrated. Recall his indignation at the fact that: 'a manufacturing firm starting with our information a week or two behind your unit ... are already making good stuff'. Making this standard also required managing the place of the patient's testimonies in any account of what a standard was and how it was made. Recall how Fletcher suggested that Dale might find the testimony of an intelligent patient useful in his research on standards, and how Dale rejected the idea saying that: 'A man like Sacks ... [his] subjective observations could be put to service, side by side with other data he could collect or record'. Labelling Sack's evidence as 'subjective' meant by definition that it had no place in his standard.

The clinicians tied into obligatory relationships with the MRC were supposed to use their incommunicable knowledge to select 'pedigree' patients on whom to try insulin. The pedigree patient exemplified the manifestations of the disease and would therefore produce an
ideal reaction to the drug. The hierarchy of incommunicable knowledge being used to recognise phenomena, to cultivate particular expertise and to standardise materials also carried through to the clinic. Clinicians objectified 'the patient' through the case. Each case was adequate evidence in itself. It seems not to have occurred to these physicians to consider statistically analysing their results. Neither did Fletcher ask the statisticians he knew to advise him. It was simply not the kind of evidence that they were after. For this to work, the patient's testimony had to be managed. The patient had to be encouraged to speak only when spoken to and to give the correct answers at that point. For instance, when Elliott reported that recovery of two of his patients, noting that one of them was a clerk, and the other had returned to her housework, he had clearly spoken to them. But for this to be evidence of efficacy, the patient's testimony had to be effaced. Elliott did not therefore admit this as patients' testimony.

Finally then, following the trail of expertise takes us back to the public and the state. It shows how individual members of the public were both subject and object at the same time. As for the patient, once he spoke out as an individual citizen offering social comment (e.g. the layman, Vivian Gabriel), he effectively stepped outside of the evidence-forming network holding him which was used to make the clinical trial. Patients could only be evidence if they had been disciplined and made into evidence by medical authorities. They could not make themselves evidence, claim to be evidence, or even to have evidence for that matter. In other words, patients did work; they did not speak. And the kind of work they did determined the kind of citizens they were. The professionals, noble scientists and eminent MRC figures who defined patients as part of their work, at the same time defined their place within the state.
PART III

HUMAN MACHINES

Establishing a Committee to organise and manage clinical trials meant setting up a regular machinery. The individual 'characters' chosen to recognise genuineness were replaced by an adjudicating body. If there was to be a machine: who would work it? How should it work? Could recognising authenticity really be formalised? Part III examines two human machines: the Therapeutic Trials Committee (which ran from 1931 to 1939), and a mass trial of the drug called 'Patulin' which was tried as a cure for the common cold which took place between 1942 and 1943. Frank Green, the Secretary of that Committee was proud to be running 'an efficient working machine'. Philip D'Arcy Hart, the Committee-Secretary for the Patulin trials was mobilising the public for a clinical trial.

If the clinical trial became a machine in the 1930s, the Patulin trial mechanised during the 1940s. In present day contexts, both these machines are seen as inadequacies and failures of the past. The Therapeutic Trials Committee (TTC) was not statistical enough, and Patulin did not cure the common cold. But while the TTC can be linked to a pre-history in which statisticians were background knowledge, the Patulin trial was a trial which involved some 1500 people and which attracted considerable interest both within the MRC and in the public domain has been written out of the MRC's history book. Sir Landsborough does not mention it once. Those who are still alive and were involved in that trial find historians' interest curious, to say the least.

In Chapter 5 I examine the formation and functioning of the TTC and show how it issued fair judgement. I argue that while this involved passing judgements on particular therapies, the Committee's more important priorities involved managing commercial and professional interests. I also show that how eminent MRC officials of the 1930s (like Fletcher until 1933 when he died, and Dale) saw the TTC's role of balancing these interests as a way
of protecting national (British) interests (particularly against the Germans). What this Committee did leave behind was the grammar of negotiations. This becomes evident in Chapter 6 where I examine the Patulin trial. More specifically, Chapter 6 shows what drove the Patulin trial and how people were mobilised to make the drug work.
CHAPTER 5

Principles, Fairness and the Therapeutic Trials Committee

The insulin trials became a precedent for other clinical tests on promising therapies after the Therapeutic Substances Act was passed in 1925. Once the Act had been passed, the MRC began to negotiate with major drug companies to set up a 'regular machinery\(^{520}\) for 'the systematic and rapid confirmation of results gained elsewhere' (as was the case for sanocrysin), or 'by the early appraisement of claims found to have been exaggerated' (as became evident in Dreyer's diaplyte vaccine). By 1931, Fletcher was able to point to a number of 'special occasions in the past' when the MRC had organised clinical trials. He pointed to 'the first introduction of insulin for the treatment of diabetes, of liver extracts for the treatment of pernicious anaemia or, again, of 'sanocrysin' and of 'diaplyte vaccine' for the treatment of tuberculosis'.\(^{521}\) The MRC established its regular machinery as the Therapeutic Trials Committee in that same year. The Committee was made up of physicians who came to run a corporate system of clinical trials that they were proud to call an 'efficient working machine'.\(^{522}\)

This chapter is about this human machine. It is about how it was made, who it served and how it was driven by the ideology of 'fairness'. I argue that the establishment of this Committee was given a distinctly national, indeed, nationalistic agenda. I show how it was the drug companies who pressed the MRC to set up this regular machinery to test their drugs; I also point to the significance of calling this Committee the Therapeutic Trials Committee (TTC) and of placing it at the centre of the system. As I demonstrated in Chapter 4, therapies would be sent out to physicians for simultaneous trials at separate centres in different parts of

\(^{520}\) PRO: FD1/2498, Fletcher to Ellis, 25/3/31.

\(^{521}\) PRO: FD1/2498, Fletcher to Ellis, 25/3/31.

\(^{522}\) PRO: FD1/3268, Note from Green, 18/1/32. Here Green refers to the Committee as an efficient working machine.
the country, where each physician tested the therapy in his own idiosyncratic way. Reports and results of particular experiments and summaries of reliable clinical judgements provided supplementary evidence for Dale's and Fletcher's program for biological standardisation of insulin. In this chapter I show that while the MRC were prepared to run a system of trials along these same lines, the doctors on the TTC used the anti-pneumococcal serum trials they had inherited to standardise trial methodology in the clinic. Focusing finally on the negotiated settlement between the Association of British Chemical Manufacturers (ABCM) and MRC which marked its beginning in 1931, I show how the body was a fair working machine.

I. First plan your 'efficient' working machine, then declare it British

In 1927, two years after the passage of Therapeutic Substances Act, the MRC set up the Chemotherapy Committee, which was headed by Henry Dale. The MRC established this particular Committee following a resolution of an ad hoc Joint Committee of the Department of Scientific and Industrial Research and the MRC, in which both parties agreed that more permanent facilities should be created for conducting clinical trials of new remedies. At the time, it was intended that manufacturers with new remedies would apply to the Chemotherapy Committee, and that Dale and his colleagues would examine the scientific and laboratory evidence for these new drugs and pass bona fide therapeutic agents on to 'a special committee' to arrange clinical trials of new drugs.

Since insulin, the MRC had organised trials of liver extracts for the treatment of pernicious anaemia, for 'sanocrysin' and of 'diaplyte vaccine' along the lines of the insulin arrangements, convening a new committee to organise a set of trials for each new remedy. Because only a few manufacturers approached this Chemotherapy Committee, Fletcher and Dale decided that there was probably no real demand within the pharmaceutical companies for a formal institutional structure for therapeutic judgement, and so they did not appoint the 'special committee' that they had initially promised to establish. The pharmaceutical companies took a rather different view of the situation.

523 See Note 2.
In 1931, representatives of the MRC held a conference with representatives of the ABCM about this question of an official machine for clinical trials. Fletcher and Dale, both of whom had campaigned for the Therapeutic Substances Act, and Elliott and Fraser, who had tested insulin in clinical trials for purposes of biological standardisation, represented the MRC. Two other MRC administrators, A. Landsborough Thomson and F. H. K. Green (who had only recently joined the MRC’s administrative staff in 1929), also attended the meeting. Each of the major drug companies sent a representative to the conference. Boots Pure Drug Co. Limited (Boots), The British Drug Houses Limited (BDH), Graesser-Monsanto Chemical Works Limited (Graesser-Monsanto), Allen and Hanbury's Limited (Allen and Hanbury's), Burroughs Wellcome and Company (Burroughs Wellcome), Evans Sons Lescher and Webb Limited (Evans Sons and Co.), and May and Baker Limited (May and Baker) were all represented, as was the Association of British Chemical Manufacturers (ABCM) itself. The meeting was held on MRC ground, at its offices on Old Queen Street in London, with the MRC’s T. R. Elliott in the chair.

Contrary to Fletcher’s and Dale's suggestion that this was not a pressing need, representatives from the drug companies argued that there was considerable demand among manufacturers for a formalised system of clinical trials. J. Davidson Pratt, the representative for the ABCM, claimed his members 'felt that some such provision for efficient clinical trials of new remedies was urgently needed'. Francis Carr, from BDH, added that Germany had a system for testing new remedies in the clinic. Carr pointed to the reasons why the drug companies were applying such pressure when he commented on the German system for clinical

524 PRO: FD1/2498, Conference with Representatives of the Association of British Chemical Manufacturers, held at 36 Old Queen Street, SW1, on 16 February 1931, p. 2.


526 See Note 5.

527 See Note 5. Italics are mine.
testing. He said that in Germany, 'these tests were generally made by individual medical men and their findings were quoted for purposes of advertisement by the manufacturers.' Carr implied that British pharmaceutical companies could not get their remedies tested and approved by the medical community in this way because, in his experience, 'doctors were afraid of publishing clinical trials of new drugs in this country lest they should be suspected of having a pecuniary interest in doing so.' The physicians on the MRC side (Fraser and Elliott) took particular offence at Carr's suggestions. Elliott 'said that in any event, such criticism could not be applied to official trials by a committee of the Council.' Besides, 'after a given drug had been officially tested and found useful, many medical men would make personal trials of it and would not then be afraid of publishing their results.'

What the drug companies wanted was an expedient way of getting their therapies clinically tested, one in which everyone understood the rules, and which would lead to their drug tests and results being publicised by the medical authorities that the doctors trusted. This was the sense of 'efficient' that Pratt conveyed, and it was echoed by Carr's contributions to the debate. With the experience of the insulin trials behind him, Elliott said 'that efficient clinical testing of a new remedy must at least take a period of weeks or months, particularly as it might be necessary for a given drug to be tested by several different clinicians.' If there was to be a clinical trial system, how would it look, and how much work would it involve? Elliott specifically asked: 'what was the largest number of new drugs likely to be submitted for clinical trial in the course of a year?' Thus, Elliott's picture of an 'efficient' clinical trial system was one that could be justified as being thorough and fair, because it could not be accused of exhibiting any 'pecuniary interest'. Clearly, the implication was that management by the MRC would allow doctors to feel professionally justified in trying and researching new drugs which had been passed through this system in their clinics.

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528 See Note 5.
529 See Note 5.
530 See Note 5.
In light of this, it is perhaps not surprising that this 'special committee', selected to manage and organise the actual trials in clinics, was deliberately made up of 'representatives of the main branches of clinical practice, who would be in touch with suitable workers to undertake the trials. The MRC and ABCM agreed to publicise the fact that such a committee had been appointed so that any manufacturer, even 'foreign ones', would know that they put in applications for their new remedies to be tested.

Fletcher and Dale had great plans for this system of formal trials. Dale envisaged that the Committee's therapeutic trials 'might even be carried out on groups of normal people'. His belief in this possibility led him to recommend that this central 'special committee' running the regular machinery be called the 'Therapeutic Trials Committee', as opposed to the 'Clinical Trials Committee', because trials on 'groups of normal people' could hardly be claimed as 'clinical' in any 'proper' sense. Fletcher recruited the members of this special committee. In the fashion which had typified the cultivating of his 'noble scientists', he wrote to Sir Farquhar Buzzard, Professor Francis R. Fraser, Dr John A. Ryle, Sir John Thomson-Walker, Professor D. P. D. Wilkie, Mr. Wilfred Trotter, Sir John Parsons, and Professor A. W. M. Ellis, telling each of them which of the eminent colleagues had been invited to join the Committee and which of them had already accepted a place. To this list Fletcher added Henry Dale, who would sit on both this 'special committee' and the Chemotherapy Committee, and T. R. Elliott who would chair this Committee. Additionally, F. H. K. Green was asked to stand as Secretary. Lord Dawson of Penn was also co-opted onto the Committee. Their role would be supervisory, he stressed. The meetings would be infrequent, 'membership will not involve any considerable amount of work', and once 'the general mode of procedure had been agreed upon', they would be able to 'transact most of the detailed business by post or by delegation of powers in

531 See Note 5.
532 See Note 5.
particular cases'. Their 'primary function' would be 'to give authority to the proposed system of testing and reporting upon approved scientific lines'.

Fletcher publicised the institution of this new machine in the MRC's Annual reports and the newspapers. Recall how, as discussed in Chapter 1, Stevens had come across its existence in the newspapers. Inventing the new tradition, Fletcher told these physicians, and then later the newspapers and the medical press, that the MRC had long been considering the 'problem of securing in the most rapid and effective way the trial under competent clinical hands of new substances or preparations which laboratory experiment may have shown to have promise of therapeutic value'. He claimed that the new committee the MRC was about to appoint would merely formalise a system of drug testing that the organisation had used 'on special occasions in the past, for instance [in] the introduction of insulin for the treatment of diabetes'. Not only did Fletcher claim the conduct of clinical trials as an MRC tradition, but when he presented this case to the doctors and the press he also implied that it was the foresight of MRC officials (acting in public interest and that of the profession) that had led to these moves to make a regular machinery out of this system. Indeed, it was precisely the potential national significance of this regular machinery that exercised Dale. Dale feared that going public in the press about this regular machinery, so soon after the structure had been erected, might have an reverse effect to the one intended. It might 'lead to the Committee being overwhelmed with requests to organise trials for foreign products, with the object of popularising them in this country.' Dale's concern about this possible imposition led him to suggest that the MRC might simply appoint the Committee, inform the ABCM of its formation, and allow a more general knowledge of its existence and authority to emerge through the circulation of reports of its work, 'rather than make a public announcement about

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535 PRO: FD1/2498, Fletcher to Ellis, 25/3/31. This letter to Ellis is an example of the kind of letter he had sent to all of these Committee members.


its formation'. Fletcher went public about the machinery nevertheless. He now stressed that the need for therapeutic testing would continue to arise in the future.

[The Council] think that advantage has come both to the profession and to the public upon each of these occasions, in different degrees, either by the systematic and rapid confirmation of results gained elsewhere or by the early [assessment] of claims found to have been exaggerated. The production of new therapeutic agents seems certain to increase rather than to diminish, and the Council think ... [it] would be useful to set up a more regular machinery for the organisation of clinical trials as need for them arises from time to time.  

This was also to be a distinctly British machine. A system in which therapeutic agents produced by British pharmaceutical companies and universities were tried and tested in Britain would show off the nation's resources (its brain power) and, more importantly, would protect the national interest. Fletcher insisted that the country needed this system because so often 'the work of University laboratories, as well as of chemical manufacturers' [in Britain] 'failed to gain its proper reward in clinical usefulness because of the practical difficulties that have hitherto prevented early effective clinical trials.' Significantly, the public was being used as a foil for making this new 'Britishness of this tradition'.

In Germany where the production of new synthetic substances is most active, physicians of good reputation are ready to publish the results of clinical trials of new and patented substances over their own names. In Great Britain, professional men, for reasons that seem obvious here, have not in the same way been willing so to use their names. It has been not uncommon, indeed, for a new substance first produced in this country to come into general recognition and use by way of clinical reports published in German journals. The profession in Great Britain have on more than one occasion had pressed upon their notice, by the medium of German literature, substances under German names that were British in first production but had escaped notice and trial by clinicians in their country of origin.

\[538\] See Note 17.  
\[539\] See Note 17.  
\[540\] See Note 17.  
\[541\] See Note 17. Fletcher's friend and colleague, Henry Dale, who was closely involved in both the establishment and the naming of the Committee, found that Germany had been given 'what might be regarded, from different points of view, as undue prominence.' Dale suggested that, for the purposes of public announcements about the Committee, that 'Germany' might perhaps be replaced by 'other countries'. Dale believed that 'it is the most conspicuous example, but the comments would apply, in
National pride continued to feature as an asset in setting up this Committee and in the conduct of its business. When Dale came across the typewritten agenda and comments of the Council on Pharmacy and Chemistry of the American Medical Association, which referred favourably to the MRC's Therapeutic Trials Committee when they appointed a Committee on the Organisation of Therapeutic Investigations of New Remedies in Hospitals in 1933, Dale took down a copy of this and sent it to Landsborough Thomson for the files. Dale wrote to Thomson:

You will see that they circulated to the members of the Council full details of the Therapeutic Trials Committee scheme, and it may interest you and Green [that one] of the members, indicated by the initials 'Be' (I have no idea who this is), comments fully and favourably on the TTC scheme, stating on p. 19 that 'The British scheme seems to me to be almost ideal in many respects'... These, I imagine, must be regarded as confidential documents, and you could hardly refer to them in a published report: but it may be some satisfaction to the MRC Office and the Council to know that the scheme is 'well-spoken of' by our American colleagues. ⁵⁴²

Similarly, in cases in which they thought British scientists were 'pioneers' in the research and development of a drug, the Committee men were keen to get their judgments of its clinical trial in print before the Germans. ⁵⁴³

The new Committee took its juridical role seriously. Not only did its members see it as an efficient working machine, but they also saw themselves as a system of fair judgement. When Sir John Thomson-Walker decided to resign from it in 1933 on account of his retirement, Green thanked him for his services regretfully because, he said, the Committee had from the outset taken the view that an expert who has himself retired from practice is in a strong judicial position for the special work of this Committee. ⁵⁴⁴

⁵⁴² PRO: FD1/2501, Dale to Thomson, 18/11/33.
⁵⁴³ PRO: FD1/2516, Green to Bramwell, 4/12/31.
⁵⁴⁴ PRO: FD1/2501, Green to Thomson-Walker, 6/11/33.
They took the position that their juridical place had two levels: one, the level of judging clinicians' reports about the trial experiments they had conducted, and the other, the level of the disinterested juror, managing the interest of the pharmaceutical industry, the public, and the profession. The new Committee inherited the clinical trial for the anti-pneumococcal serum Fletcher had began in a piecemeal fashion in the late 1930s. This trial became the focus of its establishment of a standard method for how those trials would serve as a basis for passing judgement in clinical trial results. They used the general rules of the negotiated settlement as the principles of fairness used to manage the interests of drug companies, the public and the medical profession. I turn now to how the standard trial guidelines were established.

II. Felton's serum and the standard guidelines for clinical trials.

During the mid 1920s, physicians began to write to the MRC about reports of a new American anti-pneumococcal serum that cured pneumonia. Did this drug cure pneumonia? Did it really rescue patients from their death-beds as some reports had claimed? And could the MRC please advise them on these matters? The Rockefeller Institute's Rufus Cole had produced a serum treatment against pneumococcal pneumonia, one that was, for all intents and purposes, the first successful anti-pneumococcal serum. The treatment was based on the assumption that there were different types of pneumococci -- types I, II, III, and IV -- and that against a particular type was effective against pneumonia of that type. The antiserum Cole produced was for type I pneumococcal pneumonia. By the early 1920s other workers (such as Russell Cecil, William Park, and Jesse Bullowa) were producing more concentrated sera which also included type II anti-pneumococcal sera. But despite reported successes, these sera were never popular treatments. They had to be administered intravenously, in a treatment regime which extended over several days, and the horse-based serum notoriously caused allergic reactions.

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The MRC commissioned Dr Gunn (from Liverpool University) to investigate the anti-pneumococcal serum. In 1922, Gunn reported that the anti-pneumococcal serum on the market at time was not sufficiently potent for the MRC to recommend it as a cure.\footnote{Worboys (1993).}

But a few years later, in 1924, Lloyd Felton (from Harvard Medical School) produced a 'concentrated serum' that he claimed was more potent, safer and easier to use than Cole's serum. By 1928, Felton's serum was being formally tested on patients in America.\footnote{Marks (1997), pp 60-63.} In May 1928, R. A. O'Brien, the Director of the Wellcome Physiological Research Laboratory (WPRL), wrote to Fletcher to find out whether the MRC planned to test the new 'concentrated' anti-pneumococcal serum so that the Wellcome could begin preparing to make serum to supply to the MRC for clinical trials. Fletcher was hesitant. It seemed to him that the pneumonia offered 'a much more difficult field than any in which we [the MRC] have organised inquiries hitherto'.\footnote{PRO: FD1/2367, Fletcher to O'Brien, 23/5/28.} Fletcher felt it prudent to 'wait until some \textit{prima facie} evidence [of this 'new' serum had] been presented in America', implying that the reports from America could not yet be called 'prima facie' evidence. 'If and when the proper justification is given it will become our duty to do what we can in the way of organising clinical trials here, as we have done in other circumstances'.\footnote{PRO: FD1/2367, Fletcher to O'Brien, 23/5/28.}

Pneumonia was one of the most serious diseases a person could fall prey to in the first decades of the century. It had overtaken tuberculosis to become the second largest cause of death after bronchitis during the 1920s. It was also one of the most deadly acute diseases, with an average case fatality of between 10% and 20%, rising to over 60% in the elderly. Now defined as a disease caused by the pneumococcal bacteria, it was notifiable (after 1919). There were two main types of pneumonia, lobar pneumonia (more common in adolescents and adults), and broncho-pneumonia (more common in children and the elderly).\footnote{Worboys (1993), 318-20.} In the 1920s,
when reports of the new anti-pneumococcal serum cure were emerging from America, the effects of this disease had reached folkloric proportions in the minds of physicians and patients in Britain. It would seem that few doctors in England did not have a dramatic story to tell about pneumonia. One senior medical statesman, Lord Dawson of Penn (who sat on the TTC), told his story to a group of knowing colleagues at the Medical Society of London:

> The way in which [pneumonia] descends with tragic suddenness on men still on the rising tide of their usefulness and with responsibilities of work and family on their shoulders, and in a few brief days destroys them, justifies Osler's designation of pneumonia as the 'Captain of the men of death'... One Sunday morning before the war I was called to an Eastern county. On reaching the house I found the husband dead, the wife with the rattle in her throat, and the two children engaged in a race towards death -- all from pneumonia. I realised better what the plague must have meant.\(^\text{551}\)

Penn might also have added that the prognosis was difficult, and the treatment complex, because physicians used every treatment from 'judicious non-interference' to strychnine to treat their pneumonia patients.\(^\text{552}\)

> During the spring and summer of 1929, the Wellcome Pharmaceutical Company's director, O'Brien, asked Fletcher again whether the MRC were interested in testing the new serum. O'Brien wrote:

> We corresponded last May on the serum treatment of pneumonia. Do you think the results reported since then by Park and his colleagues justify our promoting some definite clinical trials here? And would material be available?\(^\text{553}\)

O'Brien had access to one kind of 'clinical material', namely sera, which he seems to have offered the MRC for use in clinical trials. He did not have direct access to the other kind of 'clinical material', which is referred to in this letter -- patients, but physicians like Professor T. R. Elliott (UCH) and Professor Murray Lyon (Edinburgh University), who had been involved in other MRC clinical trials, were keen to provide him with the human clinical material for


\(^{552}\) See Note 32.

\(^{553}\) PRO: FD1/2367, O'Brien to Fletcher, 9/4/29.
serum trials. Elliott tried to convince Fletcher that 'the Council should take up O'Brien's offer'; it 'would not involve us in much expense', he thought. Elliott could picture a full trial of the drug. 'I would undertake the work at UCH, when all our pneumonias have been half bronchial, half lobar ... we already have some fatality data ... Bart's could certainly do it, and I should expect the London to join, and Mary's should be able to do the work'.\textsuperscript{554} Professor Lyon put in a bid for some money to purchase anti-pneumococcal serum for clinical testing from sources other than the Wellcome Pharmaceutical Company if necessary.\textsuperscript{555} He did not need to defend his expertise. He could do the tests because there was enough clinical material in Edinburgh.

In order to show the amount of material which would be available for investigation of pneumonia in the Royal Infirmary at Edinburgh, Dr Donald Stewart has undertaken a statistical review of the figures for the last ten years.\textsuperscript{556}

Dr Stanley Davidson from Edinburgh University's Bacteriological Department told Fletcher directly that:

\begin{quote}
if the MRC considers the advisability of pneumonia investigation next year immediate steps must be taken to make the concentrated serum by Felton's method.\textsuperscript{557}
\end{quote}

He, too, requested a grant from the MRC to organise serum trials.\textsuperscript{558}

Given this context of a serious disease which was prevalent, was believed to strike and be likely to kill people of any age or circumstance, backing a 'specific treatment' like the new anti-pneumococcal serum would have involved an MRC operation akin to the insulin trials. The prospects of managing public expectation, demand, consumption and anti-pneumococcal supplies on a national level may have made Fletcher shy of acting to organise clinical trials without more evidence. Be that as it may, by the late 1920s some British physicians had

\begin{footnotes}
554 PRO: FD1/2367, Elliott to Fletcher, 4/8/29.
555 PRO: FD1/2367, A. L. Thomson to Murray Lyon, 7/10/29;
556 PRO: FD1/2367, Lyon to Fletcher, 11/10/29.
557 PRO: FD1/2367, Davidson to Fletcher, 8/5/29.
558 PRO: FD1/2367, Fletcher to Davidson, 12/10/29.
\end{footnotes}
already begun to try antisera on their patients. Lederle, Parke Davis, Burroughs Wellcome and Allen Hanbury were already making the sera.\(^{559}\) Antiserum was not at the top of their prescription list because the cost was prohibitive -- a course of the treatment costing between £10 and £20 -- so panel doctors could not afford to use it on their patients. Coupled with this was the inconvenience and danger of this being an intravenous treatment usually spread over 2 or 3 days.\(^{560}\)

Fletcher decided to take up O'Brien's offer to give Wellcome's Felton serum to a select group of clinicians to test. Since requests had come mainly from Edinburgh and London, he seems to have decided to stick to these two places. But matters were complicated from the beginning, when it turned out that O'Brien might not be able to produce standardised potent serum that winter when the clinical material would be available. By October 1929 it was becoming clear that despite O'Brien's promise, and despite help from Bullowa, O'Brien would not be able to produce properly standardised sera for the MRC to give to clinicians. He had already 'used a large number of mice ... to see if one could titrate serum with sufficient accuracy to say whether a given batch was concentrated or not.'\(^{561}\) Still, by the end of that month, he said it was:

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\text{doubtful if one can on a reasonable number of mice distinguish with certainty a serum of value X from one of 5X. If this view is true, it makes any rational investigation of methods of concentration rather hopeless, and the clinician would be using something the value of which he does not know.}\]

By December of that year it was clear that O'Brien's Wellcome would not be able to supply anti-pneumococcal serum in time to recruit their pneumonia patients.\(^{562}\) The MRC arranged to purchase a supply of concentrated Felton's serum from the Lederle Antitoxins Laboratory and

\(^{559}\) PRO: FD1/2367, O'Brien, from the WPRL, was working in collaboration with Bullowa, Park and Felton to make the serum.

\(^{560}\) Worboys (1993). See also PRO: FD1/2367.

\(^{561}\) PRO: FD1/2367, O'Brien to Fletcher, 29/10/29.

\(^{562}\) PRO: FD1/2367, O'Brien to Fletcher, 29/10/29

\(^{563}\) PRO: FD1/2367, O'Brien to Bullowa, 30/10/29.
divided it between London and Edinburgh. Even with the discount Thomson had managed to procure from the company, the treatment was expensive, and so it went in dribs and drabs to select physicians in London and Edinburgh. The Therapeutic Trials Committee inherited this trial that had been put together in a piece-meal fashion mainly because of the expense of this serum, and the fact that Burroughs Wellcome were not able to supply cheaper material for testing until the following winter.

Obtaining standard serum was a problem, as was the standardisation of the Wellcome serum some were using in the winter of 1931. O'Brien confessed to having trouble in this area and had in the end resorted to taking an original sample from Felton and calling it 'standard' and identifying the sera he produced as multiples of this standard, but none of this concerned the TTC. They concerned themselves with what was going on in the clinic, and the first step was to summon reports about these expensive serum trials that the MRC were funding.

In 1932, the situation stood thus. Professor Murray Lyon was testing serum in Edinburgh, Professor Stanley Davidson was conducting trials in Aberdeen, John Ryle was supervising R. Waterfield testing serum in London, R. R. Armstrong and Francis Fraser were trying some independently at St Bartholomew's Hospital. The MRC had also given R. Cruickshank and John Cowan at Glasgow a grant of £100 to purchase serum for their clinical trials. The reports pointed to two different approaches to these clinical experiments, one in Glasgow and the other in Edinburgh and London.

The team of physicians at Glasgow Royal Infirmary acquired funds from the Red Cross and assistance from Felton to conduct their trials. The Glasgow team was headed by Cowan and Cruickshank. Cowan was familiar with clinical trials. He had tried insulin in D.
Noel Paton's department. In a fashion not dissimilar to the insulin trials, the group treated suitable cases of lobar pneumonia with serum using the patients admitted to the Belvedere Isolation Hospital. They had treated over 150 cases by this point. They based their assessment of efficacy mainly on the serum's effect in shortening the duration of pyrexia, and their impression of the patient's constitution. They also claimed to have witnessed a fall in mortality rate due to serum. And so they concluded that the serum was effective against pneumonia and was worth the effort.  

The Edinburgh and London physicians conducted their trial by giving patients in one ward Felton's serum while treating those in the adjacent ward as they would have done if the serum were not around. The patients who did not receive Felton's serum were seen as 'controls' and those he were tested formed the 'treated' group. The Edinburgh group reported a slight decrease in mortality rate, but they showed that they had been impressed by the effect of the serum by presenting the table with statistical averages of cures alongside detailed cases such as this:

Case 2 - A man, aged 28, had had pain in the left side of chest for one day before admission with a slight cough, and shivering. He was admitted on the second day of illness.

Examination: Consolidation of the left lower lobe. Patient extremely ill; collapse; cyanosis, marked Temperature 101-103; pulse 130-140; respiration 40-60 ... Progress: This patient was admitted within 24 hours of the onset of the illness, in a very critical condition. The prognosis was noted at the time as 'almost hopeless'. In all he received 12 doses of serum, injections being repeated every six or eight hours for 5 days. During that time 'life hung in the balance'. By the sixth day, however, signs of improvement were noticed and by the seventh day it was obvious that the patient was going to live ... The ward sister who also has had large experience in the nursing of pneumonia patients, attributed this to the recovery of the serum. After the third and

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569 The team comprised John Cowan and R. Cruickshank, D. P. Cuthbertson, John Flemming and A. W. Harrington. See Cowan et al., 'Treatment of Lobar Pneumonia by Felton's Serum', The Lancet, December 1930, p. 1387. See also Chapter 4 and PRO: FD1/902. Fletcher to T. R. Elliott, 21/12/22.

fourth doses of the serum both doctors and nurses clearly noticed signs of improvement.  

This was the kind of story that doctors told each other on hospital wards, in clinical meetings and at medical societies. For a physician in the 1930s reading this case, this would have captured the essence, 'the truth' of how the serum had helped to bring the patient around.

The TTC held what seems to have been the uncontested position that trials should involve control groups, that there should be alternation between control and treatment groups in order to establish a comparison between these two groups. They did not see the need to define the meaning of controls, but the term 'control' in the hands of physicians took on idiosyncratic meanings. The Committee examined the evidence produced by the Glasgow physicians along with the Edinburgh, Aberdeen and London trials. The criticisms from physicians on the Therapeutic Trials Committee also speaks of the different ideals of conducting a controlled experiment. John Ryle believed that physicians conducting clinical trials should adhere to 'the most strict conditions of trials consistent with the routine treatment of hospital patients.' By this he meant that they should conduct a close study of the case. It was not cases that made a controlled experiment, but the care and scrutiny with which those cases were examined.

Every case whether a treated or untreated 'control' case should be written up with full clinical reports which shall be available for examination together with charts and leucocyte-counts and blood pressure readings... A careful record should be made in each case of factors known to influence prognosis in pneumonia such as age, physician type, occupation and habits ... each case should be seen by independent physicians who do not know whether serum is to be given or not and who should note down his own findings and his estimate of the prognosis of the case.

Whether the experiment was controlled or not depended on the physician who could compare cases and judge therapeutic efficacy. Ryle saw the essence of these controlled clinical investigations as part of an ongoing search for causes and cures of particular diseases in

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571 See Note 51.

572 PRO: FD1/2498, Ryle to Green, 18/7/31.

573 PRO: FD1/2498, Ryle to Green, 18/7/31.
patients. Determining whether this or that treatment had a genuine effect on the disease was only one part of what a physician should aim to do when he embarked on a trial. Thus in the case of this pneumococcal serum investigation he told the Committee:

What we really want to learn is what are the adverse indications and what are the types of case which are unlikely to get better under the ordinary methods of treatments, or, in other words, what are the special indications for serum ... At the same time it we can learn to know, by clinical or other methods for quick recognition of dangerous types of organism, serum may become a very valuable addition to the older therapeutics of the disease.\(^\text{574}\)

Ryle's colleague on the TTC Arthur Ellis, had quite a different view. Ellis believed that one controlled for particular factors. A control group did not necessarily mean an untreated group. He suggested that, in addition to the series of trials already being conducted, one might set up a separate series where instead of using untreated as controls, controls were treated with similarly concentrated normal horse serum. This, he believed, would give a 'more satisfactory control of the specific nature of therapeutic action.'\(^\text{575}\) However, the sense in which physicians used the term was one in which the physician in general was engaged in a dynamic experiment, one where he held one patient in his ward against another in the same or adjacent ward. The MRC's ambivalence to the Glasgow trials indicates that while a number of things could stand as controls, it was not the case that anything could be a control. The approach of giving the patients in one hospital serum, and using pneumonia patients in other hospitals as controls, was not acceptable. Taking a statistical analysis of the mortality rate of previous years, when serum did not exist, and holding it against the year in which one gave sera to all of the suitable patients (as the Glasgow group had done), seemed to be a step beyond these boundaries.

The result of the first meeting that the Chairman Elliott called to 'draw up a standardised scheme of investigation' they agreed that in future workers should use controls in

\(^{574}\) PRO: FD1/2498, Ryle to Green, 18/7/31.

\(^{575}\) See Note 55.
their trials and that they should alternate their patients into treatment and control sets wherever possible.

Years after the Committee had disbanded and after the Streptomycin clinical trial, the Secretary, F. H. K. Green claimed that the TTC's had sought statisticians advice on a number of occasions.\textsuperscript{576} I could not find evidence of such consultations in the files which remain on the proceedings of this Committee which suggest that they may have occurred on an informal basis. Certainly, Fletcher consulted with the statisticians behind the scenes. He met with Major Greenwood at what seems to have been an informal gathering known as the Statistical Dining Club.\textsuperscript{577} The MRC also had a Statistical Committee which was headed by Major Greenwood. Much of the work of that Committee was 'not statistical at all in the academic sense of the word'.\textsuperscript{578} Quite apart from the occasional appeals to 'the statisticians' when it came to interpreting results from the serum tests for public presentation, one is faced with the issue of the idea that 25 as the minimum amount of 'clinical material' needed for a small trial was circulated as among those involved in the trials -- from the pharmaceutical companies, to the physicians without being contested. Why 25? It could have been an \textit{ad hoc} suggestion but any statistician at that time would have agreed to this as a reasonable number of patients for a trial.\textsuperscript{579} What of alternation and controls? Evidence of their statistical and experimental methodology is ubiquitous. The physicians involved in trials took the idea of dividing the patients into control and treatment groups as a given, using 'controls' and alternating groups more as a rhetorical stick rather than a category with a universal meaning. The question of who claimed these tools as their own is more fruitful and connects us to statisticians, their complex role, medical research, and more specifically clinical trials.

The statistical sphere of 1930's Britain could be reduced to a handful of people, most of whom had been trained by Karl Pearson; all knew each other. Greenwood, Pearson, and


\textsuperscript{577} PRO: FD1/7108, Greenwood to Fletcher, 8/4/28.

\textsuperscript{578} PRO: FD1/7108, Greenwood to Thomson, 21/12/27.

\textsuperscript{579} MacKenzie (1981), 105, 111-16, 211-12.
Fisher had been promoting a more scientific statistically oriented approach to medical methodology in general for some years by that time.  

Greenwood was the MRC’s favourite statistician. Major Greenwood (1880-1949) was a physician who claimed that his interest in statistics dated back to age 18 when he read Karl Pearson's *Grammar of Science*. He went to Medical school with an interest in statistics which he pursued on his own before coming under Pearson's tutelage in 1904-5 and became Pearson's protégé and friend afterwards. Greenwood was eventually appointed Statistical Medical Officer on the staff of the Ministry of Health, initially base at the Lister Institute but from 1920 onwards at the NIMR. For most of the 1920's he was employed at the Ministry of Health, the NIMR, and as chair of the MRC's Statistical Committee. From 1928 onwards the staffs of the NIMR Department, Greenwood's Ministry of Health Department, and the Statistical Committee were merged into one unit.

In 1928, Greenwood named the medical statisticians in Britain thus. The originators of the field he saw as: Brownlee, Yule, Isserlis, Henry and himself. Greenwood saw Austin Bradford Hill as one of the few first rate additions to his unit. The other promising recruit to the field was Miss Newbold but she had suffered 'a serious nervous breakdown' (and was in a nursing home at the time). Greenwood conceived of statistics as a form of critical discourse but he complained to Fletcher that because he had become a personality he was and could be vilified by physicians and scientists who took his criticisms of their work personally.

…it is not really pleasant [for] me to be regarded as a sort of devil's advocate steadily engaged in preventing young investigators having a show....But there is no statistician associated with me who can be expected to share this tiring and disagreeable business. I am the nearest approximation to an eminent person in my walk of life upon whom the Council has a shadow of claim. If upon my question of expenditure statistics can be dragged in Fletcher or Thomson, by a sort of reflex movement, dictates a letter to Greenwood.

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Greenwood was asking to be less prominent so that the statistics could speak for itself.

Although Greenwood, Fisher and Pearson promoted the use of more statistics in medicine, more generally, Austin Bradford Hill was perhaps the first to publicly claim clinical trials as his territory. He began to do this in his series of articles in The Lancet of 1937. Bradford Hill (1897-1991) was trained in statistics by Pearson and Greenwood and began his statistical career at the Industrial Fatigue Research Board. He joined Greenwood's staff in 1927. In 1937, Hill was asked by the editor of The Lancet to write a series of articles for that journal on the principles of medical statistics. He used the idea of trials on therapies as a theme taking specific cases of therapeutic trials to make broader statistical points. Even so, this was in 1937 after the Committee had been in existence for some time and Hill does not seem to have been involved in advising the TTC. In short, it seems likely that the statistician's role in devising the guidelines for the TTC's trials in the clinic, but the level of involvement and statisticians direct input remains speculative.

III. Exceptions, principles and rules

Fairness became the ideology of the TTC. My examination of these files have lead me to propose that the committee established codes of behaviour in the interest of fairness, but broke their own rules for these same reasons. How they believed they could give the public, the pharmaceutical industry and the medical profession the impression of the TTC as a fair body is the issue to which I turn. The TTC held steadfastly to certain rules in some cases. The justifications they gave for holding to the rules, the exceptions they made, and how they justified them show what fairness meant in this culture.

One of the primary assumptions was that the TTC would maintain its integrity if its name, results or 'official' status were not used to further commercial interests or advertising.

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584 PRO: FD1/7108, 'A Memorandum on the Present Position and Prospects of Medical Statisticians and Epidemiology', 23/2/28, p. 3.

From the start it was decided that the Committee would only take on 'new' therapies which could be defended on *experimental grounds* to constitute a *definite medical advance*.

Dale stressed the importance of the Committee's selecting for trial only those remedies which were really 'new' and which on experimental grounds, seemed likely to represent a definite advance in therapeutics... [There] was a likelihood of their being asked to arrange for trials of many drugs which were merely modifications of existing remedies, solely in order that their reports might be quoted for purposes of propaganda. The Committee agreed that care would have to be taken to avoid possible misuse of their reports in this way.\(^{586}\)

Refusing to allow its name to be dragged into age-old disputes between doctors and laypeople over the efficacy of therapies which had been on the market for some time was a part of establishing the TTC's place and its integrity. 'New therapies', 'experimental grounds' and 'definite medical advance' were also key words in determining what constituted a *prima facie* case of therapeutic efficacy.

The first clause of the negotiated settlement between the ABCM and the MRC in 1927 was that all manufacturers who applied for their therapies to be tested would have equal access to the system. The parties also agreed that the ABCM would hand over its membership list to the MRC, and that the representatives of this society of legitimate drug companies would pass on any information they had about drug companies both inside and outside of the Association's membership to the MRC, at the institution's request.\(^{587}\) In principle, making an application to the MRC could have taken any form, but instead of the relatively informal way that Fletcher had used to decide which drugs the MRC might test and which remedies it would not (an assessment which, as I demonstrated in Parts I and II, involved decisions about character, and on certain 'characters' assessing genuineness), the TTC designed a formal application form.

If the standardised guidelines were codes for passing judgements on therapies, the application form the TTC used for admission to the trial system was also designed to show that the Committee ran a fair system in which manufacturer who made application would be given

\[^{586}\text{PRO: FD1/5319, Private and Confidential, TTC Minutes, First meeting of the TTC, 8/7/31, p. 1.}\]

\[^{587}\text{PRO: FD1/2498, Conditions under which a special committee appointed by the Medical Research Council would undertake the clinical trial of new drugs submitted by the manufacturers. (As agreed upon in 1927 with representatives of the Association of British Chemical Manufacturers.)}\]
fair consideration. This point was made repeatedly in the Stevens case. That case also
demonstrated how this same application form could be used to exclude certain people and
elements without being appearing to be prejudicial. The application form was laid out in the
following way, and defined the following categories:

**Substance Submitted**

Manufacturers of the drug:

Purpose of the therapy:

Special advantages claimed:

Suggested mode of administration:

Chemical formula and physical properties:

Whether process is patented or not:

Pharmacological and Toxicity Tests:

Particulars of any clinical trials already made or arranged:

Remarks:

PRO: FD1/2498, Ellis to Green, 21/7/31.
The Committee had produced a formula for recognising authentic drugs. This effectively outlined the requirements for a *prima facie* case for the therapeutic efficacy of a drug. Most drugs the TTC accepted were from the major British pharmaceutical companies. Many of them could add a scientific publication when they declared the 'special advantages of the drug'. This was evidence that the therapeutic effect of the drug had been demonstrated to others beyond the laboratories of their pharmaceutical companies. Many could draw the chemical formula on the form and cite recent publications which outlined the experimental evidence and clinical experiment on one or two human beings, although the examples of trials on humans often came in the form of a typed attachment. But the application form also showed, by exclusion, what was not *prima facie*, what the Committee did not want to hear about. It did not want to know, for instance, about testimonial evidence: there is no slot for it on the form. Neither did it care for unsolicited samples of the drug to test. So when Mr Luiz Boldizsar of San Paulo, Brazil, wrote begging 'to send you all details re: my 'Cholesterine Colloide Injections', with 'an ampulla with 5 cm$^3$ of same' and asking for the MRC to 'make every possible effort to guard the secrecy of my process', his application did not look like the other forms setting out the details of therapies the Committee had authenticated. He certainly would not have helped his application with a confessional letter telling the MRC in English, which is unlikely to have been his first language, that:

Being a poor man I have much difficulty with my injection until today I have received no subsidy from anybody. It was combined my appointment to a salaried position with one of the laboratories of the Government, but owing to last year's revolution it will be impossible for a very long time. I should feel very much obliged to you if you would experiment my injections for diabetes and tuberculosis as well, but have to declare that I am unable to pay any expenses in connection herewith. This was the very reason I have sent a copy of my process to Dr R. E. Cochrane of the British Empire Leprosy Relief Association ... who was as kind as to promise me to try my injections...I shall make a collection of all official testimonials... I beg to thank you in advance for your help giving me a chance to try my injections in the British Empire. I thank you as a humble servant of science and a son of my country, Hungary.\textsuperscript{589}

\textsuperscript{589} PRO: FD1/2501, L. Boldizsar to Secretary of the MRC, 8/7/33.
In a manner not dissimilar to that used for Stevens, Señor Boldizsar was sent the brief, four-line rejection with his 'papers about it accordingly returned herewith. The Barcelona-based pharmaceutical company, 'Laboratories del Nord d'Espanya', with offices in Glasgow, did not help their case for the 'healing, antiseptic ointment on the basis of Chloramine-T' named 'Dercusan' when they included a typed list of 25 professors, medical officers, and eminent physicians from Glasgow and Spain in the 'Remarks' section of their application.

Fairness and access to the system extended beyond the assessment of authenticity at face value, when the 'face' took the form of an application. One incident, which arose out of interpretations of what came to be identified as clause 2 of the original agreement, shows how clauses could be manipulated when they were interpreted to be used in the interest of 'fairness' as a part of power struggles between pharmaceutical companies, the MRC and the medical profession. The second point in the agreement between the ABCM and the MRC was thus:

(2) The Committee shall have the right to decide without any obligation to explain their decision, whether a particular application is suitable for their acceptance or not.

When the Committee was first established in 1931, Dale suggested the TTC might bend this rule as an act of good faith to gain the confidence of the drug companies. He said:

The terms of the agreement with the ABCM give the Committee, indeed, the right of refusal, without obligation to state the reason. On the other hand, I have the feeling that the Committee might start its work under difficulties, if its first duty were to make a long sequence of such refusals. They are going to have a difficult and invidious task in any case. They will have to be constantly on their guard against attempts to use the opportunity which they offer, merely as an effective advertisement.

590 PRO: FD1/2501, Green to Boldizsar, 4/9/33.
591 PRO: FD1/2501, P. P. de J. Cusi to Secretary of the MRC, 22/3/33.
592 PRO: FD1/2498, 'Clinical Trials of New Drugs. Conditions under which a special committee appointed by the Medical Research Council would undertake the clinical trial of new drugs submitted by the manufacturers', p. 1.
593 PRO: FD1/2498, Dale to Thompson, 8/4/31, p. 2.
But Green did not have time to exercise this discretion because, in July of that same year, Drake the general manager of the ABCM, writing to Green on another matter, said he would be very grateful if you could let me have, if necessary, but not advisedly in confidence, the reasons why the Committee was unable to accept the applications on Proply guaiacol (an antihelmintic) and Parosan (an arsenical).\textsuperscript{594}

Green replied that he had 'read with surprise the remark' that it was 'advisable for the Committee to give reasons in all cases where they decline applications'. Suggesting that Drake had been misguided to make such demands, Green said: 'I take it that this represents only your personal opinion, as it is directly contrary to Clause (2) of the Agreed Conditions'. He declared Drakes' request unacceptable to the MRC, adding that the MRC:

\begin{quote}
should have supposed that your Association would not have entered into this arrangement with the Medical Research Council had the firms been in any doubt that their applications would receive 'a fair consideration'.\textsuperscript{595}
\end{quote}

Determined to find the reasons for these rejections, Drake used this same clause which was being interpreted in terms of fairness to do so. He argued that this type of disclosure was not unfair to the companies: what was unfair was keeping them in the dark. There are obviously many possibilities which might arise and which would absolutely prevent your Committee's disclosing the reasons for their rejection of an application, but I think that clause (2) of the agreed conditions was mentioned to cover only such cases and that where the reasons were quite straightforward, there would be considerable advantage in passing them on to the manufacturers. By dissemination of such information, the manufacturer will learn very quickly the criteria which determine rejection or granting of applications. Neither will the Trials Committee be troubled with applications which are always turned down for the same reason, simply because the manufacturer does not know the reason.\textsuperscript{596}

While he sympathised with Green's position with regard to clause 2, Drake spoke for the ABCM when he said that 'nevertheless, we feel that as these arrangements have been made in

\begin{flushleft}\textsuperscript{594} PRO: FD1/2498, Drake to Green, 10/7/31.\textsuperscript{595} PRO: FD1 2498, Green to Drake, 14/7/31.\textsuperscript{596} PRO: FD1/2498, Drake to Green, 16/7/31.\end{flushleft}
the spirit of the friendliest cooperation' he proposed a 'friendly discussion' on the matter.\cite{footnote:597} The two subsequently had their friendly discussion, which Green then wrote down for the record, saying that he would 'leave to [the representative of the ABCM] discretion the question as to how much of this information should be passed on to the firm concerned.\cite{footnote:598}

Another rule of the trial system was that once the Committee decided that an application for the therapeutic trial of a particular drug was unsuitable, the applicant would be free to make whatever arrangements he wished to test his remedy. This was in accord with the third agreement between the drug companies and the MRC. They also agreed that if the Committee decided to accept this application, testing the remedy would be left entirely in the Committee's hands, and the applicant would not undertake to make independent arrangements for its testing until the Committee had either a) made their report, or b) informed the applicant that their arrangements had been unsuccessful and that he was free to make his own. Successful applicants would be free to suggest the name of a particular expert to carry out clinical tests for the MRC at any stage of the proceedings. But in no case was that applicant to communicate directly with any expert whom he suspected might be testing his therapeutic agent about the progress, results or nature of those tests while the matter was still with the TTC. This was a fair enough principle, but the Committee made exceptions when it came to some pharmaceutical companies with whom the MRC had been dealing with for years if they were enthusiastic about a drug, and when drug testing came to be directly about national pride. One example of this was the case of Harmol Hydrochloride. Boots Pure Drug Company put in an application for the TTC to test this drug, whose special clinical value was as a coronary artery dilator, and it was to be tried on cases of angina (pectoris) or suspected coronary obstruction. Boots had already been dealing with Professor Gunn of the Pharmacology Department in Oxford. A paper he had published was used to back their claim for the special clinical value for this drug.\cite{footnote:599} Green wrote to Gunn, who could obviously not be asked to test

\footnote{\cite{footnote:597} PRO: FD1/2498, Drake to Green, 27/7/31.}

\footnote{\cite{footnote:598} PRO: FD1/2498, Green to Pratt, 30/7/31. The member of the ABCM with whom he met to discuss these drugs on 31/7/31 was Pratt.}
the drug, telling him which doctors he had asked to test it at the London in order to ask for his advice about a matter regarding the test.\(^{599}\)

But when Gunn told Green that the pharmaceutical company, H. Merck and Co., had recently sent him some derivatives of the Harmol compound showing even greater vasodilatory action, Dale and Green approached the drug company and told them to send in the drug for a clinical trial, saying that there was no need to go through the business of applications in this case.\(^{601}\)

The MRC and drug companies also agreed that applicants should provide details necessary for understanding the true composition and nature of the therapy submitted for trial, and that no remedy would be accepted for trial without the Committee having 'full liberty to have the relevant scientific details of its composition disclosed'. In return, the Committee would keep any information given to them as to the nature of the remedy in the strictest confidence.

The applicant was required to give the Committee full information concerning any experiments on the action of the submitted remedy, which had been made in his own laboratories or on his behalf. The Committee was free to arrange for confirmatory or other laboratory investigations to be made on their behalf before making arrangements if they saw fit. Applicants were also required to inform the Committee whether they had obtained or applied for any patent protecting the remedy, or whether they intended to use any registered trade-mark as a proprietary name for it.\(^{602}\)

The Committee had the right 'to decide whether the publication of a particular result is desirable and in the general interest, or not'. They would not publish results of a clinical trial if, on review of those results, it was decided that such results 'would not make material contribution to the general body of scientific knowledge, but would, on the other hand, adversely affect the interests of the applicant as a manufacturer.' In short, they would not

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\(^{600}\) PRO: FD1/2516, Green to Gunn, 28/10/33.

\(^{601}\) PRO: FD1/2516, Green to Gunn, 24/11/31.

\(^{602}\) PRO: FD1/2498, 'Clinical Trials of New Drugs. Conditions under which a special committee appointed by the Medical Research Council would undertake the clinical trial of new drugs submitted by the manufacturers', p.1.
publish negative results. However, should the Committee contemplate publishing the results of the clinical tests, it would be willing to inform the applicant in advance of publication, provided that such information was kept in the strictest confidence. Crucially, both parties -- the drug companies and the MRC -- agreed that applicants should not be allowed to make public use of results communicated to them by the MRC unless and until these were published. And in no case should the name of the expert who conducted the clinical tests for the Committee be mentioned in any advertisement or business publication issued by or on behalf of the applicant.

Although the application of this rule was supposed to be in everyone's interest, this was not always the case. However, the TTC stuck to this rule of disclosure more often than not. Above all, it protected the reputation of the Committee. Again, the Harmol drug case exemplifies this. The MRC were enthusiastic about Harmol and had pressed the two physicians they had asked to try it to do so quickly, before the Germans published results about this drug for angina. Somehow the newspapers had also got wind of this 'discovery'. As it turned out, the trial results were disappointing, and so the MRC held on to the conclusions of their trial, insisting on this as confidential MRC information. The trouble was, however, that the press was still promoting Harmol as a promising drug, and patients were therefore demanding it from their doctors. One physician (William Evans from the Cardiac Department) wrote to Green for advice:

I take it that it will be alright to refer to Harmol as one of the disappointing drugs tested. I continue to think that it is a pity that the reports are being held up such a long time while the Daily Press are lauding its value in angina, and patients come to one appealing for the drug which in fact had only produced toxic symptoms on a previous occasion when tried in their cases.  

Still, the TTC stuck to its guns and refused to publish a report of this inquiry.  

As for the cost of conducting trials, it was decided that the following condition should apply. First, if the investigation entailed expenditure other than personal remuneration of the

PRO: FD1/ 2516, Evans to Green, 9/3/33.

PRO: FD1/2516, Pyman to Green, 10/3/34.
experts, this would be borne by the applicant. The Committee would undertake to receive, examine and authorize any account under this heading from the expert, and present it to the applicant for payment. Second, if the expert proposed a line of investigation that involved more than minor expenditure, such as on costly apparatus, clerical salaries, or extensive travelling, the proposed expenditure would be submitted to the applicant by the Committee before it was incurred. Third, if it was considered desirable that the manufacturers should contribute funds for the personal remuneration of the experts conducting the tests, any such contribution would be paid to the Medical Research Council, and the Council would make a suitable grant from its general fund to the expert. Fourth, if such contributions were required, it would be a matter for the ABCM to decide whether the individual applicant should make a contribution in support of an investigation, or whether the Association would itself make an appropriate periodical grant to the Council on some agreed basis. In any case, there would be no question of direct financial remuneration between the manufacturer and the medical expert.\footnote{\textit{Conclusions: Fairness.}}

In 1939 the TTC was formerly disbanded because of the threat of war. During its existence it processed over 60 applications for drugs. They organised small scale trials often sending a drug out to one or two doctors (though sometimes more) which their expert committee of physicians had recommended. Once the results were in the TTC's hands believed they were in a position to decide to endorse a drug or not. Short histories of the clinical trial have focused on this Committee's trials as statistically unsound trials which came before statisticians were actively involved. More important, however, was the TTC's ideology of fairness.

The Committee operated under the assumption that establishing standard guidelines and disclosing the rules of the trial system encouraged fair dealing. The requirements for entry to the MRC's clinical trial system were disclosed in a standard application form which gave the impression that anyone who followed the rules would have access to the system. The TTC also framed the agreement between the ABCM and MRC as a set of clauses which exposed the

\footnote{\textit{PRO: FD1/2498, 'Clinical Trials of New Drugs. Conditions under which a special committee appointed by the Medical Research Council would undertake the clinical trial of new drugs submitted by the manufacturers', p. 2.}}
rules of the game. However, although these rules and standards which gave the impression of fair dealing as public activity were often in conflict with informal principles, namely: confidentiality, giving the appearance of acting in good faith, of balancing commercial interests against professional interests, and protecting British national interests. The result was that although the TTC presented fair dealing as a activity based on public rules, in private the Committee set aside its public rules in order to uphold these private principles. Both the members of the ABCM and the administrators of the TTC appreciated the decidedly private nature of fair dealing.
CHAPTER 6

The Common Man's Cold:
Mobilisation and the Masses in the Patulin Trials

It was Sunday evening, 5 March, 1944. Dr Philip D'Arcy Hart took the 9.20 am train from Euston station in London to Glasgow Central Station. Hart was on his way to Glasgow on MRC business. He was Secretary of the Patulin Trials Committee set up to organise a mass trial to test if Patulin cured the common cold. Hart would watch the morning and mid-morning sessions of the Patulin trial at the Rolls Royce factory in Hillington, then visit the Royal Ordnance Factory at Bishopton in the afternoon, with the view to taking the train back to London that evening. Hillington and Bishopton were just two of the eleven factories where Patulin was being tested on ordinary working people with common colds. Members of the public were also being recruited from three General Post Offices and three public schools. In total, some 1,300 people, up and down the country, were mobilised to try this drug.

This was not only a mass clinical experiment, it was an experiment which was being conducted in a country at war. Hart and his Assistant Secretary, Joan Faulkner (now Lady Doll) had to travel up and down the country to conduct this trial. And travelling during the war was 'a nightmare' by many accounts. Quite apart from the overcrowded stations full of military men on leave, and the disruption caused by bombs and raids, the station signs and road signposts had been swapped or removed altogether. They (as Hart recalled) had been swapped to confuse invading Germans, but it was the travelling Briton they foxed. Hart and

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606* From this point Dr Philip D'Arcy Hart will be referred to as Hart.

607 PRO: FD1/3156; PRO: FD1/3157; PRO: FD1/3158.

608 Ferneybough (1975), 173.

609 I am grateful to Sir Philip D'Arcy Hart for allowing me to interview him. During his presentation at the Wellcome Trust Witness Seminar on 8/11/94, Hart talked specifically about how difficult it was to travel during the war, mentioning the confusion which arose because of these changes in road and station signs. See Wellcome Trust Witness Seminar, 'Pneumoconiosis of Coal Workers, with Dr
Faulkner shuttled between train stations and station hotels, between this city and that, and from one factory to the next to make sure that the Patulin trials in these places were being carried out properly. When they were not on the move, they were either telephoning or writing to factory medical officers, school physicians, and drug manufacturers from their station at the London School of Tropical Medicine and Hygiene where the MRC had been moved temporarily (during the war). Hart and Faulkner needed to be in contact with these people either to visit, or to coordinate the times when the pharmaceutical company, The British Drug Houses Limited (BDH), would deliver the bottles of Patulin and control solutions to factories and so forth.  

610 They did this for about six months between December 1943 and May 1944, each local Patulin trial running for about six to eight weeks.  

611 By May 1944, Hart and Faulkner may have seen some irony in the official government slogan designed to discourage civilian travel which asked: 'Is Your Journey Really Necessary?', because the Patulin trial was a complete failure.  

Why did the MRC conduct this trial? And why did it have to be such as a massive trial? This clinical trial was quite unlike any of the trials the Therapeutic Trials Committee had conducted during the previous decade. It demanded unstinting commitment from those producing, supplying and testing the drug. It also required national resources to be mobilised. This Patulin trial was run just a year or so after the 'blitz' of 1940-41 which had caused widespread and major damage in a number of large towns and cities, and it occurred during a period when the population were mobilised on an unprecedented scale. The physical upheaval of war involved what was effectively the mobilisation of the entire population.

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610 PRO: FD1/3156; PRO: FD1/3157; PRO: FD1/3158.  

611 PRO: FD1/3157, Greenwood to Faulkner, 23/3/44.  

612 Longmate (1973), 294-6.  


614 The list of personal anthologies and accounts are too numerous to list here. For examples of literary and personal histories of the effects of bombing, evacuation and the associated mobilisation of
Britain changed from being a country in which about half of the population did not leave home for even a single night of the year, to one in which 60 million changes of addresses were recorded in 1939 alone. Indeed 'mobilisation' became a defining feature of the Second World War. It was also a metaphor for the legitimacy of unprecedented state control at that time. The Ministry of Labour had almost limitless legal powers to actively mobilise the human material resources to fuel the factories that made ammunition, engines and other essential war materials. Historians of the Second World War and the immediate post-war period record that Britain was the most thoroughly 'mobilised' of the Allied, or even the Axis nations for that matter. Similarly, Chamberlain and Churchill are also described as 'mobilising' words in their morale-building orations. But the imperative of mobilisation was sold as something that morally upright citizens volunteered for.

The context of war-time mobilisation made this MRC mass trial possible. As the events of this trial unfold, I shall show how the same Ministry of Supply that mobilised and supplied material to factories also supplied people for the MRC to test Patulin. The General Post Offices, from which civilians were sometimes recruited for war work, also provided human material for this mass trial. Thus the trial itself should be seen as an example of the kind of mass mobilisation and volunteerism associated with this period.

people, see Green (1945); Harrisson (1976); Crosby (1986), 34; Johnson (ed. 1968); Boyd (ed. 1944), 57.


616 A substantial bureaucracy was created for this purpose, based on 12 civil defense regions. This mobilisation occurred at the highest levels of resources. Oxford and Cambridge dons and academics were recruited into Whitehall as civil servants to help manage the state. The nation's 'best minds' were uprooted and dispatched to Station X at Bletchley Park in Buckinghamshire as code-breakers. See Lee (1980); Hennessy (1988), 88-119. In addition to the studies of mobilisation of labour at a national level, David Thoms' social history of the Midlands provides a study of the effects of war-time mobilisation, organisation and the effects on the economy and the social changes on a particular region due to the changes in employment profile there. See Thoms (1989); Parker (1957), 253-5; Kirkham and Thoms (eds 1995), 3-13; Dreisziger (1981), 1-23.

617 Examples of this can be found in Hennessy (1992), 8, 25.

Patulin did not prove to be a cure for the common cold. By May 1944, MRC officials were embarrassed to have been involved in a venture some now saw as worthless. How the MRC came to be testing Patulin for the common cold, and how they justified this use of resources are the issues I shall address in this chapter. The history of this trial is driven by four main actors: Hart and Faulkner, whose decisive roles made this mass trial run like a machine; Professor Harold Raistrick, the 'discoverer' of Patulin, who desperately wanted to prove this drug to cure colds; and Professor Major Greenwood, whose statistical assessment of *prima facie* evidence allowed statistics to be used to rescue the situation.

1. Raistrick: the Patulin discovery driven by what might have been

'Patulin' was the name that Professor Raistrick gave to the 'colourless beautifully crystalline' substance he had isolated from the metabolic product of a lower fungus (mould), *Penicillium patulum* Barnier. Raistrick's team published a series of articles about the antibacterial properties of substances produced by a series of penicillium moulds between 1941 and 1943, one of which was *P. patulum* Barnier. Professor William Gye, the Director of the Imperial Cancer Research Fund Laboratories at that time, asked Raistrick for a sample of Patulin to see if it had chemotherapeutic properties against cancer. Raistrick obliged. It so happened that Gye was suffering with a cold when the Patulin was delivered to his laboratory. According to Gye, he decided, by chance, to try this substance that he was supposed to use in his cancer experiments, on himself. Gye believed that the Patulin cured his cold and reported his discovery to Raistrick.

Raistrick was an accomplished chemist and biochemist. He was Professor of Biochemistry at the London School of Tropical Medicine and Hygiene (LSTMH), a professorial chair that he had held since 1929. He was elected Fellow of the Royal Society in

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619 Raistrick(1943). Raistrick's group had identified the chemical structure of Patulin as anhydro-3-hydroxymethylene-tetrahydro-y-pyrone-2-carboxylic acid.

620 Birkenshaw, Michael, Bracken, and Raistrick (1943), 625-30.

621 Raistrick (1943), 625.
1934, and was regarded as one of the leading experts on moulds in Britain at the time.\textsuperscript{622} But 'the father of the study of fungal metabolites',\textsuperscript{623} the man whom Ernest Chain described as 'one of the finest natural products chemists this country has ever produced',\textsuperscript{624} had missed out on penicillin. Raistrick had missed out on this monumental discovery because he had failed to recognise its potential. His group had investigated the three products of Fleming's mould soon after the discovery, but Raistrick had decided not to pursue the project, partly because it was an unsuitable research project for PhD students, and partly because he took the advice of medical friends who told him that penicillin was too unstable to have any practical clinical value. Raistrick's failure to grasp this opportunity seems to have haunted him to his grave.\textsuperscript{625} Two of his biographers, Ronald Bentley and Robert Thomas, captured his predicament thus:

\begin{quote}
As the poet Whittier has written,
'For all sad words of tongue or pen
The saddest are these: It might have been!'
\end{quote}

Given his brush with fame with the penicillin case, it is understandable that when Gye told Raistrick about his chance discovery that Patulin had cured his common cold in a story remarkable similar to that about penicillin, Raistrick pulled out all the stops.\textsuperscript{627} The events of how this trial came into being not only bear this out, but as the events of the trial unfold, I shall raise the question of whether the size of this mass trial might not also be attributed to Raistrick's dashed hopes and failed aspirations.

Raistrick approached the pharmaceutical industry and the military and arranged his own preliminary trials. With the war on, and the MRC's Therapeutic Trials Committee

\textsuperscript{622} Ernest Chain was the famous scientist who shared the Nobel Prize with Fleming and Florey for the discovery of penicillin. Birkenshaw (1972); Bentley and Thomas (1990).

\textsuperscript{623} Thomas (1978).

\textsuperscript{624} Bentley and Thomas (1990), 5; and E. Chain, 'Harold Raistrick, Obituary,' The Times, 19/3/71.

\textsuperscript{625} Bentley and Thomas (1990), 3; Birkenshaw (1972), 497.

\textsuperscript{626} Bentley and Thomas (1990), 6.

disbanded, arranging a clinical trial was quite a different matter to what it had been during the inter-war years. If Raistrick had dealt openly and directly with the pharmaceutical companies before approaching the MRC during the 1930s, the MRC would have been unimpressed. They might even have refused to try the drug on the basis that, with such intense commercial interest, the drug might not have received a fair trial. In the war-time context however, the pharmaceutical companies were a valuable national resource. They were producing drugs to save soldiers on the front line, and developing ways to mass produce the miracle drug penicillin, and the sulphonamide drugs. Adopting a disinterested position for the sake of the principle of fair dealing, as I showed Fletcher exhibiting during the inter-war years, would have seemed particularly rarefied.

Raistrick approached the Therapeutic Research Corporation of Great Britain (TRC) to develop his curative Patulin crystals. This consortium of the major British pharmaceutical companies -- The British Drug Houses Limited, May and Baker Limited, Boots Pure Drug Limited, Glaxo Laboratory Limited and The Wellcome Foundation Limited -- had only recently been established in 1941. Pharmaceutical companies were increasingly supplying doctors with materials and funds to research into, and to develop new drugs, so much so that some doctors accused 'enterprising' drug companies of trying 'to take over the whole field of medicine for their province.' The TRC agreed to support Raistrick in his experiments on the drug. They provided him with money and equipment, and their laboratory staff were on hand to give him advice in his biochemical investigations of Patulin.

628 For the TRC's role in developing penicillin, see Liebenau (1987), 69-86. See also Neushul (1993), 371-95.

629 This was the brainchild of the chairman of Burroughs Wellcome pharmaceutical company. See Note 23. Lord Trent represented the Boots Pure Drug Limited, C. A. Hill, the British Drugs Houses Limited, H. Jephcott, Glaxo Laboratory Ltd., T. Maxwell the May and Baker Ltd, and T. R. G. Bennett, the Wellcome Foundation Ltd. J. Slinn (1995), 180-7.

630 See BMJ (1938), 1: 1235. A description of the shift in power between doctors and the pharmaceutical companies is described by Liebenau (1987), Robson (1989); and Slinn (1995), where Research and Development of these companies is discussed in more detail.

631 Raistrick (1943), 630. In his acknowledgements Raistrick specifically thanks the Therapeutic Research Corporation for providing a number of synthetic reference samples which were of great value in identifying breakdown products of patulin. Raistrick also said that he had benefited from
Raistrick managed to convince the military to test Patulin on soldiers. The forces were interested in a cure for the common cold because it was responsible 'for more absenteeism and loss of efficiency than any other disorder or group of disorders'. Naval authorities admitted as much when they reported the results of their trials. But the Army and the Navy trials produced opposite conclusions. Commander W. A. Hopkins tested Patulin on Naval men. Captain J. M. Stansfield, Major A. E. Francis, and Major C. H. Stuart-Harris from the RAMC tested Patulin on Army soldiers. Raistrick supplied crystalline Patulin he had purified in his laboratories (at the LSTMH) and advised the officers on how to prepare buffered treatment and control solutions of the drug. Hopkins conducted three sequential controlled clinical trials: one in January 1943 on 93 men, the second in February 1943 on 49 subjects, and a third in April 1943 on 36 patients. He proved that Patulin cured the common cold. In contrast, the Army officers who conducted two sets of controlled trials by the same method, one on 50 soldiers (in March 1943), and another on 100 soldiers (between August and September of the same year), concluded that Patulin did not cure the common cold.

Raistrick assembled a portfolio of evidence -- *prima facie* evidence -- for the efficacy of Patulin, which included the biochemical evidence his research group had produced, the self-experiment of Professor Gye, the results of Commander Hopkins’ Naval trials, and a statistical commentary on the positive clinical trials from an eminent MRC statistician, Major Greenwood. He omitted the negative results. Raistrick went public with this evidence. He published it in *The Lancet* of 20 November 1943, as opposed to doing so in the *Philosophical Transactions of the Royal Society of London* and the *Biochemical Journal*, where the 53-year-old professor had published the vast majority of the 137 articles in his name (up to that point in many helpful discussions during the course of the work with the research staffs of the Corporation. The Therapeutic Research Corporation also provided financial assistance in the form of a grant for S. E. Michael, a member of Raistrick’s team, to take part in the work.

632 Hopkins (1943), 632.

633 This was not unusual in the context of war. Certainly, during the First World War a number of therapies, vaccines and drugs had been tried on soldiers and naval men.


his career. His biochemical evidence pointed to the 'natural' origins of Patulin by demonstrating that his research team had isolated and labelled the two strains of *P. patulum*.

Barnier. Raistrick proved the ontological status of the active ingredient when he gave these natural compounds a local identity within the museum of standard types at the London School of Tropical Medicine and Hygiene. He demonstrated Patulin's potent antibacterial qualities with evidence that a solution of Patulin crystals (diluted in 1: 64,000 solution) completely inhibited the growth of *Staphylococcus aureus*. Professor Gye's raw testimony showed that this antibacterial effect from experiments in a petri dish translated into a genuine therapeutic effect in human beings with the common cold. Gye told the story of how Patulin had cured his cold:

> When the supply of Patulin was received, I was in the second stage of a severe common cold which had kept me indoors for two days. A watery solution of unknown strength, but probably, judging by subsequent tests, at least 1 in 1000, was prepared and the nasal passages were thoroughly doused with it. The douching caused some pain, but since it was followed within an hour by clearing of the nasal passages it was repeated twice with solutions of about a tenth the original strength. The third and last application of Patulin was made about 9 pm [of that same night.] A night of undisturbed rest, the first for three days, was obtained and next morning I was completely well and back at work.

Gye admitted that his self-experiment was 'uncontrolled' and 'therefore of no solid scientific value', but his rank as physician and professor made him a discerning witness who authenticated the link between Patulin and the common cold. Furthermore, Gye suggested that his own experience had been confirmed in the personal trials he had made on his staff members, and on the friends he had asked to douche themselves with Patulin solution. Sifting through the stories from the friends who found 'nasal douching difficult or too much bother to carry out', those who were 'not sufficiently exact either as to duration of illness, symptoms or effects of treatment to enable one to reach any conclusions', or worse, 'appeared to exaggerate the beneficial effects', the discerning Gye claimed that reliable testimonies from his professional colleagues who 'produced the most useful information', confirmed his story of how

635 Birkenshaw (1972).

636 Gye (1943), 630.

637 See Note 31.
Patulin had cured his cold. He copied some of these down in his part of the co-authored article in *The Lancet*, to show that this was the case.\textsuperscript{638}

Commander Hopkins' clinical trials were wheeled in to prove the point that Patulin cured the cold scientifically. In three sets of trials carried out during the winter and spring of 1943, Hopkins tried Patulin and control solutions on a total of 180 naval men at the Royal Naval depot in the South East.\textsuperscript{639} Hopkins gave Patulin to 95 men (the treated group), and control solutions consisting only of phosphate buffer to 85 men.\textsuperscript{640} He tested these groups of soldiers on Patulin and control solutions in alternation, but the men were under the impression that they had all had the same treatment. The trial subjects were treated 4-hourly during the day, and then examined after 24 and 48 hours. Hopkins admitted that 'a certain number of the men, both treated and controls, had made up their minds that they were going to be cured, and claimed complete alleviation of their symptoms when asked what they felt'.\textsuperscript{641} He tried to compensate for these biases by interrogating and examining patients who said that they had been 'cured' in each case. Only those men who said that 'they felt better', and who, after questioning and examination were found 'to be symptom-free' and have 'no objective signs' immediately afterwards and within 3 days of treatment, were assigned as 'cures'. Patients whose symptoms were unaffected or who had 'improved', were defined as 'not cured'. Of the 95 patients tested during the first lot of patients in January, 54 received (1: 20,000) Patulin solutions, and 41 control solutions, Hopkins recorded that 24 of those in the treated group were cured by Patulin, while only 1 cure occurred in the control group. The second trial in February involved 49 patients: 23 treated with (1: 10,000) Patulin and 26 control solutions. Sixteen of the 23 treated patients were cured after the treatment, only 3 of the 26 control patients recovered after receiving the control. The third clinical trial of 36 patients (18 treated with

\textsuperscript{638} See Note 31.

\textsuperscript{639} Hopkins did these trials after performing experiments on the biological properties of Patulin (such as its effects on human serum, pus, blood leucocytes) and toxicity experiments on mice to estimate minimum and lethal dosages for humans.

\textsuperscript{640} They received phosphate buffered (pH 6.0) Patulin solutions.

\textsuperscript{641} Raistrick *et al.* (1943), 631.
Patulin 1: 5,000, and 18 with controls of 1: 5,000) treated in April had 15 cures in the
treatment group, and 4 cures in the control group. Hopkins' aggregating the percentage cures in
treatment and control groups, argued that his trial had demonstrated that 55 of the 95 patients
treated with Patulin had recovered within 3 days of treatment, while 8 of the 85 control
patients recovered in that time.

Finally, we come to Greenwood's statistical commentary. Appending a statistical
commentary to experimental and clinical evidence to make a *prima facie* case was unusual.
But both this statistician's input and the nature of his commentary would come to have far-
reaching implications for this trial in the months that followed. Greenwood claimed that
Hopkins' results posed a purely statistical question:

> Assuming that the treated and controlled populations do not differ in any material way,
except in regard to the fact of treatment, what is the probability that such divergent
percentage of cure would emerge [between the control and treatment groups]?

He recommended a statistical framing of the results, using what he referred to as 'a well-known
statistical method'. Greenwood was critical of Hopkins' attempts to aggregate the results to
produce an overall percentage of cures in each group. These trials had been conducted on
different occasions. They should therefore be treated as three separate experiments. So
Greenwood divided Hopkins' data into three time blocks: January, February and April. He then
examined the data in three ways, demonstrating that each of his approaches gave the same
answer: namely, that Hopkins could not have produced these results by accident.

First, Greenwood gave the expert statistician's intuitive testimony of the data. In the
eyes of a statistician, 'common sense suggested that the differences of percentage are unlikely

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642 Raistrick *et al.* (1943), 631.

643 Raistrick *et al.* (1943), 631.

644 The three groups were also different because they had received solutions of different strengths.
This may have figured in Greenwood's reasons as to why the groups should be separated, but he did
not mention it. For a detailed analysis of both Pearson's chi-squared goodness of fit test (which he
first described around 1900), and his chi-square test of independence (of 1904), see Magnello
(forthcoming). I am grateful for Eileen Magnello for allowing me to read this paper.
to be 'chance happenings'. His second examination of the data involved applying a statistical test, what Greenwood called 'an exact test', to the third data set (i.e. the April trials), which he believed was most favourable to the hypothesis of chance deviation. Greenwood did not specify why he selected this set, but it is likely that he chose it because it was well balanced, with 18 patients in both treatment and control groups, and because it was the least biased (given that in the trials conducted on the third batch of solutions, neither investigators nor patients knew who was receiving treatment and control solutions). He concluded that 'a random sampling so wide and a divergence in favour of the treated would occur about 3 times in 10,000 trials. In other words, there was a 3 in 10,000 chance that Hopkins could have obtained these promising results by accident. Greenwood's third comment on Hopkins' data, which involved an attempt to engage and convince a medical audience, was thus:

If two batches of pennies are tossed, the respective percentages of 'heads' are likely to differ, and the probability that any particular difference, or a greater difference, would occur can be readily calculated.

Greenwood discounted the possibility that the Patulin tests may have been invalid because the groups might be materially different, on the grounds that only patients with especially obstinate colds had selected themselves for treatment. Then he proved the impossibility of Hopkins' results as chance events by returning to his statistical analogy involving the coins. Greenwood presented the argument thus:

If an experiment were made with batches of coins fresh from the mint, and their respective percentages of head differed in such a way that, tested as these data have been tested, a probability of, say, less than 3 in 10,000 emerged that they came from a common universe, no sensible person would infer that the mint coins were biased.

He concluded that either a) there had been some trick in tossing, or b) a 'very improbable event had happened'. In effect, Greenwood said that there was a 3 in 10,000 chance of Hopkins'

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645 Raistrick et al. (1943), 631.

646 See Note 40.

647 See Note 40.

648 See Note 40.
data being an accident, thus lending credibility to the positive results of Hopkins' trials by saying what they were not. Crucially, they were not accidental.

Greenwood's presentation seems to have been designed to convince a non-statistical audience (the average doctor, for example) of the validity of this evidence about Patulin. By appealing to 'common sense', he implied that expert knowledge and statistical calculations were based on what sensible and intelligent people already knew to be a reasonable outcome.

Greenwood's ploy to engage with a wider audience was to hide the details of the statistical methods he applied to highlight the importance of these Patulin results. The 'exact test' he applied on Hopkins' third data set was in fact Pearson's chi-squared test of independence: a test commonly used to show whether there is a significant difference in treatment effect between one method and another. Despite the fact that this test would have been in every statistical textbook, and that it was one of the most widely used tests in medical and biological calculations at the time (and had been since the turn of the century), Greenwood never specifically identified it by name in his commentary. Instead, he directed the readers to R. A. Fisher's *Statistical Methods for Research Workers*, in which they might find the test. But when Greenwood pointed the reader to Fisher's book, he was not directing the reader to Fisherian statistics, he was pointing to an example of a statistical text accessible for the wider medical audience that *The Lancet* addressed.

Despite the fact that Greenwood translated the results of his statistical calculations to produce propositions about Hopkins' trials in ordinary language throughout his commentary, when it came to the final analysis, he recast them in a semi-technical language. He fell short of saying that because the test results were not accidental the treatment must work. In Greenwood's concluding words:

> In our case there is no such *a priori* improbability that the antibacterial substance might accelerate a cure; that it does do so is a tenable hypothesis. But, and this is the point always to be had in mind, what the statistician has shown is *not* that the odds are so and so many thousands to one against the chance that such results would emerge without *some* differentiation between the groups. Whether at other times and in groups differently chosen the same differentiation would be found can only be known when further trials have been made.\(^{549}\)
In so doing he implied that solid proof that Patulin cured the common cold could be produced incrementally by conducting more and more trials which, after analysis in each case, could be shown to have been non-accidental. Each trial would make the evidence stronger and would be *prima facie* evidence for another trial. The weight of the sum total of these units of evidence taken with 'common sense' would prove Patulin's effect on the cold. Only 'common sense' would decide the stopping point for these mini-trials.\(^{650}\)

II. *Making the prima facie evidence acceptable evidence for a mass trial*

Raistrick's evidence was enough to convince the pharmaceutical companies that Patulin had promise. But while the claim that Patulin cured the common cold may have been scientifically plausible, this disease was broadly defined as one that varied from season to season. These factors, coupled with equivocal Army trial results which, although unpublished, were public knowledge, might not have made it seem financially viable or justifiable for the TRC to invest in mass producing and marketing Patulin.\(^{651}\) Encouraged by the returns of their investment in the project, the TRC's representatives approached the General Post Office, the Ministry of Supply and the Royal Ordnance Factories to recruit volunteers from these places to try Patulin in clinical trials all over the country, while Raistrick's *Lancet* article was still in press. They had already received tentative commitments from these authorities when one representative, Dr Forgan, contacted the MRC to ask for their help in organising these clinical trials.\(^{652}\)

The MRC's Therapeutic Trials Committee had established codes of behaviour and conduct for clinical trials with the consortium of pharmaceutical companies which made up the Therapeutic Research Corporation during the 1930s. I demonstrated this in Chapter 5. But when Dr Forgan (from the TRC) approached the MRC about Patulin on 22 October 1943, he

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\(^{649}\) See Note 40. The italics are Greenwood's.

\(^{650}\) See Note 40.

\(^{651}\) These results were mentioned in the newspapers and the medical journals on this subject. How the papers acquired these acts is unclear.

\(^{652}\) PRO: FD1/3155, Note about telephone conversation by Thomson, 22/10/43.
did not begin on the defensive, but appeared to be acting on the assumption that the prima facie evidence for Patulin was a given, indeed, that it was common knowledge. Neither did Forgan propose that the MRC should take over the pharmaceutical companies' clinical trials. Landsborough Thomson filed a record of his conversation with Forgan on the day he approached the MRC. Thomson said that when Forgan telephoned he asked

> whether the MRC would be likely to accept a suggestion that they should also organise such trials, with material to be supplied by the Corporation.\(^{653}\)

Thomson recorded that: 'I [Thomson] said that the Council would' almost `certainly not interest themselves in the matter if other trials were being made at the same time'.\(^{654}\) In the same phone call, according to Thomson, immediately after he had rejected Forgan's initial proposal, Forgan said that the TRC would be willing to leave the Council a clear field, if they could assure the TRC that the MRC would act without delay.\(^{655}\) It would seem that Fletcher's social contracts in the insulin trial and the MRC's Therapeutic Trials Committee had not only established codes of conduct for trials, they had also established the grammar of negotiations between pharmaceutical companies and the MRC. And so the two parties, the MRC and the Therapeutics Research Corporation, bargained for controlling rights over various aspects of the Patulin trial, each party bargaining with full knowledge of the other's limits. This came through in the negotiations about the Patulin trial. When Thomson, in his role as administrator and civil servant, recorded his telephone conversation with Forgan, he was making a record for the files of the excellent bargain he had secured for the MRC.

> The pharmaceutical companies knew that the MRC would not conduct a clinical trial of a drug if there were other trials being conducted at the same time. And yet Forgan began the bargaining by asking 'whether the Council would be willing to include in the scheme some of those whom the Corporation have already tentatively approved.'\(^{656}\) Thomson records that he

\(^{653}\) See Note 47.

\(^{654}\) See Note 47.

\(^{655}\) See Note 47.
had refused to allow this: ‘I said that the Council would be willing to take over any such arrangements as they considered suitable’. 657

The MRC's bargaining card was that it was the state authority that had been judging the therapeutic efficacy of promising new drugs, vaccines and sera for some twenty years by this point. Furthermore, it had established a system for assessing therapeutic values. The MRC's association with this trial would lend legitimacy to Patulin. If the TRC went ahead and conducted a mass trial on their own, the MRC were likely to refuse to conduct any subsequent Patulin trials should the results of their trial prove equivocal.

Forgan and Thomson also negotiated a settlement for who should be involved in arranging the trial, and how. According to Thomson's records, Forgan had proposed that the MRC appoint an ad hoc committee to supervise the trials, which would include two medical representatives of the Corporation (probably Forgan himself, and Parish), Sir Henry Bashford (General Post Office) and Dr Amor (Ministry of Supply). 658 The pharmaceutical companies had already made tentative arrangements with Bashford and Amor. Thomson described how he had made it clear that the Council would probably wish to have such a committee, and that he saw no difficulty in principle about including the people mentioned. 659 In the meantime, Professor Harold Himsworth was asked to chair an ad hoc committee comprising the people Forgan had put forward, but with the view that the MRC would select a suitable Secretary. Five days later, on 27 October, Thomson phoned to give final confirmation of the ad hoc committee and details of its members.

Again, the absence of the Therapeutic Trials Committee undoubtedly gave the pharmaceutical companies of the TRC more bargaining power with the MRC. It was conceivable that, during wartime, a penicillium mould cure for the common cold would have been deemed important enough to be taken up by other authoritative bodies of the state. First,

656 See Note 47.
657 See Note 47.
658 See Note 47.
659 See Note 47.
the Ministry of Health had joined forces with the Ministry of Information in launching a national campaign to 'keep the nation fighting fit' by urging the public to avoid careless coughing and sneezing in order to reduce the spread of colds, influenza and other droplet infections. This campaign to educate the public through posters, vehicle bills, window displays and films such as 'The Nose has had it', and 'Breath of Danger', ran for each winter throughout the war. But it is possible that in this context, this consortium of the most important drug companies in the country at the time could have conducted a respectable mass clinical trial in 1943. Second, given their marketing approach of targeting the public, and with drug companies like Boots having their own display shops to advertise their products, these companies might have been able to successfully market Patulin without the legitimacy of an MRC trial.660 By establishing speed and efficiency as conditions for leaving the Council a clear field, the TRC implied that inefficiency was too large a price to pay for a stamp of MRC approval.

Having planned to run a large-scale trial of Patulin for the drug companies, the MRC needed to convince the masses to volunteer their common colds for the cause. But before the membership of the MRC's Patulin Committee had been finalised, and even before The Lancet had published Raistrick's paper, someone leaked news to the press that a cure for common cold had been discovered. Where the leak came from we shall never know. It could have come from Raistrick or his team, or Gye, or the Navy, or even the drug companies. Wherever it had come from, Thomson insisted that it had not come from the MRC.661 On 31 October, the Sunday Express reported 'New Cure for Colds. Coming Soon':

A new cure for the common cold has been discovered. The Sunday Express was told by a spokesman for the MRC yesterday that results of its tests of the cure would be published shortly, but he preferred to say no more about it at the moment.662

On 19 November 1943, The Star reporter wrote:


662 'New Cure for Colds. Coming soon', Sunday Express, 31/10/43.
Mrs Gye, wife of the Professor William Gye ... who is today reported to have cured a severe cold with a new substance called Patulin last February told me today that her husband had not had a cold since then... Every time he detects the slightest symptom of a cold in himself he douches his nose with a few drops of diluted Patulin.663

The following day, The Daily Mail broke the news thus:

No sooner did the news of Patulin, the new drug which may prove a cure for the common cold, hit the front pages of the press yesterday morning than the London School of Hygiene and Tropical Medicine was inundated with applications from sneezing, coughing red-eyed stuffed-nosed humanity asking for doses of the medicine. The answer was -- in every case -- 'No.' ... 'At present', a member of the MRC told me, 'there is not a lot of the stuff available', such as is there is being devoted to real tests -- tests on people whose living conditions and diet and so forth can be pretty well ascertained, checked and controlled. We have been asked to organise some tests like this on factory workers, people in the services [and so forth]. Some of the tests have proved very successful -- but the leading article in The Lancet reveals that certain other tests have not been successful. British scientists like to be very sure before they wave the flag and bang the drum ... I suggested that I was recovering from a streaming cold and might prove an acceptable human guinea pig for experiment: but the answer was again 'no', I was not 'controlled' any more than the 100 others who had applied by telephone during the morning.664

These reports were testimonial evidence designed to convince ordinary citizens that Patulin cured the common cold. Unlike the prima facie evidence Raistrick had made in The Lancet, the testimonies disclosed in the newspapers for public information were spoken through the reporter's voice. The reporters identified with the layman, and the reports were steeped in patriotism, engaging the public in the Patulin trials as a moral duty to the nation. The Daily Mail reporter's offering of himself as a human guinea-pig for experiment is particularly significant in this regard, and is a point to which I shall return in the commentary of Part III. According to the Sunday Express, Patulin had been discovered by a British scientist, and by 'one of the most famous research doctors in Britain' no less.665 The association between Patulin and the recent British innovation of penicillin was clear and direct. Like penicillin, Patulin was a mould product. Like the penicillin wonder drug, this 'entirely unusual remedy' was discovered

663 The Star, 19/11/43.

664 G. Ramsey, 'They Clamour for Patulin. But Must Keep their Colds', The Daily Mail, 20/11/43.

665 'New Cure for Colds. Coming soon', Sunday Express, 31/10/43. The emphasis is mine.
quite by accident. The lone British researcher, Alexander Fleming, had accidentally found a mould on his petri dish which killed a ring of bacteria. By chance, a new drug had found the innovative Professor Gye afflicted by a terrible common cold which his curiosity had led him to cure with Patulin. The approach of doing a mass trial after controlled tests, 'to be sure' was similarly framed as distinctly British. As the Daily Mail boasted: 'British scientists like to be very sure before they wave the flag and bang the drum.'

The newspapers said that the MRC would be conducting a nationwide clinical trial of this drug. But it was what they did not say that would turn out to be more important at the end of this trial. The papers did not give details of those 'certain other tests' which had not been successful.

III. Planning the trial with statistics in the background

The Patulin Trials Committee was appointed almost immediately after the negotiations with the drug companies. Himsworth and Sir Edward Mellanby (Secretary of the MRC at the time) asked Hart to stand as Secretary of the MRC's Patulin Clinical Trials Committee. Hart envisaged a system where he would sit with Himsworth, Forgan, H. J. Parish of the Wellcome Physiological Research Laboratories (WPRL), Raistrick, and Greenwood on the Patulin Clinical Trials Committee proper, while Amor (from the Ministry of Supply) and Bashford (from the General Post Office) would head the Sub-Committee of doctors and medical officers recruiting volunteers from factories and other public institutions. This strategy would have the advantage of giving the pharmaceutical companies their representatives on the Committee, and thus a role in organising the trials, while bringing 'the doctors more closely into the work.'

666 For more on the penicillin story, see McGraw (1991), 415-36; Wilson (1976); Sheehan (1982), 4; Chen (1992).


668 PRO: FD1/3154, Note by D'Arcy Hart, 1/11/43; Note by D'Arcy Hart, 29/10/43. Both Raistrick and MRC officials agreed that since Greenwood had 'already taken a personal interest in the subject' he should stand as the statistician in the mass Patulin trial. PRO: FD1/3154, Thomson a note. 5/11/43.
In the end the Patulin Clinical Trials Committee, which met for the first time on 23 November 1943, comprised Professor Himsworth (Chairman), Dr C. H. Andrews, Professor Major Greenwood, P. Hart (Secretary) and Dr Joan Faulkner (Assistant Secretary), B. M. Merriman (from The British Drug Houses Ltd) and H. J. Parish (from WPRL), both representing the Therapeutics Research Corporation, Professor H. Raistrick (the 'discoverer of Patulin'), W. L. Scott (Medical Officer, General Post Office), and A. J. Amor (Ministry of Supply), the last two representing the major source of clinical subjects for trial.670

When I presented the evidence Raistrick produced in The Lancet, I mentioned that Greenwood's statistical commentary formed a unique part of that evidence. Greenwood, as I discussed in Chapter 5, seemed to be calling for the personalities of eminent statisticians like himself to be less prominently associated with scrutinising (and thus rejecting) medical research plans. This simply made villains of statisticians. And, as I have shown in this chapter, statisticians like Hill and Greenwood, who focused on medicine and medical research, already believed that at best physicians saw them as villains. Worse still, they were framed as rarefied and irrelevant to the progress of medicine. Instead, Greenwood supported the dominance of their statistics in the approach that medical men took to all areas of medical practice. His part in this trial should be seen in this light.

The initial decision to collaborate in making prima facie evidence for the efficacy of Patulin, made perhaps in the corridors of the London School of Tropical Medicine and Hygiene where Hill and Greenwood were both based, might be seen as an example of the pervasion of statistics in shaping medical method and research from the late 1930s onwards.671 In any event, Greenwood was now on the MRC’s Patulin Trials Committee to organise clinical trials of the drug. At this first Committee meeting to plan the trial, Greenwood the statistician looked more like an epidemiologist when he advised caution in defining the common cold. He argued that, since the causative agent of the common cold was not a fixed entity, this changing variable

669 PRO: FD1/3154, Note by D'Arcy Hart, 29/10/43.

670 PRO: FD1/3155, D'Arcy Hart, 'Agenda. Meeting of the Patulin Clinical Trials Committee', 1/11/43.

would have to be accounted for in the design of the trial. Greenwood believed that increases in cases of influenza would cause confusion when it came to defining 'true' common cold cases, so the Committee sat down and drew the picture of the classic case. A typical patient would have: 'an apyrexial catarrhal condition, with watery or mucus discharge from the nose and injection of the fauces, associated with sneezing, fullness in the nose and head, and occasionally with cough, headache, sore throat, hoarseness or runny eyes.'

At the first set of meetings convened in late November 1943 to design the Patulin trials, Greenwood argued that seasonal variations in the common cold, evident in the epidemiological research, meant that the Committee should not only run trials all over the country to gather a variation in sample size, thus allowing for variations in the nature of the infective agent, but it would also need to 'space the trials wide apart and extend them over a considerable period', in order to obtain a true estimate of the efficacy of Patulin. As Secretary of the Committee, Hart had already established contacts with a number of factories by mid-November, before the first meeting. This suggests that he was aware of the Committee's position about this aspect of the design. Hart contacted Medical Officers (MOs) from factories and institutions all over the country, assisted by Bashford and Amor who talked to the superintendents and MOs from Royal Ordnance factories. By early December he had established a network which included superintendents and medical officers stationed at Ordnance factories in London, Cardiff, Nottingham, Kirkby (near Liverpool), Aycliffe (near Darlington), Irvine (near Glasgow), Bishopton (also near Glasgow), not to mention factory doctors and MOs at Messrs Chloride Electrical Storage, in Manchester, Messrs Rowntree's and Company, in York, Messrs Butterley Ironworks in Derby, Messrs Rolls Royce, Vickers-Armstrong (Newcastle upon Tyne), Guest, Keen and Nettleford (Birmingham), General Post Office (GPO) Parcels, GPO (London), Trucks and Tolls and GPO (London), Savings Bank


674 See PRO: FD1/3155, Amor to D'Arcy Hart, 31/12/43.
(London). Schoolchildren from not-so-common schools, with common colds, would also be tested to represent different sectors of the population. Hart had arranged with Dr Smith, the school doctor at the Rugby School, for the MRC to test Patulin on these public schoolboys. Dr Billington would gather young people from Haileybury College in Hertford.

The communications between Greenwood and Hart imply that Greenwood claimed this suggestion -- that trial volunteers should come from all over the country to represent a cross-section of people from different sectors of the British population at different times of years -- as his own.675

As I demonstrated in Chapter 5, establishing control and test groups and alternating the treatments between these groups was a part of the TTC's methodology throughout the 1930s. But the Patulin Committee decided on the design which had implications for the statistical calculations of the results. Unlike those of any of the small-scale trials which the Therapeutic Trials Committee had run, the treatments were divided into 4 blocks of 24 treatments which would be labeled Q, R, S, and T. Two of the groups of 24 bottles would contain control solutions, and the remaining two sets of 24 bottles would contain Patulin. The four bottles were mixed around so that R and T contained the Patulin, Q and S contained the controls. It was decided that the physicians testing the drug should not be informed of the contents of the bottles and that they should take the bottles. The treatments were therefore given in alternation.

Why 4 sets of 24 bottles? And why arrange them in this way? Greenwood used Pearson's chi-squared test to calculate the efficacy of Patulin statistically. Pearson's chi-squared test of association of independence tests the significant difference between observed values (i.e. the raw scores you obtain from your subjects when you give them a particular treatment) with the expected values (i.e. the theoretically expected values which need to be calculated). Within this arrangement Greenwood would have obtained a well-balanced trial

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675 Hart wrote to him later that year with a list of the names of institutions where trials were being run, the city where those institutions were located, with the population of that city and with an indication of the period during which the trial was conducted. Hart sent this to Greenwood for his 'opinion as to whether this constitutes a satisfactory experiment' so that, should it be necessary, further units could be started. PRO: FD1/3157, Hart to Greenwood, 23/3/44.
with roughly the same numbers in the Patulin and Control groups. Under the best possible circumstances, i.e. on a day in which all 92 bottles were used in a day, Greenwood would also have fixed the total number of columns \((C)\) at 48 and the \(G\) (Grand total) at 92. The expected values \((E)\) would have been whole numbers and this simplification of the calculations for his computers would have left less chance of human error due to calculation.

Greenwood did publically claim the design of this trial as his own. In an interview between myself and Hart about this Patulin trial, Hart claimed the random element as an impromptu decision of his which came to him during the pilot trial at Enfield. Faced with the sets of bottles in front of him at the beginning of that trial, he said he had the idea to 'mix the bottles up'. This, I propose, might be called a 'random element' in this trial. But its design (as we shall see in the final section of this chapter) was essentially an example of the method of assigning patients to Patulin and control groups by alternation. The issue of the random element is nevertheless significant. The idea of recruiting volunteers with common colds from all over the country, who would represent sectors of the population, was predicated on the notion that if a clinical trial was advertised in a particular part of the country, those who presented themselves were not deliberately selected. The patients, who came forward naturally, of their own accord, would have been a random selection of people, thrown up by nature and by chance. Planning the trial in this way would have been analogous to plucking common cold patients at random from the local population where the trial was being conducted. And plucking them at random would have increased the likelihood that the sample was unbiased. Greenwood was operating on the premise which, provided the sample size was large enough and the selection unbiased, it would be representative of that particular population. The statistical arguments can be traced to Greenwood's teacher, Karl Pearson. The plan I have proposed as Greenwood's, which would have assigned these randomly selected common cold victims either Patulin or control solutions, would have produced results which could be (and indeed were) conveniently analysed using Pearson's chi-squared test of independence.

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676 Personal interview with Hart, 26/8/97.
Although the Patulin Committee's employment of ideas of random sampling in their design of the mass Patulin experiment may have been directly traceable to Greenwood, and thus to Pearson, random sampling was becoming an increasingly popular and socially acceptable method of social research in British society during the late 1930s, just before the Second World War. Seebohm Rowntree's, A. L. Bowley's, and Charles Booth's famous social surveys of major cities, conducted before the Great War and during the inter-war period, all employed random sampling to develop a reliable picture of the country that would inform government social reform. During the inter-war period, newspapers and periodicals initiated readership surveys and surveys on consumer consumption, in which teams of interviewers (typically women) were employed to survey the opinions of random representatives from certain population groups. But above all the independent opinion polling system -- Mass Observation -- set up in 1937 by the self-styled anthropologist and adventurer, Tom Harrison, together with Charles Madge (poet and journalist) and the documentary film-maker, Humphrey Jennings, was in full bloom when the Patulin trial was being conducted. Across the country ordinary people (mainly middle class) took systematic records of popular feeling in the course of the chance events of their daily lives, which were to stand as a barometer of national sentiment on a vast range of important issues of the time.

Around the time that Greenwood was helping to design this Patulin trial, R. A. Fisher, the statistician well known to Greenwood (and, as I mentioned earlier, whose work Greenwood admired and directed his medical audience to) had created a statistical tool -- 'randomisation' -- which he had published in The Design of Experiments (1935). Fisher had developed these ideas in the context of agricultural experiments comparing the yields of different varieties of grain. He proposed that the experimental plots be divided into narrow strips and that grains be assigned to their place in the field by the use of a chance mechanism he designed (randomisation). Because Fisher had designed a special way of generating 'random' numbers

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677 See Stevenson (ed. 1977); Abrams (1951); Muggeridge (1967).

678 Jeffrey (1978); Harrison and Madge (1939); The Mass-Observation Diaries: An Introduction (University of Sussex, 1981).
and analysing the outcomes of his experiment, he claimed to have produced a better way of eliminating the personal biases of the individual experimenter -- indeed, a method which practically guaranteed their absence -- than any of the experimental methods investigators were using to eliminate investigator bias at the time.\footnote{Fisher (1935).}

That Fisherian 'randomisation' and the idea of 'random sampling' are two completely different statistical entities is not in dispute. My point quite simply is that the notion that obtaining a random sample of the behaviour (or, in our case, reaction, to a particular drug) would give a more 'scientific' and reliable picture of that population's activities, was increasingly popular. It seems likely that the Patulin Committee, and the doctors carrying out these Patulin trials at a local level, would have appreciated that the 'random' element in the design of this trial was aimed at producing a 'scientific' mass experiment.

The Patulin Committee organised a trial run, a 'pilot trial', to test the technique between 13 December 1943 and 7 January 1944 at the Royal Small Arms Factory at Enfield, before running the main trials all over the country.\footnote{See PRO: FD1/3155.} However, one problem remained. The negative Army trial results would not die. When the Committee had first met in November, the RAMC had not yet published a full report of their results. As it happened, the heads of the branches of the Army medical surgeons were meeting on 29 November (the day the Patulin Committee met to finish the business of their first meetings) to discuss whether they should publish the full results of their trial. Hart was asked to tell the Army heads to send their report to the Patulin Committee before publishing it.\footnote{See PRO: FD1/3155.} They sent it over immediately. Hart circulated the report around the Committee members in the interest of securing a democratic decision about what to do.\footnote{The report dated 1/12/43 was filed at the MRC on 7/12/43, and Greenwood and others had begun to file their comments on the report by the time as the pilot trial was about to begin. See PRO: FD1/3155, 'Investigation of the Common Cold. Patulin. A Report of the Director of Pathology War Office by C. H. Stuart-Harris, Major, A. E. Francis, Major, J. M. Stansfield'. PRO: FD1/3156.
The report entitled 'Investigation of the Common Cold of Patulin. Laboratory and Clinical Trials of Patulin (Raistrick), was written for the Director of Pathology of the War Office by the Army officers who had conducted the trial, namely Captain J. M. Stansfield, Major A. E. Francis, and Major C. H. Stuart-Harris, all of the RAMC. Raistrick had supplied the Army with Patulin not long after he had begun sending supplies of the drug to Commander Hopkins. During March 1943 Captain Stansfield carried out 'preliminary experiments' on 50 cases of infantrymen alternately. Stansfield asked the infantrymen how they felt after taking these treatments. Five out of the 25 patients receiving the Patulin solution were cured, with no cures occurring in the control group. So the Army officers conducted further trials between August and September of that same year. This time they engaged in closer consultation with Raistrick in preparing the treatment solutions for the trial. Crucially, all of the solutions were prepared from a single sample of Patulin which Raistrick had sent to them. Raistrick advised them that the stability of the compound in solution was largely controlled by pH, and that the substances should be dissolved in a buffer at pH 6.0. The two Army majors and Captain Stansfield devised a strict and regimented scheme involving 100 soldiers. They deliberately chose young recruits in their twenties from the armoured corps with acute onset colds -- 'the ordinary type of common cold frequent in this country in the autumn' and 'of the type commonly seen in recruit establishments'. They saw the cases and took a detailed history at 0900 hours. They asked for 'exact time of onset', 'nature of symptoms', 'character of discharge', 'number of handkerchiefs used' and 'liability of cold infection and previous respiratory diseases'. Then, with military precision, the Army investigators took the

Greenwood to D'Arcy Hart, 16/12/43; PRO: FD1/3156, Andrewes to D'Arcy Hart, 14/12/43; PRO: FD1/3156, 'Comments on the Army Report on Laboratory and Clinical Trials of Patulin', 5/1/44.


See Note 78, 1.

See Note 78, 7.

See Note 78, 7.

It was noted that only three of these were associated with pyrexia which in no case exceeded 99.6 degrees F.
temperature and pulse, examined the conjunctivae, nose (with a speculum), nasal sinuses (for
tenderness on pressure), the amount of nasal discharge (taking a swab for culture), the fauces
and the chest of each infantry man. Each volunteer was then 'told to lie on the couch' where
'he was sprayed' (using a de Vilbiss spray) up both nostrils and into the throat and a few drops
of solution (about 3 to 5 ccs) instilled into each nostril from a pipette. The patient was
instructed not to blow his nose for half an hour but simply to dab his nostrils with a
handkerchief if required, and told to report again at 1200 hours when the nasal discharge and
obstruction were again assessed, and spraying and drops were administered as before. This
procedure was repeated at 1400 hours, 1600 hours, and again the next day. The men were
instructed to return for further smears and cultures of their nasal discharge the following day,
and on this third day, the men were given a form to fill in for the next four days detailing his
symptoms and feelings 'so that some ideal of the progress of his cold during this interval could
be obtained.' On the morning of the eighth day the Army officers asked each infantryman:
'Do you think that this treatment has done your cold any good?' These results showed that their
Patulin did not have a significant effect on the common cold.

When the other Committee members studied the methodology and examined the
results, they found them difficult to criticise. For the most part, the Army and naval trials were
strikingly similar in design and organisation. As C. H. Andrewes, one Committee member, put
it:

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688 The Officers devised a system for assessing the degree of nasal obstruction and discharge. If the
subject was unable to sniff any air up through a nostril, the obstruction in that nostril was indicated as
+++. If he could sniff up with some difficulty the obstruction was put as ++, and for only slight
obstruction + was given. No apparent obstruction was indicated as 0. The same system was used for
recording amount of nasal discharge, but in this case the distinction was between degree was less
definite. The symbol +++ was used to denote a discharge visible at the anterior nares or down the
posterior pharyngeal wall; ++ and + were used according to the impression gained when the patient
sniffed up his nostrils. No sign of a discharge was indicated by 0. See Note 78, 9.

689 See Note 78, 9.

690 See Note 78, 9.
My own view is that both Surgeon Commander Hopkins and the Army workers have very creditably attempted the difficult feat of assessing the clinical value of Patulin in colds, that one report is better in some respects, the other in other ways.\footnote{PRO: FD1/3156, Andrewes to D'Arcy Hart, 14/12/43.}

Raistrick laid the blame on the solutions. First, the Army trial solutions of Patulin were made in dilute buffer plus normal saline, while Hopkins' solutions were made in dilute buffer solution with no other additives. He therefore implied that the RAMC solutions may have been adulterated. Second, Hopkins' solutions were fresh. But the Army's report suggests that the solutions were less than 10 days to a fortnight old. Crucially, Raistrick insisted that his name be struck from the title of that report.\footnote{PRO: FD1/3156, 'Extracts of Comments by Committee members of the MRC on the Army Report of Patulin Clinical Trials'.} Even Greenwood was lost for criticism. He had leant the weight of his statistical expertise and commentary on Hopkins' results, saying that these positive results could not have been produced by accident. How could results of another trial of the same treatment, made by much the same method, be so radically different? All that Greenwood could say about the RAMC trials was:

\begin{quote}

it is quite clear that there is no \textit{prima facie} evidence that the treatment had any effect. Epidemiologically, although the details are copious, they do not include information as to the time and place of observation. There is an indirect reference which implies that these colds were contracted later than spring of 1943. It would be well to know that the exact period of the year. Another omission is a statement of whether the patients came from the same area. It is quite certain that the immunising qualities of 'colds' vary and this may be correlated with changes in response to treatment. That is why, before pronouncing any judgement we should have data collected over a wide range of space and time.\footnote{See Note 87.}

\end{quote}

While Andrewes believed that the Army workers should be allowed to publish the results, other Committee members were not convinced. The Committee decided that if the Army went ahead and published the results, at that stage, this would be a huge embarrassment to them.\footnote{PRO: FD1/3157, D'Arcy Hart to Poole, 5/5/44.} Too many people had already committed themselves to this mass trial which had already begun.
There was too much was at stake to stop the wheels that had already been set in motion across the country. But how much did it take to make this trial work?

IV. Modern times: a day in the life of mass clinical trial

I began this chapter with Hart's train journey to Glasgow on Sunday 5 March. This was a 'day in the life' of a mass clinical trial, and so I shall try to recapture the events of that day, and the events and issues surrounding Hart's visit to those factories, to show the effort Hart and Faulkner exerted, and the resources that the MRC and drug companies deployed to make this mass experiment work. At the end of the day one might well ask: was the effort unjustifiable given the Army trials? Or was it precisely the equivocal Army trial results that made such a large-scale trial which promised a conclusive result imperative? Or were Raistrick's hopes and confidence in this drug a driving force? Hart's visit also exposes the techniques he and Faulkner used to mobilise the mass of volunteers who were given Patulin in these trials.

IV. 1. The visitation

Hart would have arrived in Glasgow at around 6.15 am on the morning of 6 March. He was supposed to have breakfast at the Central Hotel before being collected in a chauffeur-driven car around 8 am and driven to the Rolls Royce factory at Hillington. Dr Collier, the works Medical Officer at Messrs Rolls Royce Ltd, met him there. Hart thought the train might probably be late, 'but then again', he said to Collier, '[I] want to be at the factory well in time before you start.' When Collier was to actually start the first session of the clinical trial at Hillington, Hart told him 'is entirely at your convenience; some factories start at 9 am, others at 10 and even 10.30 am.'

PRO: FD1/3157, D'Arcy Hart to Collier, 1/3/44.

See Note 90.

See Note 90.
Collier seems to have been ready to start his trial on the Monday.\textsuperscript{698} The arrangement was for the British Drug Houses Limited (BDH) to send a van to deliver 92 colour-coded bottles with tags fastened around their necks to Collier's factory surgery: 24 with the letter Q printed on its tag, 24 with the letter R, 24 with S, and 24 with T.\textsuperscript{699} At BDH's request, these bottles were labelled 'materials supplied by the Therapeutic Research Corporation of Great Britain'. Two of the groups contained freshly-mixed Patulin solutions, the others contained control solutions.\textsuperscript{700} In the event that Patulin proved to be curative, the trial itself would have been a nationwide advertisement for the pharmaceutical companies. The BDH van would have delivered the bottles the day before (on the Sunday), probably between 5 and 6 pm, if the pilot trial at the Royal Small Arms Factory at Enfield was anything to go by, and they would have collected the unused treatment bottles on the Monday evening between 5 and 6 pm, after the first day of the trial, when they delivered the next day's consignment of bottles of Patulin and control solutions.\textsuperscript{701} This had all been tried and tested in the pilot trial at Enfield.

Hart wanted to be there on the Monday in time to talk about the trial to shop stewards, the convener of shop stewards, and the factory superintendent before they began that morning.\textsuperscript{702} This would not have been the first time that the factory workers and personnel would be hearing about this Patulin trial. Typically, medical officers at the centres were sent an introductory package with a photograph demonstrating how to give the treatment, a copy of the 'record form', leaflets with 'Instructions for Patients', 'a copy of the label from the box of ampoules of Patulin', and a reprint of Raistrick's article from \textit{The Lancet}.\textsuperscript{703} At other factories

\textsuperscript{698} PRO: FD1/3157, Faulkner to Greenwood, 23/3/44. Note the commencement date of the Rolls Royce trial at Glasgow.

\textsuperscript{699} PRO: FD/1/3155, D'Arcy Hart to Merriman, 9/12/43.

\textsuperscript{700} See Note 94; PRO: FD1/3155, Merriman to D'Arcy Hart, 6/12/43; D'Arcy Hart to Merriman, 9/12/43.

\textsuperscript{701} PRO: FD1/3155, 'Confidential. MRC Patulin Clinical Trials Committee. Minutes of first meeting', 25/11/43; Procedure for Enfield R S A F Pilot Trial,' p. 3.

\textsuperscript{702} PRO: FD1/3156, D'Arcy Hart to Collier, 25/2/44.

\textsuperscript{703} PRO: FD1/3156, Faulkner to Sargent, 14/1/44.
they pinned up posters to advertise the trial. The pilot trial at Enfield, which had formed the procedural standard for the main trial, had used this poster:

**NOTICE**

**PATULIN TRIALS**

**Investigation by the**

**Medical Research Council**

It is possible that in the new drug Patulin we have the long sought cure for the common cold. It is of *national importance* that the true value of this drug should be assessed as soon as possible, and a trial of it is taking place in this factory now. You can help in this investigation if you have a cold by reporting at the Surgery for treatment between 9 and 10 am. The treatment is simple and rapid and will be given at the Surgery during the day and at home by yourself at night. Only cases of ordinary colds will be treated. Do not report if you have hay fever or chronic catarrh. Report as soon as possible after the cold has started.\(^{704}\)

This was the standard form of advertisement for the trial, but this standard form could be tailored for local use if the factory doctor saw fit. Circulating printed matter, however, was not enough. These advertisements should ideally be accompanied by a broadcast and preferably also a canteen meeting.

**IV. 2. Personal messages**

Hart knew from his experience that there was no substitute for a visit from an MRC official to ask in person for the help of these factory workers: someone to tell them that the trial could not work without their blessing, that they were pioneers in a national effort. As Hart told Collier:

\(^{704}\) PRO: FD1/3155. This was the notice the MRC had issued for Enfield.
I must say that we [presumably his assistant, Dr Joan Faulkner and himself] have been quite convinced that such meetings are valuable, feeling that the message gets thereby carried into the shops through a large number of people who have personally seen the outside doctor and been able to ask him questions. In one factory where we did not have such a meeting there was a misunderstanding on the part of the workers that this was a cure and not a trial of a possible cure -- the results have been disastrous and that factory is our only failure to get enough volunteers.705

Hart had past personal experience of the importance of the 'human factor' in managing mass research projects in a previous MRC project. His first appointment with the MRC was as a scientific officer on a mass research project in 1937 to investigate the dust disease of the lung in coalminers in the south of Wales.706 In an interview with myself about his early career, and at the Wellcome Trust Twentieth Century Witness Seminar, Hart told how he came to be employed full time with the MRC, which shows how, in some ways, this first project prepared him for mass research. In 1937 it had been widely reported that the inhalation of coal dust produced a chronic disabling disease of the lung. Because of rising compensation costs and a need to guard against a discontented workforce when war threatened, the government asked the MRC to urgently investigate this matter. Born in 1900, Hart had, up to that point, pursued a more or less straightforward medical career, rising up the ladder to become a consultant physician in 1934 at University College Hospital (UCH). At UCH, he was a physician in T. R. Elliott's medical unit, where Thomas Lewis was doing 'clinical science'. However, Hart was not entirely satisfied in his role as consultant. He wanted to be doing medical research in a general sense of that word. Hart believes that Lewis may have noticed his discontent and recommended him for the MRC mass research project in south Wales. Hart recalls this as a 'tense period' where miners were 'extremely suspicious' of 'independent' investigators taking detailed clinical histories, examining them and taking x-rays of their lungs. He told a story designed to illustrate how financially well endowed the MRC was during the 1930s and 1940s, and how this made medical research possible. Hart called it 'the story of the half-crowns'. Hart told the story thus:

705 See Note 97.

As part of the work we wanted to see whether tuberculosis was a factor in the progression of this pneumoconiosis. There was a lot of tuberculosis around there. So we decided to do some tuberculin tests on a sample of men... They agreed... It meant an injection of tuberculin into the skin... Well, it went off very well and each one collected half a crown reward... If people were negative there required a second test about two days after. We assumed it was o.k., but it wasn't because the men grumbled and said: 'We've had one test and we don't know why we need another.' And there was a crisis. But then into the bridge stepped (Sir) John McMichael and he made the most remarkable speech and won them all over. He told them that if they give up we should have no results at all, which was absolutely true, and so they decided to do it. And then came the second crisis. Half crown again, please. Well, we had no half crowns. Time was ticking over and the second day was approaching so I rushed to the phone and telephoned Westminster and told the MRC of our predicament... That same evening, I met the local train... the guard handed me a sack of half crowns marked Medical Research Council.  

Although his half-crown story demonstrates MRC power and resourcefulness, it also shows the nature of his experience and his appreciation of how a personal speech from an official presence could persuade the ordinary working people to participate in a mass investigation initiated by the state.

IV. 4. On becoming a patient: in walks the volunteer, out walks the patient

After talking to the workers at the Rolls Royce Factory, Hart watched the treatments being prepared and advertised to factory workers. Collier and his nurse were to be stationed, preferably at separate posts and in separate rooms (but this was not always possible in factories). The MRC provided each of them with a box for filing record cards and counterfoils. The treatments were set out on a table in 4 groups of 24 colour-coded 8-ounce bottles. Each bottle had enough treatment solution to last for 48 hours. Neither Collier nor the nurse knew what was in these bottles. The doctor and nurse also had at their disposal a set of tablespoons

707 I am grateful to Sir Philip D'Arcy Hart for allowing me to interview him. This story is quoted from Witness Seminar, 'Pnuemoconiosis of Coal Workers with Dr Philip D'Arcy Hart and Sir Christopher Booth', The Twentieth Century Medicine Group, 8/11/94. Hart notes that Sir John McMichael happened to be in the area on other business. I am grateful to E. M. Tansey for allowing me to transcribe this seminar for this purpose.

708 PRO: FD1/3157, Hart to Collier, 1/3/44.
(for gargling), teaspoons (for nasal installations), and a means for boiling water to sterilise spoons.  

The plan was for ordinary factory workers with common colds to be taken through the system, starting at Dr Collier's post. Collier was to take a record sheet from the pile `in order of the serial numbers in the top left hand corner', and write the name, age and clock number of the factory worker on the counterfoil. Then, as instructed by the MRC, he would have asked the factory workers (male or female) about their colds: for example, how long had he had it? Half a day? Two days? Seven days or more? Was he sneezing? Did he have a fullness in the nose or fullness in the head? Did he have any discharge from the nose? If so, was it clear or yellow? Did he have a cough? Was he hoarse, did he have a headache, a sore throat or running eyes? Was he feeling unwell? Collier then circled the appropriate symptom on the counterfoil and examined the patient. Hart was on hand to answer any queries Collier might have had about what questions to ask, how to ask them, and why. Not only had Hart been a consultant physician in Professor Elliott's medical team at University College London before he joined the MRC, but as Secretary of the Patulin Committee he had helped to frame these questions and define the common cold for the purpose of this trial. To all intents and purposes the common cold was a 'clear nasal discharge (though it was sometimes yellow, mucus-like), sneezing, a feeling of fullness in the nose, a feeling of fullness in the head, cough, headache, sore throat, hoarseness, running eyes and malaise (often described as feeling ill). By 6 March, Hart had also watched these symptoms many times.

Hart would have then watched Collier hand the counterfoil to the factory worker, who then passed it on to the nurse's station, while Collier filed the main sheet of worker X's counterfoil in alphabetical order in a box that the MRC had provided. The nurse was instructed by the MRC's Patulin committee to double-check the counterfoil to make sure that the worker's

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710 See Note 104.

711 See Note 104.
name, age and clock number had been filled in properly, and that the form had been dated with
an indication of the time of treatment session. Hart and Faulkner had arranged for instructions
to this effect to be printed and dispatched to factories, post offices, schools and hospitals all
over the country.

Now the treatment. Hart would then have watched the nurse take a bottle from any of
the Q, R, S or T groups in strict rotation. In other words, she should give a treatment from the
Q group to the patient with serial number X, one from the R group to the next patient, and so
on. She was then supposed to write the letter of the bottle she had used on the counterfoil (with
the patient's name and details), drawing a ring around the appropriate letter. And, should it
have been necessary at that time, Hart was in a position to reiterate the Committee's suggestion
that she should write the letters and corresponding numbers down on a notepad as she went,
and tear off the coloured tag from the bottle and secure it in a box just as she was about to
treat the patient, in case there was 'a rush of patients'.

It was the nurse who gave the factory worker his first treatment from the bottle she
had selected for him or her. From this point onward, that colour-coded 8-oz treatment bottle
now belonged to that particular worker (see Appendix 6C). Having received the instructions
and photographs telling her how to give treatment, the nurse may well have told the factory
worker, as were her instructions, to pay careful attention to what she was about to do because
someone at home would have to give it to him that evening and perhaps again during the night
or in the early hours of the morning if the need arose. The factory worker was then made to lie
back on the couch with his head hanging over the end so that the nostrils faced upwards. She
told him to 'breath slowly through the mouth' while she poured a teaspoon of warm solution
down his nostrils.

712 See Note 104.

713 See Note 104.
IV. 4. i. No pain, no gain

The workers may well have flinched while this procedure was being performed. They may well have begun to regret joining the trial at this stage. At Enfield, and up and down the country, medical officers had been telling Hart that people found these treatments unpleasant. Even before beginning the pilot trial the Committee feared that, because Patulin caused irritated the nostrils, ordinary volunteers would be able to sense the difference between the Patulin and the control. If ordinary trial victims could feel the difference, plans for tagging and colour coding bottles, and for using Greenwood's chi-squared tests would have been a waste of time. The Committee had therefore arranged a preliminary trial of the proposed Patulin and control solutions on 29 medical students.\footnote{PRO: FD1/3155, 'Test to determine whether the proposed patulin solution can with certainty be differentiated by subjects from a control solution.' A stock solution of 1: 10,000 Patulin in a 0.05% solution in buffer (devised to give a pH of 6.0 in distilled water) served as the Patulin solution, while the control solution was a similarly 0.05% buffered solution without Patulin. (One of them reported no difference between them, another the solution in nostril which the investigators knew contain Patulin as the one which stung the most.)}

The students were told that the Committee specifically wanted to know whether there was any difference between the two solutions, but they were not told which solution was which.

Seventeen students were given the Patulin solution in one nostril and a control solution in the other. The investigators changed the order of application in each case so that students would not guess the identity of the solutions. Five students were given the control solution in both nostrils, and the remaining 7 students had drops of Patulin solution poured down each nostril. Of the 17 students with Patulin in one nostril and the control solution in the other, 6 believed that they could tell which nostril had Patulin in it because they could feel stinging sensation in that nostril; 9 found both solutions to be irritants, only 2 believed that the nostril with (what investigators knew to be) the control solution caused pain. Of the 5 students with control solutions in both nostrils, 3 believed they could feel a stinging in one nostril. Three of the 7 students with Patulin in both nostrils reported a stinging sensation in one nostril, the remaining 4 said they could feel stinging in both their nostrils. There is no evidence to suggest
that these results were statistically analysed, but it would appear that the Committee were satisfied that the solutions were indistinguishable, or at least that factory workers, hospital workers and office clerks would not be able to tell the difference.

The factory workers at Enfield seemed to have found both control and Patulin treatments equally vile. However, Hart and Faulkner believed that the low turnout (only 53 volunteers in total) may have been because the 'treatment was so unpleasant that workers were frightened to volunteer'. The experience forced them to look into other ways of administering it, e.g. by spray -- the method they eventually used on the schoolchildren they recruited -- and by warming the treatment before giving it to volunteers in the main trial. However, doctors giving the treatment at local centres in the main trial reported that volunteers still found these treatments unpleasant. Not a month before Hart had come down to start the trial at Rolls Royce, Dr Ronald Lane (the Medical Officer) at The Chloride Electric Storage Company Ltd, Clifton Junction, near Manchester, had written this desperate letter to Hart:

I am afraid the Patulin experiment is rather flopping here. We have had only 60 cases in 3 weeks ... and cases are coming in very slowly now. I think the reason for this is not that there are no colds, but that the treatment has fallen into disrepute, first, because so few cases seem to have resulted in cure, and, secondly, because so many of the patients have developed quite troublesome headaches following treatment. We are persevering and are giving the treatment to any volunteers who do come.

Hart had encouraged him to continue, suggesting that another publicity drive might help to get the numbers up to scratch.

IV. 4. ii. Going through the motions: following the rules

Back at the Rolls Royce factory on that March Monday, the nurse would have told factory worker to 'try to stay in this position (with head hanging over the edge of the couch) for 2 minutes if possible', even if the worker had flinched and the treatment had irritated him or her, and to: 'sit up and use your handkerchief to mop up the excess solution'. She had also been

715 PRO: FD1/3156, 'Patulin Clinical Trials Committee', 19/12/43.

716 PRO: FD1/3156, Hart to Faulkner, 12/2/44.
instructed to tell the 'volunteer' to 'try not to blow your nose for half an hour after solution is instilled into each nostril'. The patient was then be given a tablespoon of solution from the bottle to gargle with, and was then to return to the surgery after 4 hours (i.e. at about 1-2 pm) and then 8 hours later (i.e. at 5-6 pm), bringing the bottle on each of these occasions so that the nurse could repeat this treatment.717

More than in any other trial before it, this mass trial depended on patients taking the treatment at home. Since this trial depended on the participation of ordinary people, the Patulin Committee had also deliberated about how these instructions should be worded, so that patients and their spouses would understand what was required. Significantly, these instructions always ended with a plea:

Please see doctor again tomorrow (9-10 am) to tell him how you feel, and have treatments at work at exactly the same times as today, and at home at night and first thing on waking. This is the end of the treatment, but please see doctor on the third morning (9-10 am) to report, at the same time bring your bottle and leave it in the surgery ... and we thank you for your coorporation in making it possible.718

On visiting the doctor the following morning (day two of the Patulin test), these patients would have received three treatments, taking the bottle home for two or three treatments that night. The third morning, when these workers saw Dr Collier to report their progress, they would have returned the empty bottle to the surgery. No treatment would be given on this third day, but the volunteer would have to return in five days' time (i.e. on day eight of his treatment) to give Dr Collier a final progress report on the status of his health and his cold.719

Again, Hart would have been there to see that these instructions were delivered properly, and to answer any questions from workers about why it was so important for them to continue with the treatment and to return to the surgery as directed. The consequences of patients failing to do so might mean that Greenwood and his 'human computers' at the School

717 See Note 104, 3.
718 See Note 104.
719 See Note 104, 3.
of Tropical Medicine and Hygiene might have to discard these cases in their statistical calculations.

That afternoon, Hart travelled to Bishopton to visit the Royal Ordnance Factory (ROF). He had arranged to see Dr Frank Sargent, the medical officer presiding over the trials there. Hart and Faulkner had already visited Sargent briefly on a similar day trip to Glasgow nearly two months previously, on 19 January. But they had stopped at the Bishopton factory to 'discuss all of the details of the procedure during the day', have 'a very brief meeting with the shop stewards' and give Sargent a pile of 'record forms and "instructions for patient" leaflets for the trial'. Because it was a flash visit, they had promised Sargent that one of them (either Hart or Faulkner) would return to Bishopton to see how Sargent's trials were progressing.

IV. 5. Mass propaganda: driving the motor of the mass trial machine

When Hart visited Bishopton on the afternoon of 6 March 1944, Sargent's trial had been running for almost a month. He had started on 8 February, advertising his trial in the usual way with posters, broadcasts, meetings with shop stewards (word of mouth), and a personal visit from the two MRC representatives. Sargent had particularly jazzed up his broadcast to bring the workers in. He announced:

Are any of you suffering from cold in the head? If so, don't waste it on your family and your friends but take it to the Surgery where they have a use for it. You must have heard of Patulin (lots of people are now asking for a small Patulin and a Pint in Refreshment Houses!). Well, we have got Patulin in the Main Surgery and we want to try it on as many people as possible to find out whether it will cure a cold or not. This trial is one of the most important advances that have ever been made in medical practice and we want to make it as good as possible at Bishopton. But the Patulin is no good without the patient. We want hundreds of volunteers and the more we have the merrier.

For those who have already volunteered, this is a reminder that it is essential for the success of the trial that they report back to the Surgery at the end of 24 hours, 48 hours and 1 week from the first treatment, whatever the effect of the treatment may be. The full value of the experiment will be lost unless you do this.

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720 See Note 97.

721 PRO: FD1/3156, Faulkner to Sargent, 14/1/44.

722 PRO: FD1/3157, Faulkner to Greenwood, 23/3/44.
Bring your colds to the Surgery at the earliest possible moment because we want them fresh.\textsuperscript{23}

This publicity drive had brought 126 volunteers to trial. His cases must have been approaching this number when Hart turned up at Bishopton that March Monday.

Like all of the other doctors running trials at various 'units' across the country, Sargent had most likely been told by Hart and Faulkner to 'try to get a sufficient number of cases to satisfy the statisticians.'\textsuperscript{24} Two hundred was fine, one hundred would be preferable, but under one hundred was not good enough.\textsuperscript{25} It is likely that when Hart saw Sargent that Monday, he encouraged Sargent to have another publicity drive to bring the numbers up to scratch (this being his, and Faulkner's, usual instruction to doctors who report and slump in their trial cases), because within days of Hart's March visit to Bishopton, Sargent came out with the following announcement to the ROF workers:

A famous Professor used to say the best cure for a cold was a bottle of whisky and a lum hat; you go to bed and hang the hat at the foot of the bed -- then drink whisky till you see two hats. Owing to the scarcity of lum hats, this cure is not easy to carry out at present, but we still have Patulin in the Surgery, which we are willing to let you have under the counter. Seriously though, you should try the Patulin treatment if you are unlucky enough to catch a cold. The treatment is quite harmless and it may be long-sought cure we have always wanted. It used to be said that a cold properly treated would last seven day, but if left would last one week. Patulin we hope will cut it down to less than 48 hours.

In this important investigation ROF Bishopton, with 126 volunteers, has already beaten the other places trying it. But we still need a hundred more volunteers. Please remember that when you have had your first treatment, we want your opinion of it. Even if you decided not to go on with it, come and tell us what you think of it -- and, if you like, what you think of us!

\textsuperscript{23} PRO: FD1/3157, 'Patulin broadcast'.

\textsuperscript{24} PRO: FD1/3157, Lane and Faulkner, 3/3/44. This letter from Faulkner to the Medical Officer at Messrs Chloride Electric Storage Exide Works, Clifton Junction, Manchester is one example of the sorts of letters which were sent to all doctors conducting trials for the MRC.

\textsuperscript{25} PRO: FD1/3156 and FD1/3157. The following letters exemplify the demand for at least 100 and preferably 200 cases from each unit. Letters of this type were sent off to most trial centres. PRO: FD1/3157, Lane and Faulkner, 3/3/44; FD1/3157, Faulkner to Greenwood; and FD1/3157, Dixon to Falkner, 28/3/44; PRO: FD1/3157, Faulkner to Dixon, 3/3/44.
Roll up sneezers!\textsuperscript{726}

Sargent, who was himself disappointed with the turn out at Bishopton, had asked locals to suggest how he might bring in more volunteers for the Patulin trial.\textsuperscript{727} Arguably, he was diffident about putting out this advertisement. He admitted as much to Hart, adding that the advertisement appeared 'rather fatuous on re-reading'. 'But', Sargent said, 'they tell me it [is] the sort of thing that was required' to get factory workers to come to trial.\textsuperscript{728} Hart and Faulkner had no qualms about Sargent's advertisement. All they required was that he make it clear that:

to everyone in the factory that this is an investigation -- not a guaranteed cure and that we want their assistance in finding out whether Patulin is or is not effective in curing the common cold.\textsuperscript{729}

Despite his stirring advertisements, Sargent was only able to recruit a total of 157 volunteers when his trial ended 4 April, 1944.

Sargent's propagandising broadcasts may have had limited value because the ordinary people volunteering for these trials all over the country would have been bombarded in their factories, schools, post offices and hospitals by propaganda deployed by other state bodies to recruit them to all manner of national causes.\textsuperscript{730} One factory, the Royal Ordnance Factory at Kirkby, had to pull out of the Patulin trial because the superintendent had too many other propaganda drives to contend with. Sargent apologised to Faulkner for having to disappoint her, after promising to participate in this mass trial:

We are just about to start Mass Radiography for T. B. of the whole factory and we are also running a Blood Donor Campaign. This, coupled with the propaganda that we are having to put over for the introduction of the Compulsory Fire Watching Scheme and

\textsuperscript{726} PRO: FD1/3157, 'Patulin' and attachment to 'Sargent to Hart', 11/3/44.

\textsuperscript{727} PRO: FD1/3157, Sargent to Hart, 11/3/44.

\textsuperscript{728} PRO: FD1/3157, Sargent to Hart, 11/3/44. Suspecting that Hart might not understand the colloquialism, he added: 'The 'lum' hat (lum, a chimney) is a local expression for a silk hat.'

\textsuperscript{729} PRO: FD1/3157, Faulkner to Sargent , 'Not' is underlined in the text.

Pay as you Earn Income Tax, is making a great deal of work for us and is, I think, giving the operatives as much as they can possibly digest at the moment.  

Faulkner and Hart's blatant use of 'publicity drives' and propaganda to bring up the numbers in this trial, however, would not necessarily have been seen in a negative light. Whether propaganda was 'good' or 'evil' depended on who controlled it, and what their motives were. By the Second World War, propaganda and mass advertising were legitimate functions of government and state departments, being employed as tools of diplomacy and 'national projection'. Furthermore, the scientific status given to propaganda, and its ability to appeal to the herd instincts of the masses by social psychology (and by eminent scientists like Wilfred Trotter who, as we saw in Chapter 5, sat on the MRC's Therapeutic Trials Committee), made it appear to be one of the most powerful instruments in the modern world. While contemporaries of the period questioned the success of some government wartime propaganda campaigns, the campaign that Hart and Faulkner organised to promote these Patulin trials as a national 'experiment', which was being conducted for the good of the country as a whole, encouraged ordinary workers to volunteer their colds. But as is clear from Hart's Glasgow visit, the success of this propaganda depended on medical officers at lower levels being committed to this national cause. Bringing the doctors on side by coopting them onto a sub-committee of the main Patulin Committee, as Hart had suggested, writing encouraging letters to thank doctors for their help, congratulating them on their progress in recruiting patients, discussing the trial by phone, and visiting local centres, were all moves that encouraged medical officers (like Sargent or Collier) to support this national venture.

Medical officers like Sargent framed their trial propaganda to call for the kind of 'public participation' that was a part of the wartime spirit, without using the phrase 'national importance' in their posters. For instance, Sargent began his first broadcast by pointing to the fact that individuals spread their 'common' colds to everyone, while simultaneously suggesting

731 PRO: FD1/3156, Medical officer to Faulkner.

732 Grant (1994).
that this negative form of public participation could be put to positive use in the Patulin trial.  
Like other doctors, he also emphasised that people all over the country were trying Patulin.

‘You must have heard of Patulin (lots of people are now asking for a small Patulin and a Pint in refreshment houses),’ Sargent announced. ‘In this important investigation ROF Bishopton with 126 volunteers has already beaten the other places trying it.’

Officials at the Royal Ordnance Factory in Cardiff stressed public participation in this trial as a democratic exercise in which everyone was being treated the same. They pinned up a notice saying: ‘A sufficient number of employees (suffering from colds) have already volunteered to assist the Medical Research Council with this important experiment... This same treatment will be available for any employee suffering from a cold.’

Hart and Faulkner particularly encouraged medical officers to take a one-for-all and all-for-one tack. Everyone needed to participate to make the experiment work and, without everyone’s help, all would be lost. As they said to Sargent, it should be made ‘quite clear to everyone in the factory that this was ‘an investigation’, not, they stressed, ‘a guaranteed cure and that we [the MRC] want their assistance in finding out whether Patulin is, or is not effective in curing the common cold.’

Sargent had done this when he ended his broadcast with the words: ‘Please remember that when you have had your first treatment, we want your opinion of it. Even if you decide not to go on with it, come and tell us what you think of it -- and if you like what you think of us!’

Some medical officers, like Dr Irene Dixon, who was bringing people to trial at the Savings Bank Department of the General Post Office on Blyth Road (London), promoted the mass trial as a patriotic duty. She was so persuasive in campaigning for the trial that Faulkner

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734 PRO: FD1/3157, Sargent to Hart, 11/3/44.
736 PRO: FD1/3157, Faulkner to Coulthard.
737 PRO: FD1/3157, Patulin, 11/3/44.
wrote to congratulate on how 'magnificently' she was doing and that hers was 'undoubtedly one of our best units to date'. 738 Operating from a GPO may have given Dixon a certain advantage over medical officers at other centres. 739 Unlike other government departments, the GPOs were well equipped, and were efficiently-run businesses which sold commodities. Dixon may also have been helped by the fact that the GPO had a permanent publicity policy in which this particular MRC campaign could be slotted. 740 In the end, she managed to recruit a total of 164 volunteers in the six weeks of the Patulin trial at the GPO Savings Bank by convincing ordinary people that they were pioneers, and by involving the whole bank in the spirit of the MRC trial venture. But there was a price of this kind of success, as is shown by Dixon's letter to Faulkner, written after she had filed her trial results off to the MRC:

I shall be much interested in your findings and I know the Savings Bank and especially the pioneers who offered up their colds for experiment, would greatly appreciate any summary if the results that you felt able to give them at a later date. Everyone has cooperated magnificently. 741

In short, ordinary people could be seduced into public participation by patriotic propaganda, but because they often felt that they had 'volunteered' their services, they wanted to know that they had not laboured in vain. This request was also echoed by Dr Ronald Lane (MO at Messrs Chloride Electric Storage Company), who told Hart that in his experience 'of using workpeople in experiments of this type', it was 'a bad mistake' not to let them know 'when the results were available'. Just 'a short note of a few hundred words ... in simple language, which he could circulate to those who had taken part' would do. 742


739 Grant (1994), 82-123; Hansard, 6 June 1934, vol. 290, col. 1019; and cols. 963-4, 993-5, 1014, 1030.

740 Grant (1994), 82-123.

741 PRO: FD1/3157, Dixon to Faulkner, 28/3/44.

742 PRO: FD1/3156, Lane to Hart, 25/1/44.
The buffered end

By the end of April, Greenwood's statistical calculators began to file their results for the local trial centres. They were as follows. Enfield Royal Ordnance Factory: 'no significant difference' in the effect between Patulin and control solution; Rolls Royce (Crewe): 'no significant difference'; Rolls Royce (Derby): 'no significant difference'; General Post Office, Mount Pleasant and Trucks and Tolls (London): 'no significant difference', and so forth. In each case, at almost all of the trial centres, the reports from Greenwood's people said that there was no significant statistical difference between the effect of the Patulin and control solutions. Meanwhile, the Army, knowing the MRC's trial was now over and that the results were filing in, wanted to know the outcome and whether they could publish their results. Then on 4 May, when the Patulin Trials Committee met to discuss these disastrous results, Raistrick dropped a bombshell. The actual Minutes of this final meeting are missing from the files but we can piece together the disclosure on that day from a summary of the situation that appears in the records. Concerned about the outcome of the trials, and seeking an explanation for what he must have heard were disastrous results, Raistrick had asked Dr Peak at Messrs Boots to do some urgent experiments on the solutions. Raistrick now implied that the problem was with the buffers. The trials had started with the solutions in a phosphate buffer in the pilot trial, but the main trials were carried out with citrate buffer owing to 'technical difficulties of dispensing'. Peak's experiments seemed to show that:

Patulin was almost immediately destroyed in citrate buffer solution, but not in phosphate solution; furthermore stability, as estimated by spectroscopic and bacteriostatic tests on which reliance had hitherto been placed, did not correlate at all accurately with the results of extraction in estimating the amount of Patulin present in buffered solution.

Hart was more direct arguing that if Peak's results were confirmed the whole of the main trials were worthless. These would mean that the trials had been carried out on inert material. Hart reported that there was now

743 PRO: FD1/3157.

744 PRO: FD1/3157, Summary of clinical use of Patulin.
a further complication: the navy trials were carried out with Patulin freshly prepared in phosphate buffer; Peak's reclamation tests, carried out both immediately after solution and after storing for 2 months, indicated that Patulin was stable under these conditions. But the army trials were carried out using phosphate stock solutions of greater strength and age which, according to reclamation tests, may well have lost practically all of their Patulin. Hence these negative results were suspect also.\textsuperscript{745}

Even the \textit{prima facie} evidence was now in question. Hart now had to confess this to the Army officials, while Himsworth, as Chairman of the Patulin Committee, summarised the situation for Mellanby.

The Committee was resolved to reinvestigate Peak's results, but they closed the matter publicly by praising the essential power and value of statistics. Raistrick conducted experiments to see if the Patulin precipitated out in the citrate buffer. Peak continued with his experiments. In addition, the MRC initiated two independent investigations at the NIMR.\textsuperscript{746} Raistrick's experiments and that of the NIMR concluded that Patulin was stable in the citrate buffer solution. Peak's later experiments also confirmed this.

On 2 June Raistrick told the MRC that his brief experiments had established the following facts. First, the buffer mixture supplied by BDH was in fact pH 6.8 and 6.0 as directed. Second, there was no evidence of any serious decomposition of Patulin in citrate buffer solutions of pH 6.8. This meant that the failed trial results could not be explained on purely chemical grounds. Third, Peak's initial results had a chemical explanation.\textsuperscript{747} On 7 June, Joan Faulkner reported that Raistrick and the NIMR groups had each independently concluded from their tests that 'there was no serious decomposition of Patulin in citrate buffer' and that 'it would therefore appear that the results of the clinical trials are valid'. She confirmed that the

\textsuperscript{745} PRO: FD1/3157, Summary of clinical use of Patulin.

\textsuperscript{746} PRO: FD1/3158, Hart to Harrington, 9/6/44; PRO: FD1/3158, Hart to Peak, 9/6/44.

\textsuperscript{747} PRO; FD1/3158, Raistrick to Hart, 2/6/44. Raistrick said that his results showed that when the Patulin was extracted with ether and recrystallized from ether there is progressive decomposition of the patulin due to some cause at present unexplained. If, however the Patulin was extracted with ethyl acetate and recrystallized from benzene, although the recovery yields are not 100\%, they are sufficiently large, bearing in mind the difficulties of quantitative recovery, to justify the belief that there is very little decomposition of Patulin in citrate buffer pH 6.8 solutions after standing for 24 hours.
Patulin Committee would not prepare a draft report of the results for publication. The following day Dr Peak dispatched a letter from Boots Pure Drug Company Limited. He explained that his initial failure to recover Patulin quantitatively from citrate buffer solution had been found to be due to extraction of material from buffer solution during the extraction which causes decomposition of the patulin during evaporation of the extract. He said that when he modified his extraction method to overcome this, his results indicated that there was no immediate appreciable decomposition of Patulin in citrate buffer solutions of the strength used in the trials. Peak claimed that he had always had reservations about his initial results, but that he had thought it only right and proper to bring them to the Committee's attention given the obvious implications of these results.

The Patulin Committee published the results of this trial in The Lancet. The editor published this mass trial proving that Patulin did not cure the common cold next to the small Army trial which had suggested that the drug did not cure the common cold. In a leader later on that month, the same journal now wrote the history of events thus: there had been two early small trials of Patulin both with good, sound methodology. One of them had suggested that Patulin was a cure for the cold, the other was equivocal. The MRC had a large-scale trial to determine the whether Patulin was a cure or not. This large-scale trial proved that it was not. The message: one could not tell whether there had been a cure for the cold unless there had been a large-scale clinical trial. Statistics had rescued the day.

**Conclusions: Mobilisation and Public Participation**

More than any other trial, the Patulin trial illustrates how personal ambitions drove the organisation, planning, and in this case perhaps even the size of clinical trials. Raistrick was determined for his Patulin to cure the common cold. If he could prove he had found a cure for this age-old incurable disease he would be more famous than Alexander Flemming. I showed him pulling out all the stops to demonstrate that the drug was efficacious. He did this by

748 PRO: FD1/3158, Faulkner letter entitled, Patulin Clinical Trials Committee', 7/6/44.

749 PRO: FD1/3158, Peak and Stroud, 'Stability of Patulin in Citrate Buffer Solution', 8/6/44.
recruiting experts from a number of disciplines in order to assemble a prima facie case for the efficacy of the drug, and then later by hurriedly conducting experiments to show that the preparation the MRC had tested in mass trials was not inert. Major Greenwood was amongst those people Raistrick recruited. Greenwood's ambition was for statistics to have a more important role in influencing medical methodology. He had been campaigning for this cause for some decades by this point. In his support of Raistrick's clinical experimental evidence in *The Lancet*, Greenwood suggested that a large number of trials should be run in spring and winter in order to account for seasonal variations in the disease. Committee reports do not give a complete picture of who influenced whom, or of how a particular policy was made. But it is significant that the trial was organised along the lines Greenwood had suggested. In this sense one could argue that Greenwood's ambitions also influenced the shape of these clinical trials.

The way in which advertising was used to mobilise the public undoubtedly shaped these trials. Mass trials could not be ‘made’ until the notion of ‘the public’ had been constructed, and this was done through an ideology of public participation. This points us to the methods of mobilising large numbers of people who were themselves being tried and defined in these clinical experiments. On one level, it would seem that the MRC’s ‘publicity drives’ which advertised the common cold trials generated participation amongst factory workers, schoolchildren and so forth. The MRC poster advertisements and broadcasts appear to have recruited some workers to the cause, but word of mouth remained the most important way of publicising the clinical trial. The trial at Bishopton illustrated that even the liveliest of poster advertisements might not, in its own right, recruit a large crowd of subjects. Frank Sargent's second broadcast only brought 31 volunteers to the 126 people he had recruited during the first month of his Patulin trial. Nevertheless, the value of the network of contacts Hart and Faulkner established to publicise this MRC trial should not be underestimated. Hart and Faulkner's organisational approach of commandeering human resources on a national scale, through personal contacts and individual meetings, produced the fuel which made this trial run like a human machine.

Setting up routines also made the Patulin trial machine efficient. Each cog knew when to turn. Patients, doctors, drug companies all knew their place in the general scheme of things.
There was a routine for the delivery of bottles of treatments and control. The set of standard forms organised what doctors put to certain patients, at what stage they asked these questions, and where they penned their answers. Sending photographs of how to administer treatments was also designed to standardise behaviour of the investigators. Sets of colour-coded bottles, suggestions for cross-checking the information the investigators collected, and lists of instructions for patients also gives the impression of a mechanised trial.

These techniques of mobilisation were themselves on trial. They were an integral part of the definition of a clinical trial. Conducting a trial now meant running an efficient machine, and to run a large machine, MRC researchers had to convince the public that everyone was participating in the same venture for the good of the nation, and after the war, for the good of mankind.
CONCLUSION

In this history of the clinical trial I have examined what appears to be a strictly medical methodology and opened it up as a historical issue which speaks of how British society worked in the first half of this century. In so doing I have shown that the making of the clinical trial in Britain was as much about the meaning of disclosure, integrity and character in English culture as it was about the place of standardisation, fairness and statistics in the first four decades of this century. The clinical trial was the product of MRC attempts to assure a future in which the British public would know which medicines were genuine and safe. It was also the product of attempts to establish rules of best conduct for the medical profession, the pharmaceutical industry and the public. I have argued that the clinical trial was made through the moral management of these groups. It was made by creating special kinds of expertise to make fair and balanced judgements about the therapeutic value of certain medicines. What was at stake in creating a 'standard' system for determining the therapeutic efficacy of medicines was nothing short of the future of the nation. Thus the clinical trial system came to be the very embodiment of what it meant to behave with British integrity and discretion, and what it meant to uphold proper standards in public affairs.

One of the central points I make in this thesis is that the system of clinical trials was made within the state by scientists and physicians like Fletcher and Dale. These figures claimed the right to speak for medical research, medicine and science by assuming administrative parts on the stage of state, appearing sometimes as bureaucrats, sometimes as scientists and other times as statesmen. I show that although the MRC assumed the legal authority to control the biological standardisation of therapies and to standardise them in the way that they had standardised insulin -- through clinical trials -- it was the drug companies who pressed the MRC for a more permanent system. This was the Therapeutic Trials Committee. The system was in the drug companies' interest because it formalised the assessment of therapeutic authenticity. It also allowed those companies to have their therapies tested and approved by the medical community and to increase their sales amongst doctors, moves which set them apart from proprietors of secret remedies and quack medicines.
Controlling a permanent system for therapeutic evaluation gave the MRC authority, and introduced more physicians to 'medical research' and clinical trials.

The TTC was disbanded in 1939. Statisticians have conceived of this inter-war Committee as a predecessor of the RCT. They have focused on the fact that the Committee made passing judgments about therapeutic efficacy, and have noted that the trials were small and that many of them were not statistically sound. While I agree that this is the case, I have argued that fair dealing seems to have been one of the Committee's most important priorities. This, I have proposed, should point us to its more important function of managing commercial and professional interests. Crucially, the Committee was protecting British interests in this area of therapeutics against German interests.

The 1940s began a new era for trials because the Second World War changed the face of British culture. The ways in which the war changed Britain were beyond the scope of this thesis. However, Chapter Six, on the Patulin trials for the common cold, demonstrated that not only did the war change the politics of negotiating clinical trials, but it made mass trials possible and justifiable in ways that they had not been before this time. The institutional structure of the NHS has been seen as an important factor in making the streptomycin trials work. However, the ways in which the patients and physicians were mobilised for that trial are similar to those of the Patulin trials. Significantly, Dr Philip D'Arcy Hart played a pivotal role in both the Patulin trials and the ground-breaking streptomycin trials.

Throughout this thesis, I have pointed to the many ways in which trials engaged the public. The public was a resource on which the MRC drew in order to make the clinical trial. At the same time the MRC defended themselves and their approach in setting up this system as being for the public good and in the public interest. But the Patulin trial showed that the mass clinical trial could not be made until the public had been constructed as a participating collective of bodies who were convinced that they acting for the common good.

Those who have fought for the RCT as a strictly medical methodology over the past fifty or so years, and who have defended it against attacks of ethicists and philosophers, might imagine its history as a linear progression of the development of these issues and of the gradual input of more statistics into its methodology culminating in the introduction of randomisation.
This is because their making of the RCT, whether explicitly, or not, has been about ignoring its historical and contemporary ties with non-medical issues in society and an insistence on starting the history of the clinical trial with Bradford Hill. I take the position that the most important period in the making of the clinical trial was in fact the pre-Bradford Hill period. Clinical trials became firmly associated with state authority, with moral management of the public, and with public participation. Without these associations, the RCT would not have had the importance and far-reaching implications that it has had for this century. Neither would Hill have occupied a central place in the RCT's history.

Although statistics and randomisation have not been the driving themes of this thesis, I have shown that certain statisticians and their efforts to defend a place for statistics in medicine during this period may have shaped the trial in a number of ways. First, the Secretary of the Therapeutic Trials Committee claimed that the TTC consulted the MRC's statisticians from time to time. Second, I showed Greenwood's central role in the Patulin trials. However, I argued that Greenwood's complaints about his prominence as an eminent statistical personality suggests that he wanted a more primary role not for individual statisticians themselves, but for 'statistics'. But whereas being in the background in the 1930s meant being behind the scenes of the Committee, by the 1940s statisticians had a place on the Committees for organising trials.

As for the issue of randomisation, I have taken a clear stand on this issue. First, it did not have an important role in shaping the clinical trial before 1945. Second, in the period before 1945, 'randomisation' should be taken to have two kinds of meaning: one, a strictly statistical meaning and the other, a more general, popular sense of the word 'random', namely, 'mixing things up', or drawing a sample from a population in such a way that the selector could not know what kind of selection he would make. It is important to recognise these two meanings. In attempts to assure Bradford Hill's place as the person who brought the statistical tool of randomisation to the clinical trial, accounts of the subject have tended to write any other notions or ideas or random elements in assigning therapies to patients before Hill. Hill undoubtedly deserves the credit for seizing this opportunity to put his ideas in practice, but striking the existence of related notions of randomness from the history books makes for an unconvincing historical account of why the streptomycin trial occurred and why randomisation
remained an element in the trial. Giving these other existing notions a place helps to explain why this notion had meaning for those involved in the first streptomycin trial. It is, in effect, not unlike the situation I presented for standardisation earlier this century. Hart, who said he had 'mixed things up' in the Patulin trial, would have understood the intuition behind, and purpose and plausibility of, a strictly statistical notion of randomisation.

Finally we come to the ethics and moral issues about the making of the clinical trial. The approach of dividing the thesis into three parts has in itself been a deconstruction of the master narrative. It has also been a deconstruction of the medicalisation of certain historical phenomena that happened to have evolved in the medical domain. In so doing I would like to raise the question of how one might open up historical developments like the clinical trial for cultural critique. How one writes the history of the clinical trial has implications for opening up the moral issues about clinical trials. Thus, my point with this history is that the moral issues surrounding clinical trials are not simply questions about the ethics of randomisation: they are moral questions which revolve around how disclosure is managed in English culture, the extent to which character and characters should be allowed to assess authenticity, and what it means to be fair. In short, they are moral questions about how society works.
EPILOGUE

Major Greenwood retired from the directorship of MRC's Statistical Committee in 1945, the year after the mass trial of Patulin. Austin Bradford Hill took his place as head of what became the MRC Statistical Research Unit, and also as Professor of medical statistics at the University of London. In 1946, the MRC ran a mass clinical trial to test the effect of the drug streptomycin on tuberculosis. Hill, Philip D'Arcy Hart (Director of the MRC’s Tuberculosis Unit), and Marc Daniels (the Assistant Director) designed this trial together. It was a randomised controlled clinical trial. Randomisation was Hill's idea. With Hart's and Daniels' support this first randomised controlled clinical trial was conducted. The trial ran from 1946 to 1948 when the results were published. Forty-nine years later, there are plans for a high profile international meeting, to be held in 1998, to celebrate the birth of this medical revolution.

Austin Bradford Hill played a central role in writing this grand narrative of the clinical trial. Hill established the clinical trial as a strictly medical methodology in which the trial was a model clinical experiment and was ethically defensible. The streptomycin trial stood as a 'classic' example of this model. Hill's interests in framing that trial as a model clinical trial are a part of the professionalisation of medical statistics, epidemiology and the more widespread use of statistics in medicine.

During the 1950s and 1960s Hill promoted randomisation in the controlled clinical trial through papers and lectures in Britain and internationally. Archie Cochrane, Iain Chalmers, Richard Peto and Richard Doll are some of the more prominent people who have developed the trial methodology, and who have promoted it internationally and continue to do so. These physicians and statisticians have defended the RCT against attacks from ethicists and members of the general public who see randomisation as an inherently unfair, unethical, undemocratic statistical tool, in other words, that trials are illicit human experiments. They have also had to defend it against some statisticians and philosophers who argue that both the methodology and analysis are seriously flawed. One of main points of my thesis, however, is that focusing on randomisation draws out attention away from what I feel are the most important and chilling implications of the establishment of this medical methodology in our
times, namely the role of the state and the public in making of the clinical trial. Hill's focus on the ethics of clinical trials and of randomisation was culturally bound. He was defending this methodology during the 1950s and 1960s, in the aftermath of the Nuremberg trials and amid growing concerns about experiments on patients in the clinic. He did not want this 'revolutionary' medical innovation to be tarnished. He wanted and, indeed, needed to set it quite apart from these emotive issues. Examining post-war issues surrounding the emergence of 'ethics' as a part of the language of public debate about clinical trials points to the changing relationship between ‘clinical trials’, ‘the public’ and ‘the state’.
Dear Mr Elliston,

Many thanks for your letter of the 10th November and its enclosure. I agree that these will illustrate the difficulties that quack remedies raise. I can also sympathise with your desire for some arrangement that would effectively dispose of false claims: as our files here abundantly show, Members of Parliament are not alone in having to deal with this kind of propaganda.

I am quite clear, however, that the matter is not one for the Medical Research Council to take up. Their concern is the advancement of knowledge, and that would not be helped by the examination of claims which have neither a rational basis nor the support of any trustworthy practical evidence. The Council have therefore always refused to divert resources in men and money, badly needed for vastly more important work, to the investigation of claims for which a prima facie case is not properly made out. It has also to be remembered that they can secure clinical trials only by the co-operation of the hospitals: this they have at present for the testing of new remedies of an authentic kind, but I am sure that they would soon forfeit it if they went beyond that.

A further objection, which would apply equally in the case of any other body, is that most quack remedies are secret preparations. To test such a remedy is to report upon a substance which is identified only by the invented name attached to it by the makers, and of which the composition may therefore be changed by them at any time. Apart from that, a secret preparation may contain dangerous components, and at best it usually consists of substances of which the medicinal properties are already well-known.

In any event, an unfavourable result in an official test would not necessarily end the matter. We have had experience of testing methods of treatment that were sufficiently respectable in themselves but that happened to have a partisan backing. The adverse report has merely provided a fresh battleground for the propagandists.

The machinery for testing genuine new remedies already exists in our Therapeutic Trials Committee. What is needed for the other sort is legislation forbidding the sale of secret
preparations, or indeed any preparations for which no case can be made out or that are merely well-known substances disguised under fancy names. This has already been done in the case of remedies for venereal diseases, and also, under the Therapeutic Substances Act, in the case of vaccines and some other substances.
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