

Chapter 23 An Ethical Assessment Professor Sir Ian Kennedy

23.1. Introduction

The question I am asked to address is whether the trials involving volunteers which are described in the Survey were conducted in an ethical manner. I interpret this to mean: did those carrying out the trials behave in a way which right-minded others would think at the time was ethically appropriate and justified, taking due account of prevailing values and circumstance. Of course, this proviso only goes so far. While it is important to recognize that views may change over time, for example, as to the balance to be struck between paternalism and freedom of choice, it must be said that there are outer limits to what is ethically appropriate conduct. Conduct which exceeds these limits cannot be justified by appeals to the prevailing values or circumstances of the times. Examples of ethically impermissible conduct in the context of research on humans, which no amount of references to the context or circumstances of the day could justify, would include “experiments” involving the intentional infliction of torture, or the intentional causing of a person’s death. These were regarded as repugnant long before the modern development of human rights following the horrors of the Second World War. And, necessarily, it follows that appeals to cultural diversity, or the subjective right of states to determine for themselves what is morally acceptable, in this context cut no ice. Some moral prescriptions are universal in nature, if the notion of a common humanity is to mean anything.

What I will be asking, therefore, is whether the trials at Porton, even if carried out with honourable intentions (that is, the belief that the interests and rights of the volunteers were not being put improperly at risk and that the ends pursued were good and justified), in some way either went beyond the ethical standards of the day, or even beyond what should ever be contemplated by a civilized society. In the context of the Survey, the latter question, of exceeding the limits of what may be permissible whatever the times or circumstances, is largely of academic interest only. But, it must not be ignored, particularly given the backdrop of war and the threat of war which may be offered to justify conduct. For, this is the context of the research at Porton. It must be borne in mind that the temptation always exists to invoke external threats and the national interest as a means of justifying what would otherwise be thought morally doubtful or impermissible. The temptation may be to stretch the limits, or even to go beyond them. It is important for me, therefore, always to keep in mind what, if any, influence war or the threat of war and the consequent invocation of the national interest should be allowed to have on the conduct of research into aspects of warfare, (see the discussion in Chapter 22.3.5) *

The trials conducted at Porton are described in the Survey. The Survey was conducted with very great diligence. The amount of research and analysis was considerable. The expressed intention was to examine and report openly on all the various sources of documentary evidence. I did not review the sources themselves. My comments here, therefore, relate to what was produced as a consequence of the research undertaken. I have no reason, however, to doubt that the Survey reflects its stated intention.¹ I did review some films (which I refer to). I did not see all of the very

* Hereafter, previous chapters will be referred to as, e.g., 1.1.1, (without the word “Chapter”)

¹ For completeness, I add a further observation. When I had completed and submitted the original version of my chapter, the facts on which I based a particular view were reviewed and amended and I was asked whether I wished to amend the view which I had taken. As it happened, I did not alter my view. But, I expressed concern. If some facts could be reviewed, why not others? Were my views, already tentative, even more so, since the factual basis for them might be open to doubt? The MOD responded responsibly. They undertook to review all of the references throughout the Survey on which the author, and necessarily I, had relied. This review has delayed the publication of the report for some time. In the event, the MOD concluded, after reviewing around 90% of the references, that the Survey had been accurately compiled (subject to the occasional unimportant detail). One amendment, however, has remained and I have commented on it (see footnote 2 at 23.7.4)

many films which are held in the archive of the Imperial War Museum, the quality of which, in terms of preservation, varied considerably. To that extent, I gained only a partial picture and do not, therefore, greatly rely on them as evidence (although I do refer to them briefly at one point (23.6)). I was, however, involved in the conduct of the Survey in one regard: from time to time I requested that further information be gathered which would allow certain central ethical concerns to be addressed. My requests were always met, subject to one exception which it was beyond the Survey to meet and which I refer to later (the recording of the recollections of the research scientists working at Porton during the relevant time). Moreover, my independence was respected at all times. As agreed, there was no editorial control on the part of the MOD over what I might say.

23.2. Guiding Principles

In writing this appraisal, I adopted certain guiding principles, or assumptions. I set them down here, so that my approach to the material contained in the Survey can be understood (and, if appropriate, challenged). They are, in effect, a series of first principles, rather than the product of a synthesis of various Codes or Guidelines, though in large part, they reflect what Dr Maclean sets out in Chapter 22.

1. The ethics of research on human volunteers is an area of systematic study and enquiry which was relatively neglected until as late as the 1980s. Codes and Guidelines had existed for some time, and appeared more frequently from the mid-1970s onwards, but the awareness of them varied, as did the understanding of what they might mean when applied to the reality of actual research. Moreover, it is in the nature of the subject that there have always existed differing views as to what conduct is appropriate. Indeed, a book could still be published in 2001 by the British Medical Journal with the title *Informed Consent in Medical Research*, in which what most would regard as the core notion of research ethics, that of consent to research, is the object of critical and, in some cases, skeptical appraisal. [1] Thus, we are not dealing here with an area of clear, agreed rules akin to a statute (if ever even statutory language were clear!). We are dealing with general precepts, largely in the form of exhortations to good conduct. The translation of them into practice has been left until recently, (with the advent of the supervisory role of Ethics Committees), to the integrity, the good sense and the conscience of the researcher.

2. It is crucial to recognize that my assessment represents my judgement based on the facts as they appear in the Survey. Being a judgement, there always exists the possibility that others may disagree. Such disagreement, to be valid, however, must be reasoned and not merely based on prior unproven assumptions, or bias.

3. Conduct may only fairly be judged in the context of the times (subject to what was said earlier about the existence of limits which do not change over time). This means that it would be wrong to use as a standard of assessment the developed concern for human rights which is part of current discourse about research, when considering conduct which happened 40 or 50 years ago. The ethical evaluation of research has been an evolving process. It is still going on.

4. Research on human volunteers was not only conducted at Porton Down over the relevant period. It has been an established feature of the development of medical science and of pharmaceutical products for decades. Indeed, one of the first formal attempts to prescribe how researchers should conduct themselves appeared at the end of the 19th century in the form of the Prussian Code of 1900 (see, 22.2.2). Any assessment of the conduct of research at Porton, therefore, must be informed by some understanding of how research was conducted and monitored elsewhere at the relevant times (see, for example, 22.1.2 and 22.4).

5. The context in which trials were conducted at Porton was one of war, the threat of war and of civil disorder. The Survey covers first the period before the Second World War, when the horrors of the use of gas by the enemy in the First World War were still etched in the folk memory of the

nation. Secondly, it covers the period of the 1939-45 War, when the nation's survival was at risk and the perceived risk of the use of gas and other chemical agents was great, as was the perceived need to retain an offensive capability. Thirdly, it covers the period of the Cold War, interspersed as it was with localized conflicts, during which the Soviet Union and other countries were understood to be developing a range of deadly chemical agents for offensive use. And, during this third period, there were times of civil disorder, both in the United Kingdom and in its Colonies, which the governments of the day saw as calling for responses which included incapacitating chemical agents. In short, the aim of the research at Porton was the defence of the realm, the protection of its military and (to a lesser extent) police, and the protection of its civilian population. The nature of the threat and, therefore, the challenge to the researchers at Porton are set out in the first two Chapters of the Survey. The trials conducted at Porton, as summarized in Chapters 3 and 4, reflect Porton's response to this challenge.

As has been said, the extent to which this context may justify that which in other circumstances may be judged impermissible, must be examined. But, it is not hard to imagine that those pressing for results in government and those carrying out the research saw the work at Porton as of a different order from the conduct of research by, for example, pharmaceutical companies developing new medicines. This is not at all to say that they regarded themselves as free from constraints. The Survey demonstrates that there was constant reference to safety and risk. It is merely to say that in their eyes, and I venture to suggest, in the eyes of the population generally, the work might have been regarded as simply more important in the scheme of things. And, it would be wrong to ignore this sense of the importance of the work being carried out.

6. Despite the best efforts of those conducting the Survey, the picture which appears is necessarily incomplete:

(a) Documentary evidence exists. It is what the Survey relies on to a very great extent. But, it cannot tell the whole story. For earlier decades it is sparse or non-existent. Later, it is more complete, but must be seen against the background of other information, instructions and exchanges which did not find their way into documents but which were undoubtedly part of the context in which volunteers were recruited and took part in trials. In the absence of this undocumented evidence, there is a tendency to treat the documents which do exist as if they told the whole story. They do not. Moreover, because it is written down, there may be a tendency to give more weight to a particular entry in a record than it should properly be asked to bear. Selected quotations may be useful as giving an impression of what went on. To that extent, I shall use them. But, they are incomplete evidence, at best. They do not tell the whole story. They can lend support to a view, but they cannot serve as definitive proof of what was going on.

(b) The Survey is assisted by the recollections of volunteers. But, many, indeed most, of the trials took place long ago. Memories, therefore, may not be reliable. This is not to impugn the integrity of those volunteers whose recollections are reported in the Survey. It is merely to acknowledge that what may be remembered is inevitably filtered through and affected by the experience and events of intervening years. Moreover, the volunteers were not, of course, a homogenous group, nor do they all tell the same story. Furthermore, those whose recollections are recorded do not constitute a scientifically designed sample, such that their recollections may be relied on as representative of all. They are, in fact, a tiny proportion of all the thousands and thousands who took part in trials over the decades. At best, therefore, their recollections are anecdotal evidence. That said, however, the volunteers whose recollections are recorded all have one thing in common. They were all on the receiving end of the trials which were carried out at Porton. To ensure as complete a record as possible, therefore, their recollections ought to sit alongside those who conducted the trials. This is not so as to set up some sort of opposition, which may not, in fact, exist. It is merely to enable the researchers' recollections to add to and thereby enrich the account which the Survey seeks to construct. Unfortunately, for contingent reasons, having to do with the involvement of the police, the Survey was not apparently able to take account of the researchers' recollections. This is a serious gap.

It is serious not only because we are denied their evidence. It is also serious in terms of fairness. To the extent that the evidence which is available may suggest that the conduct of a trial (or trials) was not proper, this, directly or indirectly, may constitute an adverse comment on those carrying out the trial(s). Without the opportunity to hear their response, it must follow that, for the sake of fairness, any conclusions which I reach which reflect adversely on researchers must be regarded as tentative only: amenable to being displaced should further evidence be made available.

(c) There are some questions which I have not asked, even though they are clearly of considerable (some might say crucial) importance. These relate to why certain trials, or categories of trial, were carried out at all. An example may be the lengthy and risk-prone research on liquid nerve agents, such as GB. The effect of GB vapour could be said to be far more important, in the scheme of things, than the effects of liquid GB, not least because, if delivered, for example in a bomb, relatively few would be affected by the liquid who would not also have been affected by the explosion of the bomb itself. The critical effect to be studied would be that caused by the vapour produced and spread by any bomb. Yet, trials related to liquid GB went on for years.

One reason why this question might properly be asked is that it is an accepted rule of thumb that bad science is bad ethics: if a trial is scientifically flawed, it should not be carried out. To carry it out, therefore, is unethical. (An example might be the testing of the substance in the captured German shells, described in 8.2.1 and discussed later (23.5.1)) I have chosen to leave this question unanswered, but others may wish to pursue it further. My reasons are as follows. First, I am not a scientist and thus do not know, nor does the evidence tell me, enough to reach a firm conclusion. Secondly, there may have been evidence from intelligence or other sources which justified the research, but which is not revealed in the Survey. Thirdly, the research at Porton was, as I shall explain later, carried out under the supervision of various committees. It might be thought that these committees would have satisfied themselves that any proposed research was necessary. On this view, it would be difficult, though not impossible, to second-guess the judgement made at the time. In fact, however, the committees seem to have been concerned either with wider strategic questions as to the direction of research, or with the particular, and critical, issue of safety. The Survey does not identify how the territory in between, in which the questions whether Porton should, in fact, be doing these particular trials at all, or whether the information sought was necessary, was covered, if at all. So, the question lingers.

23.3. The approach adopted

It is important to state at the outset that it is not the aim or intention of this assessment to examine each and every trial carried out at Porton during the period covered by the Survey. The reasons are obvious. There were many thousands of trials. They varied greatly in nature. And, the quality of the evidence available as to how they were conducted also varies greatly. Instead, the approach I adopt is to identify:

1. the mechanisms for supervising the conduct of trials
2. the general patterns or trends in the conduct of trials which emerge
3. specific issues or cases which warrant particular attention.

In following this approach, I draw on the chapter on the ethics of research written by Dr Maclean (Chapter 22). In particular, I take account of the rather gradual recognition among researchers (and more so among the general public) that research on healthy human volunteers ought in some way to be supervised (the word “regulated” may be too strong). Scientists did not feel the need to be told how to behave, (and some still do not!): to a degree it would have been seen as insulting in the tenor of the times. The strong assumption that scientists, especially if they were

also doctors, could be relied on to act properly prevailed for much of the period under review, and, albeit in an attenuated form, survives to this day. Paradoxically, the emergence of the Nuremberg Code was thought by researchers here in the UK to have little to say about the research which they carried out, because it grew out of the atrocities committed by the Nazis before and during the Second World War. As Professor Beeson put it in 1964, as recorded in the *Journal of the American Medical Association*, "I think we must read the Nuremberg Code in reference to the conditions under which it is written. This is a wonderful document to say why war crimes were atrocities, but it is not a very good guide to clinical investigation which is done with high motives" [2]. This comment is not repeated here to endorse it, but merely to record what influential commentators at the time thought.

Subsequent Codes and Guidelines were also seen as, to a degree, remote from what researchers actually did. A major incentive towards developing a greater engagement with ethics came with the involvement of organizations which funded research, not least the Medical Research Council. Its first formal statement on research ethics appeared as early as 1953, but it, like many that followed, was directed at clinical, therapeutic research on patients and its special problems, rather than research on healthy volunteers. It was only later, in 1963, that reference was also made to the latter form of research. By making the observance of certain ethical standards a condition for receiving funds to conduct research, the attention of researchers was obtained. But, perhaps the single most important stimulus was the decision of the Royal College of Physicians to take a lead both in championing the cause of the ethics of research and in setting down Guidelines which were accessible, comprehensible and measured. It was not until 1973, however, that the Royal College formally addressed the question of research on healthy volunteers.

Government then became engaged and from then on the ethics of research have received increasing attention. Guidelines have been refined; sub-areas, such as for example, research on children or the mentally incapacitated, have been developed; a scholarly literature has grown up; and teaching and training in research ethics is widespread. But, this particular flurry of recent developments has only occurred over the past fifteen years or so. Much of it post-dates, therefore, the period covered by the Survey. Moreover, there is inevitably a considerable gap in time between the promulgation of what is represented avowedly as advice and its translation into the practice of those actually carrying out research. This being so, it is of the first importance to avoid looking back through the perspective of hindsight. This leads us again to the proposition that the only way fairly to assess the conduct of the trials by the researchers at Porton is by reference to the standards of the time.

23.4. The Commissioning and Supervision of research at Porton

Porton conducted research at the behest of the Services, through the War Office, later the Ministry of Supply and still later the Ministry of Defence and its Chemical Defence Research Department. This does not, of course, mean that Porton was obliged to do everything that it was asked, particularly, from the point of view of my assessment. It, meaning those who directed Porton and worked there, remained responsible for the conduct of the research undertaken. If conduct was improper, it remained so whether or not it was done in compliance with requests from others, even the government of the day. This is not to say that governments asked for research to be carried out which was acknowledged to be improper. It is only to say that, from the standpoint of ethics, it is not open to Porton to plead some form of "superior orders" to justify whatever was done.

There is clear evidence that Porton recognized this. On a number of occasions, the evidence shows that those at Porton indicated that certain research:

1. should not be carried out on ethical grounds, for example, research on agents whose primary mode of action was to induce hypo- or hyper-tension (12.1.2-3), or

2. would have to be carried out first on animals (see, for example, 8.5 and also the insistence of the Committee for the Safety of Human Experimentation (COHSE) that dyes be tested first on animals, 18.2.2),
or
3. would perhaps take longer than envisioned (human studies of T4423 were only begun after 10 years of work on animals (16.4)).

Equally, there is evidence of constraints moving in the opposite direction, placed by government and its Scientific Advisory Committee (SAC) on what Porton might be allowed to do in fulfilling what was asked of it, (for example, in the case of V agents, described in 10.1, and in the conditions laid down by the Adrian Committee, set out in 9.1).

In carrying out their research, Porton, was supervised by committees which went by different names at different times, as is set out in detail in 4.2 and 4.3. The word “supervised” is important, since it appears clear that the committees not only monitored the strategic direction of research into chemical warfare, but from time to time gave technical advice, particularly advice on safety. As the final paragraph of 4.3 makes clear: “...the work at Porton, since it was opened in 1916, has been directed according to the needs of the Armed Services. Approval for work done at Porton with volunteers was obtained for types [*my emphasis*] of human studies up to the mid-60s. Thereafter, it became usual to seek approval for every human study [*my emphasis*]. From the mid-60s this approval was sought from a committee with members from outside Porton”. Thus, there are numerous examples in the Survey of the relevant committee approving a research project and of stipulating that research was not to be carried out, at all or until certain conditions were met. One such example is the refusal by COHSE in 1976, on grounds of safety, to allow the carrying out of a trial into exposure to high concentrations of CR over a short period of time (15.6.2).

The importance of referring to this system of supervision is twofold. First, it meant that Porton was accountable to others who might properly be assumed by those working at Porton and those outside (ultimately the general public) to represent and reflect the values of the day and, thereby, offering not only scrutiny but also validity to what was done. Secondly, the various supervisory committees over time contained a proportion of members who were outside the communities of the armed forces and research into chemical warfare. About half of the members of the Chemical Defence Advisory Board (CDAB), from 1946 onwards, were independent “outsiders”. Further, about half of the members of the CDAB’s 5 Sub-Committees were equally independent, including the important Applied Biology Committee (ABC). The same was true of the subsequent Medical Committee (MC). The ABC was established in 1965, following internal disagreement in Porton about the safety of trials on incapacitating agents, specifically to be the “Father Confessor” for Porton’s staff and to “damn the proposals [for research] of those who were trying to go too far too fast” (13). The Survey describes how, at least after the ABC had become the MC in 1973, these “outsiders” had the right, which they exercised, to meet as a separate group in “closed meetings” to discuss particular aspects of the research at Porton (see, for example, the closed meeting to discuss trials of drenching with CR gas in 1973 (15.4.3)). This reinforces the proposition that the research at Porton was subject to external scrutiny, supervision, and approval.

Perhaps the most crucial development, described in 4.3, is that, from 1965 onwards, the ABC, with members from outside Porton and government, was given responsibility for advising on safety and ethics and for approving studies on human volunteers which Porton proposed. This superseded the supervision which had been exercised from 1963 by the internal committee, COHSE. An example of COHSE’s supervision can be found in the decision not to conduct further trials of TL 2833 because of the risk of cerebral hypoxia (12.2.4). The more wide-ranging discussion of safety which this decision formed part of is considered later. Further, in 1972, both the MC and COHSE exercised close supervision of the trials involving drenching volunteers with CS solutions (14.4.4) and CR solutions (15.4.3). It follows that the researchers at Porton were not free, (even had they wished it), to ignore the views and values of the wider community. (There is at least one example which seems to suggest otherwise: the use of GF in studies in 1963-64.

The Adrian Committee had stipulated in 1953 that, of the G agents, only GB should be used in trials. No explanation is given for why this condition was breached, but it is suggested in the Survey that the fact that the results were widely published suggests that Porton may have received authorization to conduct them (9.4.6) There is no evidence offered to support this view, but it appears to be plausible).

It is important, however, not to press this point concerning supervision so as to suggest that the research carried out at Porton, therefore, always was in accordance with the general ethical principles of the day. This is because, as was said earlier, the supervision seemed only to go so far. In translating any general permission that they received, the researchers still had discretion as to how exactly to proceed. Thus, although constrained generally, for example, to ensure that research was conducted with due regard to the safety of the volunteers, it was still open to the researchers in principle to interpret this constraint in ways which went beyond the permissible. This is one of the questions which I will consider in greater detail later.

But, the important point here is that the existence and exercise of scrutiny and supervision from outside suggest that it is hard to argue that the researchers engaged in egregious departures from the principles of proper conduct of the sort which would be condemned by all civilized society, unless it is argued that the "outsiders" were all committed to the conduct of research in an unethical manner and colluded with the researchers at Porton in this. The existence and exercise of scrutiny and supervision do not demonstrate, however, that the researchers never behaved unethically, in the exercise of their discretion in conducting a particular trial. This is still to be examined.

In this examination, it will be necessary to bear in mind that the researchers at Porton did not always speak with one voice. The Survey refers to examples when researchers disagreed among themselves as to how properly to proceed, and when there was disagreement between researchers and senior staff. One example of particular importance is described in Chapter 13. Tests of incapacitating agents on human volunteers were suspended in 1965 because of concerns over the programme. The Head of the Medical Division at Porton doubted the evidence that the agents were safe and expressed the view that "it would be unethical" to conduct trials in peacetime. He banned all further trials involving hallucinogenic agents. The medical staff at Porton were also concerned. One was described as "very near breaking point". Two resigned. The Director of Porton, however, perhaps reflecting the pressure he was under from the Services, challenged this "question of medical conscience" (13). He convened a meeting of outside experts at University College London specifically to determine what "our medical colleagues outside Porton would consider justifiable", that is, to discover what were the prevailing standards of the day. The Head of the Medical Division was ultimately reassured by the views expressed and trials on incapacitating agents began again. The significance of this expression of concern and subsequent discussion lies in the fact that there was clearly an awareness of the need to conduct research in an ethically proper way and a preparedness to discuss how this should be achieved. This is not to say that the appropriate course was always adopted. But, it does say that those at Porton were sensitive to ethical concerns, rather than proceeding in some kind of ethical vacuum.

23.5. The conduct of research

As I said at the outset, I intend to concentrate here on what may be called general trends or patterns in the research at Porton. I will refer to specific examples when they may illustrate the discussion, but in doing so, I am conscious of the need to prevent a particular example from becoming the basis for a general conclusion. Examples belong in a context and I will seek to see them in this way.

It may be helpful to consider what I call general trends by reference to the various central ethical concerns which are relevant to the conduct of research on healthy human volunteers.

23.5.1 Prior research

Given that research on healthy human volunteers should not expose them to risks of harm, (something which I will explore in detail later), it was accepted during the period of the Survey that research should first be conducted on animals, where appropriate, and that the relevant literature should be searched and studied. (An unusual exception appears in 8.2.1 when, in 1945, the substance in captured German shells was tested simultaneously on rabbits and human volunteers. When one of the rabbits promptly died, the trial was immediately ended, and the substance washed off. The reason why this approach was adopted may be that it was assumed that the substance was a vesicant, similar to mustard gas. It turned out, however, to be an otherwise unknown gas, GA. The approach may be criticised as exposing the volunteers to unnecessary danger. Routine tests carried out to determine which of the known substances it was would have shown that, in fact, the substance was unknown. At that point, suitable precautions could have been taken. Instead, volunteers were put at risk of serious harm. Compare the appropriately cautious approach described in 15.3.3 which involved putting the particular concentration of CR gas in liquid form into the eye of a rabbit 30 minutes before putting it into a volunteer's eye). One example of extensive prior research can be found in the considerable work on GA, GB and GD carried out on animals, as described in 8.3.2.

The aims behind the extensive use of animals included the identification of responses to particular substances and the point at which those responses became dangerous and even fatal. Assuming that the information obtained was transferable across species, from non-human animal to human, (different animals were used for different tests), the tests allowed researchers, in principle, to control the risks to which the volunteers were exposed.

There is ample evidence that research on animals was seen as an essential first step before trials of the effects of a substance on humans were carried out. Indeed, on some occasions, the research on animals took place over a number of years before researchers deemed it safe to proceed to trials on humans, (see, for example, 8.5, describing tests on animals which took four years (1947-51), before nerve agents were tested on the skin, although, as I shall describe later (23.7.4), volunteers were still exposed to danger. See also the work on V agents which was pursued from 1953-58 before human studies were begun).

The exception to the prior use of animals was in the case of psychoactive agents. The view taken was that prior research on animals would be of no benefit when what was being explored was the effect of an agent on a human's motivation or powers of concentration. Instead, the researchers relied on prior studies carried out on humans and reported in the open literature. For those incapacitating agents about which little was known or reported in the literature, the medical staff at Porton carried out tests on themselves before exposing volunteers, setting the initial doses very low and gradually increasing them until an effect was observed. That said, animals were, in fact, still used in the initial stages of research into these agents in 1961-63 (11.1).

23.5.2. Consent

Consent is undoubtedly the most important ethical pre-requisite of research on healthy human volunteers. The word "volunteer" signals as much. The guiding principle is that people are being asked to come forward to participate in research, the results of which are not intended to be of any direct benefit to them, and, as such, they should not be taken advantage of, or exploited. They should only be involved in research if it is clear that they have agreed (consented) to do so. In this way, proper respect is shown to each person's right to choose.

While the general principle of the supremacy of consent is simple to state, the emergence of consent as being of crucial significance, its meaning and its application to concrete circumstances are less clear. As regards its emergence, it is important to note that the need, or even desirability, of consent has prompted debate over the period covered by the Survey. But, it

is fair to say that this debate has focused on what is called “therapeutic research”, that is, research designed directly to assist the research subject while at the same time generating information of a generalisable nature, pursuant to recognized scientific principles. Such research may well be conducted on the very ill and there have been those who have argued, and still argue now, that to seek consent in all circumstances may, in some circumstances, be inappropriate and even cruel. The same argument has not, however, been employed in the case of “non-therapeutic” research, that is, research on healthy volunteers. In my view, it has no place in the context of such research. Thus, it has no place in my assessment of the research conducted at Porton. Nor is there any evidence that the argument was reflected in the approach to research adopted at Porton. Although, as will be seen, there is room for discussion as to the quality of the consent obtained in some circumstances, there can be no doubt that, as a matter of principle, the need for consent was recognized throughout.

Turning now to the meaning and application of the notion of consent, in what follows I will use the term “real consent” to describe consent which can be said to be ethically sound. To be real, it is now accepted that consent has to meet certain criteria, although these criteria were only effectively articulated over the last two decades. Previously, it was more a case of their being intuitively understood, rather than expressly articulated. Three criteria are ordinarily identified, each of which itself calls for closer analysis. In short, real consent is not straightforward. The three criteria are:

1. that the volunteer be competent to consent
2. that the consent be based on sufficient information to allow a choice to be made
3. that the volunteer truly is a volunteer.

The issue of competence need not detain us here. It is largely concerned with the mentally ill or the mentally disabled, children of tender years, and the elderly who may be confused. The assumption may properly be made that those who volunteered to attend Porton did not fall into these categories, nor were they otherwise mentally incompetent to consent.

So, I turn next to the issue of information. This is of central importance. The accepted view is that a researcher has a duty to give to each research subject that information which will allow the subject to make a considered choice whether or not to take part in the research. Such information operates at a number of levels. At the most general level, it means that the research subject must be aware of the purpose for which he is being recruited: that is, that he is involved in some form of research, (a test, or trial, or some such word). At its most specific, it means that the subject should be made aware of the particular features of the particular test or trial in which he is being invited to participate. (I add, by way of parenthesis, that the Survey in the paragraph of 21.3.1 immediately before Figure 21.7 gives too specific a meaning to the word “purpose”, interpreting it as referring to what a specific trial would involve, rather than to the general idea of being involved in research).

23.5.3. General Information

The distinction between general and specific information is of considerable assistance in understanding and assessing the material described in the Survey. In my view, the distinction is helpful in understanding the approach adopted towards recruiting volunteers for research at Porton. The system is set out in general terms in Chapter 5 of the Survey and described in detail in Chapter 21.

Prior to 1964, general calls were made for volunteers in a series of stages. The calls went out from the War Office to Service Departments, which then wrote to Units (as described in 21.2.1). After 1964, the system changed. Notices calling for volunteers appeared in the official administrative instructions issued by the MOD and the Service Departments, to which all service personnel had access. Notices issued by the MOD were then translated into Notices issued by the various Services. Porton also began in the 1960s to recruit directly from Units in the form of

“special intakes”, (as described in 5.3.2). While there is a wide range of evidence in the Survey of the formal Notices which appeared after 1964, there is no direct evidence, other than the recollections offered by some of those who volunteered, of what was said or done later in the process of recruitment.

As regards the earlier calls, before 1964, that went from the MOD and Service Departments, the available evidence suggests that the proposed forms of words to be used contained little or no specific information for potential volunteers concerning the nature of the trials which they would be exposed to. The calls were general in nature and, at the same time, couched in reassuring terms. The Army’s wording in 1961, for example, stated that “the tests carried out at [Porton] are carefully planned and are arranged so as to eliminate foreseeable danger. They are carried out under expert medical supervision”(21.2.1). Reference was made in the Army’s Notice to possible physical discomfort, which is described as “usually very slight”. The Royal Air Force’s Notice described “any physical discomfort which may result” as “very slight”. The Royal Navy’s Notice was silent on the issue. Taking account of the generality of trials, however, what was said is undoubtedly true, though not particularly revealing (21.2.1)

As regards the Notices which were issued after 1964, in the form of Defence Council Instructions (DCIs), it is clear from the Survey that the various Notices differed among themselves and over time. Some were more specific on some matters, others did not mention matters which could, as a matter of first impression, be regarded as important in affecting the choice made by the volunteer. One such matter is whether or not the volunteer would be exposed to danger, and, if so, to what degree of danger. In fact, long before 1964 and the change in the method of recruitment, references were made to danger and to risk. The words used, however, were clearly intended to play down risks (although, by and large, the risks of harm were indeed remote). In 1950, for example, a War Office recruitment notice stated that “Tests are carefully planned to avoid the slightest chance of danger” and this expression was used in a letter to Royal Air Force Units, and by the Army and Royal Navy (21.2.1). But, the assertion that there was no danger or risk at all, particularly after the fatal incident in 1953 (which I shall discuss later), prompted a review of recruitment notices. The Survey refers to the advice of the Treasury Solicitor. His advice is clearly right, that the notices ran the risk of appearing to offer a guarantee of safety when “there was always some possibility ... of a danger being discovered” (21.2.2). This cautious advice, although accepted by the War Office, was not, in fact, translated into practice in Notices produced by the Royal Navy or the Royal Air Force between 1958-63, although it was by the Army.

That there was a tension between the desire of Porton to recruit volunteers and not discourage them, and the need to be careful (and honest) in the words used, is clear. A meeting was convened at Porton in 1962 at which the concerns of Porton’s staff were expressed. New wording, adopted in 1962, did not mention danger or risk (21.2.2). It did, however, and this is of equal importance in assessing the openness of the process of recruitment, state that the research was concerned with “chemical warfare agents”; identify a range of tests which were commonly undertaken; and state that each test would be explained to the individual volunteer, who could refuse to take part if he wished (21.2.2). That said, the Royal Air Force’s Notices still made no reference to the right to withdraw in 1962, and 1963.

One view of these discussions and their outcome could be that volunteers were being misled. Another view is that words such as “foreseeable danger” may be thought to be too question-begging and also could dissuade servicemen from volunteering, when, in fact, the very great majority of trials were routine, any dangers were, at best, remote, and the assumption was that the volunteers would be given detailed explanations before any trial, thereby allowing potential volunteers to withdraw. The fact that some Notices did not, in fact, mention this right to withdraw is arguably of less significance if, as is suggested in the Survey, this complied with the approach suggested by Porton. Those drafting the Notices could perhaps legitimately take the view that, after all, it was the researchers at Porton who administered the trials and could be assumed to cover such matters.

In my view, the paucity of direct evidence precludes any firm conclusion. A number of grounds exist, however, which may explain and justify the approach adopted. First, it is entirely plausible and tenable for those engaged in the initial process of recruiting volunteers, at whatever level, to take the view that it was their job to encourage volunteers to go to Porton. The words chosen to accomplish this objective might well vary on this view. That they did vary, and vary considerably, is clear from 21.3.1. Equally clearly, the precise wording used, particularly after 1964, was for individual Service Departments. From the point of view of those at Porton, the wording was not their responsibility, even though they might make suggestions. Thus, it could not be said to constitute an attempt on the part of Porton to mislead potential volunteers. From the point of view of the Services, once the initial recruitment had taken place, it could be said, that it was then the job of those at Porton to explain in detail what was contemplated in the particular research and to offer the volunteer the opportunity to take part or not, based on that detailed briefing.

Viewed from this perspective, the actions of those drafting and circulating the Notices is comparable to the actions of pharmaceutical companies which, to this day, post general notices calling for volunteers for trials of drugs in such places as Students' Notice Boards in Universities. The details of the specific trial and the method of obtaining consent are then left to those conducting the trials. It is important here, however, to enter one caveat. From 1964 until at least the 1980s, with few exceptions Notices not only made no reference to risks, but positively asserted that there was "no danger" involved in taking part in trials. This clearly ignored the advice in 1953 of the Treasury Solicitor. On its face, such an assertion is misleading as regards those volunteers who saw the Notices and relied on them, even though, as regards the great generality of trials, it was true. The fact that a volunteer had died in 1953 demonstrated that there was some degree of danger, even if the death could be explained as an idiosyncratic response (an explanation which I will consider (and reject) later) and even if, as was the case, no further studies of the kind were again carried out during the period covered by the Survey (9.3).

In my view, these Notices, during this period of time, placed a greater priority on securing volunteers than on entirely preparing them for what they might be exposed to. But, the word "entirely" is important. The view could still have been taken that, as has been said, the large majority of trials posed only the remotest risk of harm and that, in any event, Porton could be expected, indeed could properly be relied on, to give the volunteer the particular, specific information he needed to allow him to choose, once he was at Porton. The wording of the Notices at that time, therefore, could in my view be justified, as being in the larger public interest, even though not entirely forthcoming.

Secondly, Units were left in no doubt that Porton needed a steady flow of volunteers. Those who led the Service Departments saw it as desirable to encourage men to volunteer. In such circumstances, it is not surprising that the Notices were couched in reassuring terms. As was said earlier regarding the Notices issued before 1964, on one view, this could be seen as a deliberate attempt to deceive and trick volunteers into attending and taking part in research which was in fact likely to expose them to danger and harm. On another view, which on balance I prefer, if, in fact, there was any systematic, long-standing attempt to trick volunteers in this way, it is very likely that word would have quickly got round among the servicemen. Porton would have been avoided. Moreover, and perhaps more telling, I repeat again that many thousands of trials were carried out at Porton during the period of the Survey. They varied enormously in nature. Very many, indeed what appears to be the large majority, were routine variations of long-established trials, which posed no risk of foreseeable adverse consequences. In such circumstances, to stress the idea that volunteers would be exposed to danger would have been to distort what was, in fact, the case. It would also have undermined the legitimate campaign to recruit volunteers. Of course, this is not to ignore the fact that some trials did expose volunteers to the risk of harm and, on occasions, were intended to cause some harm, for instance, burns or blisters, as I discuss later. These raise questions not about the general calls for volunteers but about the adequacy of the information given to volunteers in particular cases and I will examine them in due course, when I consider the actual consent given by volunteers.

Thirdly, while the various Notices differed in their language, all of those identified in the Survey after 1964 and most beforehand refer to “Volunteers” and to “Chemical Defence” or “Chemical Warfare”. While it is not clear whether servicemen who volunteered actually saw these Notices, if they did, they cannot have been left in doubt as to what, in general terms, they were volunteering for. Of course, if they did not see the Notices (such that the Notices played no part in their decision to volunteer, and 21.2.4 suggests that not all volunteers were recruited through Notices), then the concerns highlighted in the Survey about the reference, or otherwise, to danger fall away, since the volunteers cannot, on this reasoning, have been misled by them.

23.5.3.1 Research on the common cold

Before leaving the issue of general information as a basis for initial consent, it is necessary to comment on the recollections of many that they were, in fact, volunteering to take part in research on the common cold, rather than chemical warfare. Chapter 6 describes at length the trials that were conducted into the common cold at the Common Cold Research Unit (CCRU) and elsewhere. Assuming for the sake of argument that those who recall attending Porton for research on the common cold did not see any general Notice headed “Chemical Defence”, the extent of this recollection, both in terms of numbers and over time, demands attention, notwithstanding the material differences in the practices used to recruit volunteers as between Porton and the CCRU.

The evidence described in the Survey makes it clear that no research on the common cold was conducted at Porton. Equally, while research involving service personnel was conducted into the influenza virus in the 1950s, according to 6.2.2-3, these trials were not conducted at Porton, but, rather, were carried out at servicemen’s Units.

Thus, if the recollections recorded in the Survey are accurate, that volunteers were agreeing to take part in research on the common cold, the evidence set out in the Survey is wrong. Moreover, a picture would emerge of wholesale and discreditable deception of volunteers over a long period of time as to why they were being recruited by the Services and by those at Porton. It has to be said immediately that whether such a deception could be sustained is open to doubt. But, more problematic still is the existence of direct evidence, from 1960-61 and 1964-77 (21.4.2), which on its face appears to contradict the volunteers’ recollections. The evidence takes two forms. First, there was a survey from 1960 to 1961. Secondly, there is a card index, created from 1964-77, which is still retained at Porton, containing about 2250 cards in all, one for each volunteer who came to Porton during that period. As for the survey, it shows that, of 334 volunteers interviewed, only 2 said that they had volunteered for research on the common cold. As for the card index, it indicates that, when asked why they had come to Porton, only 5 of the 2250 made any reference to research into the common cold. And, moreover, according to the Survey, the evidence relating to the 5 is “less than direct”. Admittedly, the card index only covers a period of 13 years and may not be representative of volunteers’ views over the whole period during which research into the common cold took place. That said, however, its significance lies in its consistency.

My conclusion on this matter is that recollections have become confused over time. I do not suppose that there was any deliberate distortion of the truth. I only suppose that this is merely another example in which the passage of time and events has produced a “folk memory” which appears to have no basis in fact.

23.5.4. Specific Information

It was the duty of the researchers at Porton to ensure that those who volunteered to come to Porton, were given such specific information about the particular trial which they took part in to allow them to make a considered choice whether to take part or not. (I will consider later whether the fact that they had been brought to Porton by the Services as servicemen meant that the option not to take part was more theoretical than real).

Ordinarily, the specific information regarded as most important from an ethical standpoint is that which relates to:

- the risks which the volunteer will be exposed to and the likelihood of their eventuating
- the consequences of taking part in the trial, including what may happen if the risks eventuate, and more generally any discomfort which may be suffered, its nature and duration

It is good practice now to prepare an information sheet for would-be volunteers, which they can study before deciding whether or not to proceed. This sheet will contain a fairly detailed account of the research and will cover, among other things, the matters referred to above. The practice of preparing such sheets, however, only became routine or standard towards the end of the period of the Survey and is commonly associated with, although its development is independent of, the emergence of ethics committees. Beforehand, the information given to the volunteers was not necessarily recorded. This would have been common in trials generally and not just particular to Porton. (As will be noted later, information sheets, called "Lay Statements" were formally introduced at Porton in 1987)

Thus, the Survey contains little or no direct evidence of what transpired between the researchers and volunteers over the whole period which it covers. (There is some documentary evidence, but the Overview to Part VIII of the Survey, quite rightly, in my view, makes it clear that such evidence does "not provide a complete picture of recruitment practices"). It must be added that there is on this issue, as on many others, evidence of the recollections of some of the many thousands of volunteers who attended Porton during the period of time covered by the Survey. While not, for a moment, doubting the genuineness of these recollections, it would be wrong to rely on them as settling any issue. As I have said, those offering these recollections are very few in number, they are a self-selecting group, they do not constitute a group which has been so designed that its evidence is representative of the views of all volunteers, and there is no evidence available from the researchers as to what their recollections are.

Thus, it follows that there is very little material on which to base any firm conclusion about the information passed on to the volunteers, prior to their embarking on a trial. 21.6.1 describes occasions, recorded in documents, on which specific information about trials was given to volunteers. The list is not long. The Survey cautions, however, that where a report does not mention that information was given to volunteers, "it is not safe to assume that none was given" (21.6.1). This must be right, not least because the tendency to record these matters may have been a development which grew only gradually, mirroring, perhaps, the slowly growing recognition generally of the importance of the ethics of research. From 1979 onwards, the practice grew of stating in the record of a trial that it had been "conducted in accordance with the provisions of the Declaration of Helsinki", (21.6.1). This assertion does not, of course, constitute proof that the trial was so conducted. But, given the central importance placed by the Declaration on consent and the provision of appropriate information, it may well constitute a form of shorthand statement that the volunteer had been appropriately informed before consenting.

In the absence of direct evidence, I have to rely largely on secondary evidence. First, since the trials required the cooperation of the volunteers, some explanation of what they were to do and what they could expect to happen was obviously called for (see, for example, 21.7.1). Secondly, in those trials in which the volunteers would be exposed to discomfort, it is fair to assume that this would have been explained, not least so that the volunteer would continue to participate, for example, by staying in the chamber when exposed to gas.

Of course, being told what is going to happen is not the same as being advised of the risks and consequences associated with taking part in a trial. Mere information, without any explanation of its significance or meaning, is not sufficient to allow a considered choice and thus does not, of itself, make the consent an informed consent. One example, which I also mention later in the

context of risk, perhaps goes to the very edges, if not beyond, the permissible as regards obtaining real (in this context, informed) consent, even allowing for the fact that it was conducted in 1942 when the fear of H (mustard gas) was great. It involved a trial to explore “the full extent of the danger” of H vapour to the scrotal region (20.1.2). It is hard to believe that servicemen would have volunteered for such a trial had they been adequately informed what the aim was. If I am right, and servicemen were not informed of such an obviously painful experience (even if short-lived and even if treatment was available), this trial was an unjustified departure from proper ethical standards.

Overall, however, the only conclusion available to me is that there is not enough evidence to allow me to reach a considered view on the amount and quality of the information given to the volunteers throughout the period covered by the Survey. There are occasional references to the information given to volunteers (for example, during the conduct of the trials described in 19), but not enough to indicate how common the practice was. I am persuaded that the possibility that a trial might expose volunteers to risks, the likelihood of those risks eventuating, and the consequences for the volunteers if this should take place were all actively considered and discussed by the researchers at Porton, particularly in the case of certain trials. I am not, however, able to reach a view as to whether these considerations were consistently passed on to the volunteers. The Survey does contain one example of detailed information being passed on to volunteers. It is described in 19.1.3. But, as I have said, it is not possible, on the available evidence, to determine whether it represents common practice, or was exceptional. That said, it is a good model of its kind, even now. It relates, in fact, to a trial in 1955 of various routes for administering atropine.

By way of comment at a very general level, I can say that the degree of information deemed necessary to obtain real consent is significantly greater now than at the beginning of the time covered by the Survey. Until at least the middle of the 1970s, paternalism tended to hold sway in practice, in the conduct of research. It was reflected in the propositions that the volunteer need not be concerned about details, which he might well not understand, and that his safety and welfare could safely be left in the hands of the researchers. This approach was thought to be justified, if challenged, by the argument that the duty of the researcher was to convey such information as was necessary to allow the volunteer to make a considered choice. The unstated assumption was that the best judge of what was necessary was the researcher. The recital of risks which were remote and of consequences which were hypothetical was regarded, on this view, as counterproductive and likely, unnecessarily, to put the volunteer off. Implicit in this approach, of course, was the assumption that if there were a conflict between pursuing research deemed important (by the researcher) and telling the volunteer about unlikely risks and consequences, the deemed imperative to carry out the research should prevail. This was the tenor of the times. If reflected in the approach adopted at Porton, would have been in accordance with practice at the time. It would also have had the added perceived justification that the research being conducted was in the national interest. But, this is speculation.

There is one area of research which warrants special attention: the trials involving psychoactive agents. I shall need to come back to these trials when I discuss the notion of risk and the limits to what a volunteer should be exposed to. But, here I am concerned with consent and whether it was sufficiently informed. The approach adopted by Porton in their trials relating, for example, to LSD was that it would defeat the purpose of the trials if the volunteer knew what he was being exposed to, since what were being tested were psychological responses and attitudes. So, these trials were deliberately conducted without giving the volunteers certain information. They were told in general terms what they were expected to do and precautions were taken to respond to any untoward occurrences. But, they were not informed about what they were being asked to take and, it follows, what were the likely risks and consequences. As is stated in 12.2.2, volunteers were given a “general outline of the purpose of the trial and assured of their safety. For obvious reasons they could not be informed of the nature of the compound to be used”, (and see also 11.2.4). (Another example of deception is described at 9.4.3, when men were caused to believe that they were to inhale a small amount of nerve gas, when in fact they were inhaling air.

Given the importance of determining the effect of GB on pulse rate, and given that the volunteers were not, in fact, exposed to any agent, it would be hard to argue that this trial went beyond the accepted standards of the time).

Two points arise. The first is that the fact that there was discussion at Porton about what information should be given to the volunteers lends further, albeit weak, support to the proposition that, ordinarily, volunteers would have been given more detailed information as to what they were being exposed to. The second point is that, in the case of the trials involving psychoactive agents, a deliberate decision was taken to keep information from, if not deceive, the volunteers. On the face of it, this may seem to constitute unethical conduct. But, as in all things to do with ethics, the picture is not as clear as appearances might suggest.

There has long been a debate over the existence and extent of exceptions to the researcher's duty to obtain the informed consent of volunteers. One particular area of debate has been the deliberate deception of the volunteer in, for example, research in the social sciences. Currently, the chances are remote that a research proposal in the area of the medical sciences, which did not include a requirement that volunteers be given appropriate information, would be approved by the relevant ethics committee. But, before the advent of ethics committees, and in the area of psychological research in particular, the insistence on informed consent was not always as strong. Indeed, the issue has been one of some controversy. It has long been argued strongly that if the only way to discover what was thought to be of importance was to engage in some form of deception, then this was permissible. The provisos were that the research should be of sufficient importance and not trivial and that, on available evidence, the volunteer would not come to harm, (but see the notorious Stanford experiment (which involved one group of students delivering what they believed were electric shocks of increasing strength to a group of actors who feigned being shocked)) [3].

These, I would suggest, were the standards of the 1950s and 60s. They are the standards against which the researchers at Porton should be judged, whatever the Codes or Guidelines of the time may have said. For, as has been said, these Codes were not paid great attention, being thought to apply to others, rather than to *bona fide* researchers engaged in work of national importance. Thus, I conclude that, judged by the standards of today, the trials involving psychoactive agents would be difficult to justify, but by the standards of the time they were not so at variance with accepted practice as to merit being described as unethical. (I leave out of account here any discussion of the legality of the trials involving, for example, LSD. Consideration of the law is not part of my task. I am aware that the trials involving the use of LSD have recently attracted the attention of the police and, therefore, make no further comment.)

23.5.5. Voluntariness

The last element in this consideration of consent is the issue of voluntariness. The question can be put simply: were the servicemen who took part in the trials truly volunteers? It is too simple to respond that they answered a call for volunteers and went of their own accord to Porton. What has to be established is that, both initially and once they were at Porton, they did what they did of their own free will and did not feel and were not placed under improper pressure.

At the stage of their initial recruitment, the point has already been made that there is very little direct evidence of the process of recruitment, save for the Notices which were posted but may not have been seen by all those who volunteered. The first question which needs to be asked is, given that they were serving soldiers, were they, in fact, ordered or otherwise placed under pressure to come forward? The answer is that there is no direct evidence to suggest that they were. The available documentary evidence points in the opposite direction. Early Notices to Commanding Officers urged them to "allow" or "permit" men to volunteer. The picture is one in which Commanding Officers were reluctant to lose men and thereby deplete their Unit's strength, rather than ordering men to volunteer to meet Porton's, or the government's, targets (see 21.2.1).

The calls for volunteers made it clear that extra pay and a certain relaxation of the discipline of military life, such as wearing civilian clothes, were also available to those who volunteered. The question raised is whether these could be said to have constituted an improper inducement. An inducement is considered to be improper in the context of research when it causes someone to volunteer for that which he would not otherwise wish to do, merely to obtain that which is offered. It is not deemed improper if it constitutes reasonable recompense for the contribution made by the volunteer and for any inconvenience or discomfort experienced.

The payment of volunteers taking part in research has long been the subject of discussion. There are those who, for example, in the past have criticised the pharmaceutical industry for recruiting students and the unemployed for trials of drugs, through the offer of money. It is an area in which differing views have been and are held, as is described in Chapter 22, (see, for example, 22.3.5 and 22.4.6). The differences of view, however, tend to be about whether the money or other material inducement offered is too much. Few hold to the view that no money at all should be made available. Moreover, at the level of principle, there is no reason to suspect that an offer of money *ipso facto* undermines a person's capacity to choose what to do. It might provide a reason for choosing, but rarely will dictate the choice. The best that can be said, therefore, is that reasonable judgement is called for. And, on that basis, I would suggest that the offer of financial and other inducements to the volunteers at Porton did not prevent them from being volunteers. It may be worth adding that, as 5.5 makes clear, the ethical issue of inducement was recognized and considered by Porton in the late 1970s. The Medical Committee noted in 1978 that the Medical Research Council was not in favour of paying volunteers, but, nonetheless, decided to continue its practice of offering payment.

The next question to ask is whether, once they were at Porton, the volunteers effectively lost the capacity to change their minds. At least two grounds can be advanced for holding this view. First, a volunteer might feel under what is called "peer pressure" not to pull out. In the ethos of the armed forces pulling out could be seen as weakness. But the argument has to be pressed further. It is not simply that this pressure may have existed, but that the researchers at Porton should have been aware of it and made allowance for it in their procedures for obtaining consent. For my part, I take the view that this feeling is not limited to the armed forces, but is a commonplace in all walks of life. Of itself, it cannot, in my view, be said to have converted the servicemen into non-volunteers. Furthermore, the researchers at Porton, on the available evidence, seem to have emphasised that volunteers could leave if they wished. It is difficult to see what else they could have done, without treating the servicemen as if they were unable to decide for themselves. Had they done so, it would, of course, have constituted precisely the kind of paternalism which the notion of consent is supposed to displace.

The second ground which can be advanced to suggest that the servicemen were not really able to change their minds and leave, (were not truly volunteers), is more substantial. They were serving soldiers and therefore attuned to obeying orders and doing what they were told. In the language of the ethics of research, they were a vulnerable group. The idea behind the notion of vulnerability, as undermining voluntariness, is based on the existence of a relationship of power, in which the researcher is the more powerful. As a factor to be considered when examining the ethics of research, the vulnerability of the research subject has been discussed for some time. The most obvious example was the use of convicted prisoners in research. It was said that they were easily induced to take part, (not least, out of the hope of some reward), and were rarely true volunteers. The more subtle application of the notion of vulnerability to research on employees, students, and members of the armed forces, is more recent. During the 1970s and 1980s, and even into the 1990s, the use of employees, for example, was still commonplace in some pharmaceutical research. (Porton abandoned the practice of recruiting members of its staff as volunteers in 1978, on ethical as well as scientific grounds (5.4)). Moreover, the use of those who might *prima facie* be vulnerable will still be defended, provided extra care is taken to ensure that they are in fact making a free choice. Indeed, few would argue that in no circumstances should members of these groups, merely by virtue of the fact that they are employees, students or

whatever, ever be allowed to volunteer to take part in research, if it is to be carried out by their employer or professor. Given that the issue of vulnerability is the object of continuing discussion in current reflections on research ethics, (see, 22.3.1 and 22.4.2), it would be wrong, in my view, to conclude that the use of servicemen in research at Porton was ethically improper, simply on the basis that they were servicemen and, by this fact alone, unable truly to volunteer and give real consent.

I turn now to another and extremely important feature of voluntariness. Intrinsic in the notion of consent is the notion of refusal. Someone is only truly a volunteer if he feels that he may refuse to take part in a particular trial, having once been informed of what is involved, or, having embarked on the trial, may withdraw at any time during it, without attracting any sanction. As regards the evidence in the Survey, there are various Notices referred to, beginning with the wording suggested by Porton in 1962, which explicitly drew attention to the fact that a volunteer need not take part and could withdraw at any time (22.2.3, 22.3.1). Even assuming that the volunteer saw these Notices, however, this does not tell us what happened in practice. There is also evidence (described in 21.7.1) of a Note in 1944 which refers to “full freedom to refuse”; of discussions in the BC in 1958; and of a Briefing Note by Porton’s staff in 1959. Moreover, 21.7.3 refers to MOD documents which record that the right to withdraw was explained to volunteers. But, as has been said, these documents and Notes do not, of themselves, necessarily reflect what was done in practice. There is also some limited direct evidence, in various experimental logs, of volunteers refusing to take part (described in 21.7.2 and Annex J). Again, it is not possible to say how comprehensive these logs are, nor how typical were the cases recorded. Further, it is not possible to say what their relative infrequency demonstrates: that, ordinarily, volunteers felt unable to refuse; that they were ordinarily content to proceed; or, simply, that refusals and withdrawals were not regularly recorded.

The most instructive evidence, perhaps, of what may have happened in practice can be found in the way in which many trials were designed and carried out. For example, those exposed in a chamber to gas were told that they could leave the chamber at any time and, indeed, many did (see, for example, 14.1.1). Also, in the design of some of the trials of riot control agents, considerable attention was given to allow a volunteer to withdraw (see, for example, 14.2.2-3); to facilitate the escape of a volunteer should he be unwilling to carry on with the trial, (see, for example, the arrangements made so that volunteers could escape from CS gas, either by getting through a gap left at the bottom of the hessian “wall”, or through escape panels cut into the walls at intervals, each of which was attended by staff from Porton ready to lend assistance (14.2.4)); or to have access to assistance, (for example, COHSE insisted that the trials of drenching with CR be carried out close to the showers to minimize the delay in decontamination, should a volunteer wish to terminate a test (15.4.3)). An example of a volunteer refusing to continue a trial is described in 14.4.4. It involved drenching with CS gas. Another, in 1942, during wartime, involved 2 volunteers who refused to take further part in a run over an assault course, while being exposed to harassing agents, despite the existence of financial inducements (17.3.3). Moreover, the offer of financial inducements if they were prepared to tolerate being exposed to gas in the chamber for longer periods of time, described, for example, in 14.2.3, carries the necessary implication that the volunteers had a choice as to whether to carry on, and did not have to do so, if they did not wish to. And, incidentally, I do not regard the offer of these additional sums of money, in the context, as an improper inducement. It seems to be a good example of reasonable compensation for undergoing additional discomfort.

My conclusion is that there is no direct evidence of volunteers being coerced to take part in trials or to carry on when they wished to stop. There is, on the other hand, evidence of general statements to the effect that volunteers could refuse or withdraw. And, there is evidence of practical arrangements to give effect to the exercise of this choice by the volunteer.

One postscript might be added to the discussion of voluntariness. On a number of occasions, the researchers at Porton subjected themselves to tests before conducting trials on volunteers. Currently, this is a practice which is not encouraged for a variety of reasons, not least that the

resulting information may not be sufficiently objective, that some researchers, in their enthusiasm may exceed what is safe, that atypical tolerance of certain substances may be acquired, and that it is a process which bypasses the procedural arrangements now in place to monitor research. But, historically, it was not uncommon. Researchers, in accordance with what was a commonly held view, felt that they should not expose others to the possibility of harm which they themselves would not be prepared to be exposed to. Further, initial tests allowed the researchers to calculate more accurately what volunteers could safely be exposed to. There is no evidence that the research staff at Porton were under pressure to submit themselves to such tests. Rather, it seems to be a case of selflessness, born perhaps of a sense of the importance, in their eyes, of the work that they were doing.

23.6. Formality of consent

I turn now to what may be described as the formality of the process whereby consent was obtained from volunteers. By the 1960s, it was being argued that consent, particularly in the case of research on healthy volunteers, should be recorded in writing, signed by the volunteer. The practice was not always observed, but certainly by the time that ethics committees emerged, it was regarded as a standard requirement. It is important to notice immediately, however, that a written consent form is not a substitute for real consent. A person may, for example, sign a form without really understanding what it says, or the implications of signing it. A signed consent form provides evidence of consent, but is not conclusive. Equally, the absence of written consent is not proof, nor is it even evidence, that consent was not given. What is important, therefore, is not so much the formalities of consent as the process whereby consent is obtained: the imparting of necessary information and the testing of voluntariness. But, some record in writing might be said to be a useful start.

In general terms, the absence of consent in writing, of course, makes it that much more difficult to determine what in fact took place, and thus to decide whether the process for obtaining consent was appropriate. And, this is true of Porton during most of the period of time covered by the Survey. Written consent was not obtained from volunteers. Only in 1987 was a written consent form introduced (see Annex K), presumably at the insistence of the newly created Independent Ethics Committee. Of its kind, it seems brief but satisfactory. It appears that it was accompanied from 1987 onwards by a "Lay Statement", (see Annex K for an example of such a Statement), the purpose of which was to give the volunteer more specific information (as discussed earlier). This combination of Consent Form and Lay Statement (or Information Sheet) brought Porton into line with standard practice. But, they were only introduced at the end of the period covered by the Survey.

Thus, for the time prior to 1987, I have had to rely on less direct evidence to form a view as to whether the volunteers at Porton really consented to take part in trials. It is important from the point of view of establishing the context, however, to recognize why written consent did not form part of the formal arrangements at Porton. It seems that the desirability of recording consent in writing was already recognized in the late 1950s. 21.7.4 describes the discussion, prompted by the Admiralty in 1959, and the response of the War Office. Whether the initial intention of the Admiralty was to ensure that consent was recorded as a "safeguard" (the word used in the original Admiralty document) against future complaint, or arose simply from the desire to allow a volunteer to record his exercise of choice is not clear. Officials at the War Office were initially opposed. The grounds stated are worth repeating: "...either the certificate [essentially a consent form, in the form of a declaration that the volunteer had read and understood the description of the test and was willing to undergo it] would become pure routine which men sign without reading or it would make them suspect that they were about to be subjected to something very dangerous, the responsibility for which we are trying to pass to them" (21.7.4).

Officials also raised two further objections: security; and the fact that volunteers had not been prepared to come forward on those occasions when they had been required to sign something.

The principal objection, however, appears (from 21.7.4) to revolve around the idea that the certificate to be signed would be seen as what is graphically called a “blood chit”: a document purporting to absolve the War Office of responsibility if a volunteer were harmed. Thus, Ministers were advised to encourage a procedure whereby volunteers “clearly understood what they were being asked to undergo” (21.7.4), but advised to reject the idea of a signed document, because of the connotation of its being a “blood chit”. The Admiralty tried again in 1960 but without success. 21.7.4 also describes an occasion in 1980 when a form of written consent was considered but was still “deemed undesirable”. Finally, in 1985, the idea was accepted.

The initial discussions between the Admiralty and the War Office follow a pattern which anyone remotely aware of the workings of government departments will recognize: wires got crossed. What was canvassed by some as a formal demonstration of consent was seen by others as an agreement by the volunteer to waive liability. Such a waiver was thought, quite properly, to be inappropriate. Thus, forms were not to be used. That this inaction lasted nearly 50 years is a tribute to the longevity of decisions once taken, no matter that they be wrong-headed. It also suggests that “political” considerations and concerns over security took precedence over considerations of what were seen as formalities. It does not suggest that the need for consent was to be ignored, or was unimportant. That forms were not used is unfortunate from a historical perspective. It says nothing, however, about the conduct of the trials at Porton and whether or not they were conducted with real consent.

A second postscript may be added. In 1964, a film was made about the process of recruiting volunteers. A transcript of the material parts of the film appears in Annex I. On its face, the film could be said to provide evidence concerning the consent and voluntariness of volunteers. In the event, I do not place any reliance on the film, for two reasons. First, it is not of itself evidence of what actually took place at Porton. Secondly, it was made by the MOD as part of the process of encouraging recruits and so cannot be said to be an objective and impartial account. This is not to say that it was intended to, or did, misrepresent what went on at Porton. It is merely to say that it may be wiser not to rely on it.

By contrast, other films which are held by the Imperial War Museum and which I was able to see, are of some assistance. A few of the ones I saw recorded trials being carried out. I have no reason to believe that they were selectively biased to present a particular picture of what went on. Two specific factors struck me as significant. One was the degree of supervision by staff during the conduct of trials, suggesting the availability of assistance if a volunteer suffered discomfort. This tends to reinforce the description of the approach adopted by Porton described in the Survey: “during studies, physiological functions likely to be affected by the study were taken, and the study stopped if limits were approached” (12.1.5 and see further Annex E). The second factor was the presence of what appeared to be medical care when a volunteer did, in fact, encounter distress or discomfort. These observations are relevant as I turn now to discuss risk and safety.

23.7 Risk and Safety

In the conduct of research on healthy volunteers, it was an accepted principle from the start of the period of time covered by the Survey that the safety of volunteers should not be put at risk. What is more problematical is what this principle was understood to mean. The first question is: risk of what? The answer is initially clear. The volunteer may not be exposed to the risk of death or significant injury, physical or mental. Significant is to be contrasted with trivial, but there is a large middle ground over which disagreement may exist. This is because the answer to this first question depends in part and is inextricably linked with the answer to a second question: what risk? A risk of some deleterious consequence may be very great or remote. Further, the consequence of a risk eventuating may be great or slight. In concrete terms, there may be a slight risk of something catastrophic, such as death, and there may be a real risk of something trivial, such as a temporary headache. Putting these parts of the principle together produces a sharper proposition: that the researcher should not expose a volunteer to any risk which involves

even a remote chance of death or significant, serious harm, nor to any risk which involves anything other than a remote chance of harm which is more than trivial. This suggests that in the case of trivial harms, the risk may be run if it is unlikely to occur. In these last two cases, the researcher must have taken all reasonable steps to prevent the risk from occurring.

If this is not complex enough already, there is a further, distinct, strand which runs through the modern history of research on healthy volunteers: that the risk to which a volunteer may be exposed may be proportionate to the importance of the information which is sought. It can be found in the first (1964) Helsinki Declaration's reference to, and thus apparent endorsement of, a balance which can be struck between risks to a research subject and importance of the objective, and, thus, the benefits to others. Although this notion of proportionality cannot be read to justify exposing a volunteer to a real risk of death or significant injury, it is clear that it can serve to tip the balance somewhat towards taking greater risks if the prize (of information) is great enough. It does not say that the interests of society should *prevail* over those of the research subject, but merely suggests that the balance may be struck more subtly. Moreover, it is an issue which remains to this day the object of debate, such that distinguished commentators were able to write in 2002: "...there was, and still is, uncertainty over the circumstances in which the potential benefits of research to many people might outweigh inconvenience and risk to a few" [2]. Thus, a remote risk of death may come into the equation, as may a somewhat more likely, though still unlikely, risk of more than trivial harm. This notion of proportionality, of course, takes on great significance in the context of research relating to defence against weapons of war and of appeals to the national interest. Indeed, there is specific reference to the "good of society", as justifying research being carried out which might otherwise be impermissibly dangerous, in the meeting in 1965 convened by the Director of Porton, following the ban on trials of incapacitating agents (13).

It is necessary also to include in any account of safety and risk the observation that the mere fact that someone may be willing to expose himself to a risk, aware that it may cause him more than trivial harm, does not mean that it is thereafter proper to proceed. There is at some point a duty on researchers not to expose volunteers to such harm, despite their preparedness to be exposed. The reasons are complex. It may well be in the public interest to promote research. But, it is also in the public interest to protect people from themselves, at some point. Freedom of choice, at some point, is made to give way to benevolent paternalism. One obvious justification is that the cause of research would be damaged if a volunteer were to be exposed to something which was expected or likely to harm him significantly. But, this may not be the real reason. At bottom, the reason may have more to do with the researcher than the volunteer, or the cause of scientific research. It may be that there is a sense that to permit such activity would brutalise or desensitize the researcher and, by association, make society, by permitting or encouraging the activity, complicit in it.

How do these general reflections relate to Porton? They form the background to the enquiry whether the researchers exceeded the limits of what was ethically proper. Did the researchers expose the volunteers to trials which carried too great a risk of harm and thereby improperly endanger their safety?

Before addressing these questions, there is a prior point of some importance to be made. The researchers, before they conducted trials on human volunteers sought to establish from research on animals, study of the available literature, and, on occasions, tests on themselves what might be the expected consequences of research on humans. They sought, in other words, to establish as best they could the nature of the risk, so as to avoid any reasonably foreseeable risk of serious harm to volunteers, (see, for example, the efforts, not entirely successful, to establish normal levels of ChE described in Annex C). It is worth noting, for example, the tests involving T3436, described in 11.3.3. Between 1969 and 1971 and 1971-72, COHSE and ABC closely monitored the dose used, starting with low doses and approving gradual increases, as evidence emerged about safety. The general approach adopted, therefore, was one of seeking to work in the realm of the known or the reasonably predictable, so as to be able to control the consequences and thereby protect the volunteer. This is in keeping with the researchers' ethical

responsibility. There were occasions, as will be seen, when this approach was not followed, but these were exceptions which tend to prove the rule.

Secondly, as has been seen, on a number of occasions until the practice was stopped in 1978 (5.4), researchers first tested compounds on themselves, particularly in the case of nerve agents and incapacitating agents (11.2.2, 12.2.2, 12.4), (and see also the preparedness of an RAF ophthalmologist to expose his eyes to GB, so as to understand its effects and thereby to design appropriate trials, described in 9.5.2). Although this approach is not approved of now for the reasons already set out, at the time it may have been said to demonstrate a commitment to doing what was ethically proper in the realm of risk in two ways. It gave the researchers further information about the agent being tested and thus allowed them to design better and safer trials. Also, it reflected, as has been said, a commitment to what, for a long time during the period under review, was thought of as the “golden rule” of research ethics: that a researcher should not expose a volunteer to a test which he would not be prepared to undergo himself. Thus, in at least two ways, the researchers sought to respect and give effect to what they understood at the time to be the ethical standards underlying research.

Returning to the questions posed above, it may be helpful in answering them to proceed in stages, which reflect, in general terms, the degree of risk involved.

23.7.1. Routine trials

First, a large majority of the volunteers were exposed to trials at Porton, which were almost humdrum or routine in nature. They involved no recognised risk. They often consisted of painstaking variations on established themes, such as the testing of different fabrics, or of protective clothing (see, for example, 2.3). They raise no issue as to ethical propriety.

23.7.2. Intention to cause discomfort and distress

Next, there was a large number of trials which exposed volunteers to discomfort and distress. It was known or predicted that this would be the case, indeed many of the trials were conducted to measure the extent of the distress, (not whether it would occur), and how long it could be withstood. Thus, distress and discomfort were intentionally caused. Did such trials exceed what was ethically permissible? In my view, they did not. The volunteers, as has been said, appeared to be aware of what was likely to happen and consented. The risks were not such that they should not have been asked or allowed to consent. The distress could be expected, ordinarily, to be of short duration, for example, a matter of minutes. The risk of any long-term effects was remote. The volunteers were accompanied and attended by medical staff who could intervene and render assistance if it was called for, (see, for example, 12.1.5 and Annex E).

On occasions, the distressing effects of being exposed to a particular agent lasted longer than could have been expected, or a volunteer’s distress was atypically more pronounced (see, for example, the trial in which miosis lasted for 5 days (9.5.2)). Medical assistance was available and, where necessary, a volunteer remained at Porton until he had recovered (see, for example, 12.2.2: an unexpectedly long depression of a volunteer’s blood pressure “did give some cause for concern” according to the BC).

Such occurrences, even if unusual, could give rise to the suggestion that the researchers, at least on these occasions, exceeded the limits of the permissible. But, a distinction needs to be made between responses which could ordinarily be expected and those which were unpredictable, or out of the ordinary. If the researchers took measures so to control the trial that they could reasonably be said to be able to predict the range of responses and to be entitled to expect that the responses of the volunteers would be within the predicted range, then this may have been enough by the standards of the times to comply with their ethical responsibility.

It may be objected that the unexpected should be expected and, thus, provided for. Leaving aside the obvious logical paradox, it should be remembered, first, that, with a very few exceptions, the researchers were working with young fit men, who could be expected to respond in a predictable manner. Secondly, from at least the 1950s onwards, volunteers underwent a careful medical assessment before being involved in a trial. The extent of this assessment is described in Annex E. It will be seen that the examinations became more extensive over time, particularly as trials of different agents were carried out. Moreover, the examinations covered not only what may be described as routine matters, such as blood samples, but susceptibility to certain agents, for example, mustard gas, and also psychological well-being. It seems clear from Annex E that significant precautions were taken to assess volunteers and exclude those who might be predicted to be put at undue risk in any trial.

Thirdly, particular efforts were made in the trials involving psychoactive agents, to eliminate unsuitable volunteers. This resulted in the fact that, from 1961-65, 80% and in 1967-8, 66% of the volunteers reporting to Porton were excluded from these trials (11.1). The stringent application of the tests and their results, which resulted in volunteers being excluded, provoked tension between Porton and the ABC. It was felt that the need to conduct trials was being frustrated by Porton's concern for safety. Eventually, Porton gave ground by admitting into the trials those who were categorized as "borderline" (11.1). In my view, this relaxation of their position does not warrant criticism since it was at the margins and was the result of legitimate differences of opinion as to where the balance was to be struck (see further 5.1 and 11.1). Had Porton gone further, my view may well be different, particularly given the fact that the risk that studies might "set in train some irreversible effect" (11.1) had been discussed in 1959 at a meeting of CDAB concerned with the safety of trials involving psychoactive agents. A further example of excluding potentially vulnerable volunteers can be found in the introduction of a new eye-testing regime in relation to work on miosis in 1982, because of the suspicion (which I consider later) of a relationship between myopia and detached retina (9.6.3), (and see also the description of the introduction of SFEMG at the behest of the Medical Committee in 1987 (9.6.4) and EEG in 1979 at the behest of COHSE (9.6.5)). And again, some volunteers were barred from studies of CR because they were hypertensive (15.2.2).

Fourthly, idiosyncratic reactions, not otherwise predictable, do happen, even despite efforts to make the trial as safe as current knowledge allowed. An example may be that described at 15.5.3, in which a volunteer developed microcysts but "no significant residual damage" after the trial of a CR squirt.

The conclusion I am drawn to, therefore, is that in this second category of trials, the researchers did not exceed what then or now would be thought to be ethical in terms of the risks to which volunteers were exposed to. Moreover, this view is reinforced if account is taken of the context, that of defence against chemical warfare, and the proportionate value of gaining information as compared with the extent of the risk to which the volunteers were exposed.

23.7.3. Intention to cause harm

A third category of trials is more problematic. These are the trials in which the purpose of the trial was to inflict harm on the volunteer. That is to say that the researchers intended that harm be caused, rather than sought to discover the effects of an agent in circumstances in which some might suffer some distress which would be temporary, or from which they could remove themselves if it occurred. This distinction is not, of course, clear-cut, as the trials of nerve agents described in 8.4.3 illustrate. In one trial, the aim apparently was to estimate the "threshold" dose of GB vapour. Such a trial clearly, by its nature, carries a risk of harm, though it may not be intended to cause it. In fact, all three men in the particular trial who were exposed to GB without protection suffered what is described as "early signs of systemic poisoning".

An example of this third category of trials is the trial into the effect of CS gas on the eyes, described in 14.4.2: the concentration sought was that which would produce "severe pain and

sustained blepharospasm”, albeit for a brief period of time. Other examples of trials which were intended to produce harm were those involving vesicants and other agents, described in Chapters 17, 18 and 20, in which the intention was to cause blistering and burning. Here there was more than a risk of harm. There was an inevitability of harm, and harm which was not trivial. It may, of course, be said that the volunteers may have consented knowing what was intended. But, this may be one of those cases in which the consent of the volunteers does not necessarily make the trial ethical, because of the degree of harm which they were exposed to.

It is very unlikely that the sort of trials which fall into this third category would be countenanced now by an ethics committee. But, this does not necessarily help us, since it imposes the standards of today on research conducted decades ago in very different circumstances, including during a World War. In my view, three arguments in particular can be advanced to suggest that the trials, in principle, can be justified as having been ethical at the time. First, in most cases, particularly in the later years covered by the Survey, as more information became available, the trials were carefully controlled. Secondly, the outcome was predictable and, therefore amenable to being managed and controlled. (Certain trials of nerve agents, however, may be an exception and I will consider these separately). Localised blistering or burning, for example, was the expected and intended outcome (although the severity was not always accurately predicted, (see 17.2.4)) and treatment was known, effective and available.

Thirdly, applying the notion of proportionality, it could be argued that the information sought was sufficiently important to warrant exposing volunteers to harm, if the harm was limited and the trial was conducted in a controlled environment. It may be one of those cases in which the concern for defence against chemical warfare agents and the tenor of the times may justify that which otherwise would be difficult to justify. Many of the trials falling into this third category were conducted during the Second World War and later in the 1940s. Furthermore, after the abandonment of the development of new offensive agents, the imperative for the Services and, hence, the main thrust of research, were to develop effective forms of treatment for service personnel who might be exposed to nerve agents and to H (mustard gas) and other vesicants, (it should be remembered that H was regarded as a threat throughout the whole of the period covered by the Survey). Indeed, Chapter 19 describes decades of research into developing protection against nerve agents.

To develop treatments, the researchers had to establish the point at which the agent became effective. Hence, there were the trials which involved causing some degree of harm, such as blistering and burning. There is little doubt that some of the trials produced and were intended to produce injuries of “casualty severity”, that is, sufficiently serious that the man would not be able to take part in military activities. The trials walked a tightrope between “controlled harm” and significant injury. Sometimes, the line was crossed, safety was compromised and trials were stopped. Chapter 17 describes this tension in trials involving H. The effects of a trial in 1942, for example, were described as “much more severe than expected” (17.4.1) and all 3 volunteers required treatment in hospital.

These trials make for uncomfortable reading now, particularly those described in 17.4.1, when, for example, 2 of 4 men, deemed “casualties” after a trial, “required immediate admission to hospital” and another was admitted some days later with burns to his scrotal region. This sense of discomfort exists even though more than trivial harm may only have been suffered in a few of the thousands of trials which took place. While it may not be enough to say that the country was at war, the nature of the perceived threat from the enemy, in my view, justified the trials, notwithstanding the fact that, on occasions, the harm caused was considerable. It was not disproportionate in the context and against the background of efforts made to ensure that volunteers were not put to what would then have been viewed as disproportionate risks. For example, volunteers in 1943 were given a full ophthalmic examination before a study of the effect of HN-1 on the eyes (17.2.4). That said, while the trials, as trials, may have been justified in principle, as I have already made clear earlier (23.5.4), I entertain the most serious reservations

about the reality of the consent obtained in, and thus the ethical propriety of, some of the trials, particularly those described in 17.4.1 relating to H weapons.

That volunteers came forward during the early years of the War from all sections of Porton's staff, not just the medical but also the administrative staff, (and some research was conducted exclusively on staff at Porton), serves as a further reminder of the standards of the times and what those working at Porton, who might be considered to be aware of trials and their implications, considered to be proportionate.

I accept that views may differ. Indeed, the researchers themselves expressed concerns on occasions, as, for example, when, after initial trials of BZ, the researchers doubted that further tests could be justified in terms of the risks of psychological harm posed to volunteers (11.3.2). Equally, Porton opposed the use of agents the primary mode of action of which was to induce hypo- or hyper-tension, as being "very dangerous", despite pressure from CDAB (12.1.2-3) (and see also the whole of Chapter 13). But, the fact that views may differ suggests, in my view, that it would be wrong to conclude that the trials which fall within this third category were, for that reason alone, ethically improper.

23.7.4 Trials at the edges of knowledge

I identify from the Survey a fourth category of trials which is the most problematic. It relates to the trials of nerve agents. There seems little doubt that there was great concern in the late 1940s and the 1950s about the possible use by the Soviet Union of G agents which were not previously known. Much work was needed and it was painstakingly carried out. But, as Chapter 8 indicates, on some occasions, researchers were operating at the edges of their knowledge when exposing human volunteers to various trials

Because of the importance to my assessment of this category of trials, it may be of assistance if I separate it into two sub-categories, so as to analyse as carefully as possible the trials to which it applies.

1. The first subdivision consists of those trials in which the outcome was not really predictable from the knowledge available to Porton. This meant that the trial and its outcome could not effectively be controlled. And, since the ability to control what might happen is a crucial ingredient in safeguarding those exposed to the trial, the inability to exercise this control meant that volunteers were put in danger. Moreover, the level of danger was equally unpredictable: it could include death or serious injury. A number of trials fall into this sub-category.

- In a trial described in 8.4.7, six volunteers were exposed in 1951 to a dose of GD vapour weaker than one fortieth of the dose estimated in 1949 to be lethal. Yet, "the symptoms suffered were much more severe than expected". On one view, therefore, the lethal dose was not known with sufficient precision and must have been underestimated, exposing volunteers to danger.
- 8.5.4 suggests that the reliance on ChE inhibition measured in a particular way, as the means of calculating the lethal dose of G agents, and the maximum dose to which volunteers could be exposed, was less than sound.
- The maximum dose of GB to which volunteers could be exposed was reduced after the case of severe poisoning in April 1953 (8.5.5), but this reduced dose, when used in a subsequent trial two weeks later, still led to a fatality, as will be described later.
- In 1963, trials were conducted into the effects of the nerve agent GF (contrary to the conditions laid down by the Adrian Committee, as previously mentioned (23.4)). The

results of the research (involving 30 men) were described as “unduly variable”, particularly as regards ChE depression, and further work was banned (9.4.6).

- As a sign of a growing sense of caution and concern, in the light of previous experience, Porton, in 1964, applied a “local safety margin” by setting the level of ChE depression lower by some 20% than that approved by the Biology Committee (9.4.2).
- The trials in 1953 which resulted in a fatality, which I will now review in detail.

For the purposes of my assessment, the most significant trial which falls into this sub-category is the “main human study with liquid G agents”, which resulted in “a case of severe poisoning and a fatality” in 1953 (described in 8.5.5). The death of the volunteer is a matter which is currently under review by the courts and the Wiltshire Coroner. I have no more information than that which appears in the Survey and, therefore, confine my comments to this. Clearly, the death of a volunteer is an appalling tragedy. It does not follow, however, that its occurrence *ipso facto* points to improprieties in the conduct of research. The question which I must address is whether the volunteer was exposed to a trial which was so much at the edges of knowledge and so fraught with risk of serious harm or death that it should not have taken place. An initial answer would appear to be that a number of volunteers were exposed to the same or similar trials and did not suffer serious harm. (the other seventeen men in the study were contaminated in the same way but “showed no signs or symptoms of GB intoxication” (8.5.5), and subsequent reports stated that 182 out of 396 volunteers had “received contaminations equal to or greater than [that which] the man who died [had received]” (8.5.5). But this answer, (which, in any event, is not entirely true: leaving aside the case of severe poisoning, “[n]ine of the 14 men who took part in [the initial studies] showed symptoms of GB poisoning” (8.5.3)) may not go far enough. Two further matters must be explored. First, were the risks involved in the trials of nerve agents, of which the one involving the death of the volunteer was part, sufficiently known and understood so as to allow the researchers to guard against or manage them? Or, were these trials so far at the edges of what was known, that the researchers were exposing volunteers to risks which they could neither calculate nor guard against?

Clearly, in so important a matter, it is crucial that any view must be based on the particular details of the trial in 1953 as a consequence of which the volunteer died. That said, however, the trial must be seen in a context. And that context, I repeat, is one of researchers operating at the edges of knowledge and understanding. An example, not related to the trial in 1953, may illustrate this context. The review by Porton in 1982 of its past work on miosis in trials of GB is instructive: “good fortune rather than wise decisions have [sic] been responsible for the safety record” (9.6.3, and see further 9.6.4 and 9.6.5). Of particular concern was the relationship (if any) between miosis and detachment of the retina after exposure to GB. While any such relationship was thought to be speculative, it is clear that the trials were conducted against a background of incomplete understanding of the dangers to which volunteers were exposed. While researchers should not be criticized from the vantage point of hindsight, it was agreed at the time of the review that the ophthalmic screening procedures were “inadequate and inappropriate” (9.6.3).

Certainly, reading the available evidence concerning the trials of nerve agents, there is, as has been said, a very real sense that the researchers were at the edges of danger and suspected it. (Another indication of the context at that time, not involving work on nerve agents, can be found in the discussion surrounding the suspension in 1965 of the trials of incapacitating agents, referred to earlier (23.4) and described in Chapter 13. The ABC acknowledged in 1965 that some of the work on the newer incapacitating agents went “very far into the realms of the unknown” in terms of assessing the safety of trials (13)).

Returning to the fatal incident, the information base in relation to the effects of GB in 1953 was limited. Insights were being gained experientially and factored into the next set of trials. The agent which researchers were dealing with was lethal at an appropriate dose. Its effects, for

example, on skin appear not to have been wholly understood, notwithstanding the several years of tests on animals, (see, for example, 8.5.4 and its description of the variation in inhibition of ChE). As the reports on the fatal incident indicated: "Comparatively small variations in absorption might therefore encompass the lethal dose" (8.5.5).

In the case of the volunteer who died, everything appeared to turn on the amount of skin fat in his arm, since his RBC ChE activity (another critical indicator of the effect of GB) was found on post-mortem examination to have been within the normal range. The role of skin fat (both surface and sub-surface) in the penetration of the skin by GB had been demonstrated by earlier research in 1951 and 1952 (see 8.5.3 "...the amount of surface or sub-surface skin fat affects the degree of penetration of liquid GB").² Then, in April 1953, one of six volunteers suffered "severe poisoning" (8.5.5) when a dose of GB was administered to fabric fixed to his arm. The man recovered after being hospitalized and suffering convulsions and temporary cessation of breath. After the incident, his surface skin fat was measured and found to be much lower than the average. While other factors were thought to have contributed to his reaction, the role of skin fat, particularly in the light of the findings in 1951-2, maybe thought to be significant. This view is reinforced by the very fact that his surface skin fat was measured after the incident (evidence also that researchers knew of the role of skin fat even though the Survey points to the fact that the results of the initial studies in 1951-2 were not published until 1954). Furthermore, as a result of the incident "the maximum dose of GB to be used subsequently in the main study was reduced from 300 mg to 200 mg, and a second layer of clothing was interposed between the liquid GB and the skin" (8.5.5).

The trial involving the volunteer who died took place in May, 1953, only two weeks later. 200 mg of liquid GB was applied on top of two layers of cloth fixed to his skin. His surface skin fat was found on post-mortem to be below, but not greatly below, the average. But, his sub-surface, or subcutaneous, skin fat was found to be "practically absent" (8.5.5). Given the view as to the importance of the role of both types of skin fat, gained from the initial studies, the first question which I must ask is whether a procedure for measuring surface and sub-surface skin fat existed at the time, or could have been developed. If such a procedure was available, or could have been developed, then failure to employ it in the case of the volunteer who died constitutes improper conduct. It also means that it was wrong to expose any of the volunteers to this trial, since they would all have been at risk.

If such a procedure for measuring both types of skin fat was not available nor could be developed, I must ask a second question. In the light of the serious incident two weeks previously, were the researchers at Porton justified in carrying out further trials, particularly the trial in which the volunteer died? (All nerve agent studies with humans were banned thereafter, until after the Report of the Adrian Committee). Skin fat affected the response to GB. Assuming, for the sake of argument, that a procedure did not exist to allow it to be adequately measured, then volunteers clearly ran the risk of being exposed to serious harm. Moreover, it appears to be the case that skin fat not only affected the response to GB, but affected it in such a way as to make a significant difference to the risk to which a volunteer was to be exposed. On the hypothesis that no procedure for measuring skin fat was or could have been developed, I am drawn to the conclusion that, knowing its importance and being unable (on this hypothesis) to measure it, meant that volunteers were exposed to an uncontrollable danger of serious harm, or

² In a later amendment to the text, made after I submitted my initial draft, it is pointed out on three occasions (8.5.3 and 4) that the report of the initial studies in 1951 and 1952 was not published until January 1954. I do not take this as intending to suggest that researchers at Porton were, therefore, unaware of the results of these studies until they were reported. If it is so intended, I reject it. The community of researchers studying the effects of GB cannot have been so large and diffuse that results were not known and shared between them. Writing up the results cannot have been the only and exclusive means of becoming aware and keeping abreast of what was going on in such a community.

death. That being so, on these assumptions, it was wrong to carry out the trial both on the volunteer who died, and on the others involved.

It could, of course, be objected that the volunteer's response was idiosyncratic, and thus, by its nature, could not be predicted nor guarded against. There have been occasions in which volunteers involved in trials of new drugs have suffered injury, or even died, as the consequence of an idiosyncratic response [4]. No blame attaches because the tragedy was both unforeseeable and unpreventable. But, this argument does not hold water here. The trials in 1951-2 had pointed to the role of skin fat and the trial in April 1953 had then raised questions about skin fat (admittedly surface skin fat), such as to implicate it as affecting the volunteer's response, even though RBC ChE activity was also implicated. Indeed, it had led to the reduction of the maximum dose and the use of two layers of clothing. If the idea of an idiosyncratic response were advanced here, it would amount to blaming the volunteer for having fat-free arms.

If the assumptions advanced above are valid, the volunteer died because the trial was not safe, not just for him, but for all, since none of the volunteers in the various trials appears to have undergone any procedure for measuring skin fat. And, if such procedures were not available, the trials became uncontrollably dangerous. This is not, I submit, the judgement of hindsight. The pressure to develop knowledge about G agents was great, above all to develop forms of treatment to protect service personnel and the wider society. This pressure, this imperative, must not be overlooked. But, in my view, there were trials carried out as a consequence which went too far.

2. The second sub-category of trials which I have described as being at the edges of knowledge relates to what I might call a conscious and deliberate flirtation with danger. It involves two studies described in 10.2.2. It did not involve volunteering servicemen, but the medical staff at Porton. Again, perhaps they were seeking to follow the "golden rule", but in this case going beyond courage to foolhardiness. The report of the studies talks of "careful consideration" being given to continuing the trials part way through the second study. But, it involved trials in 1958 of the nerve agent VX, whereby volunteer medical officers were exposed to what was then accepted as the *lethal* dose, a dose which was only later revised. It cannot be doubted that despite any "careful consideration", the trials could reasonably have been expected to flirt with the risk of serious injury and death. Any such trials cannot be justified and should not have taken place, nor have been condoned by others at Porton.

As regards this fourth category of trials, my conclusion is that there were clearly occasions on which the safety of the volunteers (including the medical staff) was put at risk, and that this was acknowledged by Porton. By this I mean the risk to safety amounted to something more than a particular predicted harm, which, it could reasonably be assumed, could be controlled and managed. As has been said, it is clear that in the case of nerve agents, the imperative to know was, of course, deemed to be high. Good examples of this imperative are the work on miosis described particularly in 9.5.2, and on VX described in 10.2.3 (and see 10.1.1). Equally, the pressure to find out was high. But, I am of the view that at least a *prima facie* case exists that there were trials involving nerve agents which posed such a risk of serious harm as to go beyond what was ethically permissible, notwithstanding the context of defence and the threat of war.

The crucial issue is the researchers' ability to vouch for the safety of the volunteer. When this was in question, there is a case for saying that the researchers crossed the line from the proper to the improper. It is not for me to speculate on their motives, which may have been of the best. I can only say that in these apparently rare cases the boundaries of what should be done were exceeded, even by reference to the standards of the time. I list the trials which I regard as having exceeded these boundaries in my Conclusion (23.11).

23.7.5. Long-term effects

Before concluding this section on safety and risk, two further points warrant attention. First, it is clear that researchers were concerned about any long-term effects which could follow from being exposed to certain agents. There were follow-up studies, for example, of exposure to GB (9.6.2) and a detailed examination over a long period of time into the possible carcinogenicity of CR, carried out in conjunction with experts at the Chester Beattie Cancer Research Institute (15.2.1-2).

Concern about long-term effects was particularly present in the case of psychoactive agents (see 11.2.5 and 11.3.2). The risk of short-term effects and their consequences were explored and, once identified, were monitored and managed. But, whether there were long-term effects was not known. This might suggest that trials should not have been embarked on at all if, however remote, they were risks of really serious harm, such as permanent changes of personality. Indeed, as has been seen, the Survey describes how the safety of tests was discussed by the CDAB concluding that “it was difficult to know whether or not ... studies might, in some volunteers ‘set in train some irreversible effect’” (11.1).

Again, any judgement is not clear-cut. There was, for example, very real concern that psychoactive agents could be used against the armed forces or the civilian population, from which grew the perceived need to understand and, if possible, counteract their effects. This creates the ethical background against which the trials must be judged. Thus, notwithstanding the fact that the available literature did not provide a definitive picture of the extent of foreseeable reactions, the decision was taken to devise a test, so as to exclude from the trials those volunteers who might be more vulnerable to these agents. The intention was to remove, or at least reduce to a remote possibility, the risk of long-term harm. As was commonly the case when the researchers were uncertain, the test was designed by experts from outside Porton (from the Maudsley and other Hospitals). The advice from experts at the Maudsley Hospital was that “as long as subjects for human studies were chosen carefully and small doses used, irreversible effects were unlikely” (11.1). This may invite the conclusion that, if the proposition that it was imperative to carry out the work is accepted, the researchers, by consulting outside experts, took such precautions as to suggest that they did not offend against the standards of the times.

This view may perhaps be reinforced by the decision to follow-up volunteers over time so as to monitor any long-term effects. The volunteers’ Service medical records were routinely annotated to record the fact they had attended Porton, which would have put medical personnel elsewhere on notice, should something untoward and otherwise inexplicable arise at a later date. Monitoring long-term effects was the responsible thing to do. That it was not always, in fact, done effectively, by relying, for example only on Service medical records (see 9.6.2), speaks of administrative ineptness and, perhaps, cost-cutting, rather than any ethical impropriety on the part of the researchers.

The case of H and the long-term effects on volunteers, and servicemen generally, of exposure during training or trials was different. As described in 18.1.4, this concern did not involve monitoring volunteers in the future, but having to decide whether to abandon the practice then current of exposing service personnel to H, because of the possibility of long-term risks of cancer, raised in 1977. COHSE took outside advice in 1978 and concluded that, although the risk was low that a single exposure would result in adverse consequences in the long-term, the use of H for a “confidence test”, as part of every serviceman’s training, should cease. Porton initially did not regard this as applying to their research work, since volunteers were only exposed to a single dose. Porton also did not regard it as necessary to warn of what it regarded as a “non-existent risk”. COHSE, for its part, recognized the tension between the safety of volunteers, on the one hand, and the perceived needs of the Services for information about the effects of H which would help them to protect their service personnel, noting that if work on H were abandoned, the further development of protective clothing would be “seriously affected”. But, the interests of safety

prevailed and penetration studies of clothing using H were suspended. The MC subsequently discussed the issue. No further tests were carried out.

I turn finally to three matters which an assessment of the ethics of the research at Porton should mention. I can deal with them somewhat more briefly.

23.8. The role of ethics committees

Ethics committees are, in effect, institutional mechanisms to superintend the conduct of biomedical research so as to ensure that scientific advances are made while protecting the interests of research subjects. Described in this way, it will be realized that from at least 1965, if not before, as was pointed out earlier (23.4), Porton had such a mechanism. Initially, it was the Applied Biology Committee, then the Medical Committee. A significant feature of these bodies was that from the outset they included independent members from outside Porton and the armed forces. Equally significant, as was referred to earlier, they exercised a supervisory role over the conduct of the research at Porton and, in particular, appear to have reflected on a number of ethical issues which arose.

To this extent, Porton might be thought to have been sensitive to the need for external supervision and, as important, advice on the ethics of proposed research, long before the general emergence of ethics committees took place. In 1987, an Independent Ethics Committee was created, characterized by its wholly independent status and membership. The requirement that all proposals for research should be submitted for approval was continued. In this respect, Porton brought itself into line with the practice of other institutions where research was carried out. But, a supervisory mechanism, with a significant degree of independence and authority, (which, on occasions were exercised, for example, through "closed meetings"), had long existed.

23.9. Compensation

One of the more contentious issues surrounding the conduct of research on healthy volunteers is whether researchers have a duty to compensate (in terms of money) those harmed as a consequence of participating in the research. A duty exists in law, but only if the research subject can show that the researcher has been negligent and that he has suffered harm as a consequence, (leaving aside the (very rare) situation in which the volunteer's apparent consent was vitiated by fraud or duress). The existence of an ethical duty, regardless of the requirements of the law, is not, however, universally accepted.

Against this background, the Ministerial statement in 1930, referred to in the Survey (21.7.5) appears to stand in some contrast. By this Statement, the Secretary of State for War explained that volunteers at Porton would be covered by what was called the Injury Warrant, and could, therefore, receive "compensation under the procedure of injury attributable to service" (21.7.5). There is virtually no evidence in the Survey of the extent to which this Statement reflected actual practice then or later. The two exceptions are when the widow of the serviceman who died after the trial in 1953 is described as having been paid a pension under the Injury Warrant and when COHSE is described as reaffirming the continued applicability of the Warrant in 1980 (21.7.5). If the practice adopted did indeed mean that compensation was available without the need to bring any legal action, or even the need to show conduct which was actionable in law (for example, negligence), it suggests that, in this regard at least, the government of the day and later successors were alive to what many would regard as an ethical obligation, as being the counterpoise to the willingness of the volunteer to come forward for the good of research.

That said, the newly appointed independent Ethical [sic] Committee reviewed arrangements for compensation at its first meeting in 1987 (21.7.5). Crucially, the Committee indicated (21.7.5) that the future approval of research would depend on an "appropriate" system of compensation. A

draft was prepared, drawing on the Guidelines issued by the Royal College of Physicians and on those proposed by the Association of the British Pharmaceutical Industry. The Medical Committee at Porton accepted the draft and formal arrangements were introduced to provide for compensation for anyone suffering “injury, disability or death as a result of participating as a volunteer in research...”. These arrangements were set out in a document which, it appears, was intended to be given to all volunteers. It contemplates that compensation may be claimed without the need to demonstrate negligence or take legal action. It leaves open to the claimant the option to pursue legal action should he wish to do so. The claimant must, however, demonstrate that the harm complained of was “as a result of participating ...” (21.7.5 and Annex K). This approach is consonant with accepted practice and constitutes a recognition of the ethical responsibilities owed to the volunteer by the institution engaged in research.

23.10 Awareness of and compliance with Codes and Guidelines

The Survey says little about the role which Codes and Guidelines on research ethics had on the conduct of research at Porton or on the minds of the researchers. There are occasional developments which, on one interpretation, can be said to reflect the emergence of a particular Code or Guideline, if only because they are roughly contemporaneous. But, it is not until 1979 (21.6.1) that entries begin to appear in documents indicating that a particular trial was conducted in accordance with the Declaration of Helsinki. Given the importance that this Declaration gives to consent, these entries may be intended to demonstrate that volunteers’ consent was obtained. But, as has already been said, bald assertions of this kind are no evidence of what in fact transpired. At best, they are evidence that there was an awareness of the existence of the Declaration and the need to comply with it. Why it became routine practice to record this is not revealed. It needs to be said, however, that while there is little formal acknowledgement of Codes and Guidelines, it must not be thought that they were necessarily ignored. The debate in 1965 over the ban on trials of incapacitating agents sees references being made both to the (then) recently published Guidelines of the Medical Research Council of 1963 and to the Nuremberg Code of 1947 (13).

23.11. Conclusion

In this assessment I have concerned myself, as I indicated at the outset, with the general pattern of conduct at Porton in carrying out trials during the period of time covered by the Survey, and certain specific issues and cases. I have not examined each trial, not only because there were very many thousands, but also because of the wide variation in the evidence available.

I have come to the conclusion that research was carried out at Porton in a thorough, painstaking, careful and often ingenious manner. Examples include the trials relating to nerve agents described in 8.4, 8.5.1-2 and 9.4.1. The elaborate and extensive trials of riot control agents described in 14.2.2, (not least because the safety of the wider public was also at stake), provide a further example, as do the very large number of tests on the penetration of agents through a wide variety of fabrics described in 18, and the trials relating to atropine described in 19.1.2. The results were obviously of great importance in assessing military effectiveness, (and see the laconic, but deadly serious observation that a soldier suffering from miosis may discern a shape as a tank, but “would be hard pressed to say if it was Russian or British” (9.5.3)).

Secondly, I have come to the view that there is no evidence to justify a conclusion that the conduct of the trials at any point went beyond the limits of what should ever be contemplated, far less tolerated, in a civilized society.

Thirdly, however, I am persuaded that there were trials, albeit a few out of the many thousands of trials conducted at Porton, (and, as the Overview to Part VI of the Survey makes clear, there were “many hundreds of human studies” conducted just in the period 1939-45), when it may be

said that the research may not have met the ethical standards required of the researchers and, where relevant, those who approved the trials. They are the following:

- The trials of liquid nerve agents on bare skin, carried out between 1951-3 and described in 8.5.3-5: they include, but are not limited to the trial which led to the fatality in 1953
- The trials in 1951 of the nerve agent GD, described in 8.4.7, in which the lethal dose was not known with sufficient certainty
- The trial in 1958 of the nerve agent VX, described in 10.2.2, which involved the use of what, at the time, was regarded as the lethal dose
- The trials in 1942, described in 17.2.4 and 20.1.2, involving the exposure of volunteers to H vapour in the scrotal region, if, as seems likely, there was no real consent
- The trial in 1945 of the substance in the captured German shells, described in 8.2.1, which exposed volunteers to danger without first seeking to determine the nature of the substance

In addition, a question mark can also be raised in relation to the trials conducted from the 1950s to the 1970s to determine the extent to which GB induced miosis, described in 9.5, in so far as a real danger that a volunteer might suffer a detached retina existed but was not controlled (9.6.3). The trials might be said by some to have constituted too great a step into the unknown.

These trials clearly amount to serious departures from what should have been done. But, on the evidence of the Survey, they are few in number and spread over several decades. Indeed, that they are few in number may be thought, perhaps, to be worthy of note and a tribute both to the volunteers and the researchers. The work was conducted at Porton in difficult times: during the 1930s with the memory of the Great War and the threat of more war to come; during the Second World War, when the survival of the nation was at stake; and during the acute tensions of the Cold War and, later, of civil disturbance. It involved research into agents which were deadly, or agents which had to be made safe. This must not be forgotten. Nor must the past be viewed with hindsight, or from a perspective which is far removed from the tenor of those times. As is clear from the Survey, a very great debt of gratitude is clearly owed to those who volunteered to take part in the research at Porton and to those who carried it out.

References

Chapter 23

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