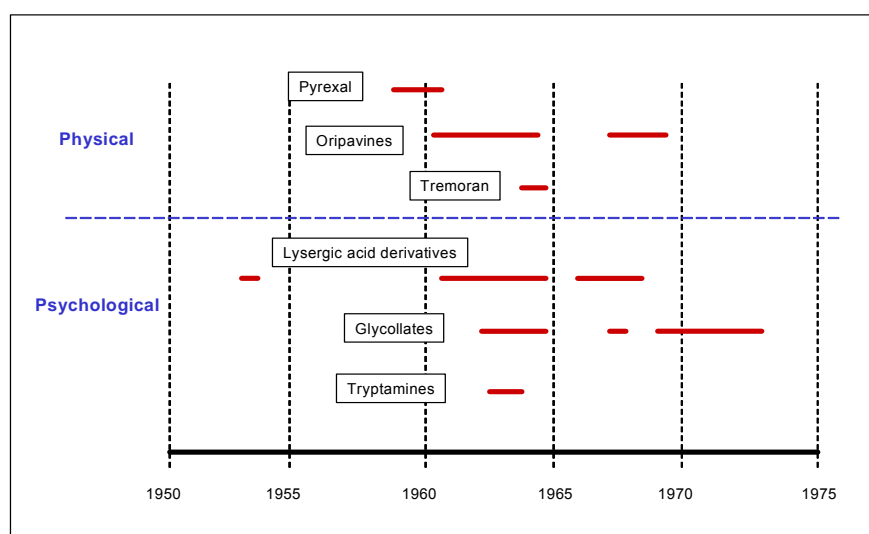


Part IV. Human studies with incapacitating agents

Overview

Interest in incapacitating agents was the main theme of the paper produced by the Defence Research Policy Committee in 1960 and agreed by the Chiefs of Staff in 1962. In fact this interest was anticipated by the Chemical Defence Advisory Board (CDAB) in 1958. The main programme of human studies with incapacitating agents started in 1959. A human study was carried out in 1953 and 1954, but it was commissioned specially and unrelated to the main programme.

A distinction was drawn between physical and psychological incapacitating agents. The distinction was not clear cut, as psychological agents often had a physical effect. The distinction used here follows that used by Porton in 1962. The figure below shows the classes of incapacitating agent tested in human studies at Porton.



Incapacitating agents posed problems. For lethal agents animal tests helped to establish the toxicity and to estimate threshold, harassing and lethal doses for man. Although the degradation of physical performance of animals under the influence of physical incapacitating agents could be measured, assessing motivation in animals was clearly difficult.

Many of the incapacitating agents shown in the figure were known to the world outside Porton. Indeed, some were used as medicines. So, rather than extrapolating dose estimates for man from the results of animal studies, initial doses for some human studies were based on information available in scientific journals and reports. For those incapacitants about which relatively little was known, initial doses were set at very low levels and gradually increased until some effect was observed.

The descriptions of human studies with incapacitants which appear in Chapters 11 and 12 are hampered by the absence of detailed experimental logs covering the period February 1963 to October 1964. Other records covering this period, such as summary books and ward diaries, often give no information about the studies which were conducted. The annotation "experiments in the station hospital" or "studies in the experimental ward" appear frequently. Apparently, detailed records of these studies were maintained by hospital and ward staff but none has survived. Therefore, some uncertainties remain about some of the studies with incapacitating agents. These uncertainties are explained in Chapters 11 and 12.

Chapter 11. Psychological incapacitating agents

11.1 Selection and screening

The potential for psychological incapacitating agents to impair judgement, initiative and leadership had been recognised in 1957 [1]. There were many substances known to have some deleterious effect on man: in 1963, for example, 150 new substances were investigated [2]. As it was impracticable for all these substances to be tested on man, in 1960 Porton set about identifying physical and behaviour tests for animal work to screen new substances [3].

The idea was that when new substances were administered to animals, the screening tests would show which ones were likely to have an effect on man. The ability of screening tests to show this effect was investigated in preliminary work, in which incapacitating substances already known to have an effect on man were administered to animals [4]: those screening tests which returned positive results could then be used in animal work with new substances and be relied upon to predict those substances which would have an effect on man. In 1961 67 psychological incapacitants were screened using such tests [5]. Animal tests continued to be used thereafter to screen incapacitants.

Attention then turned to screening for human tests. CDAB discussed in 1959 the suitability of volunteers to take part in studies with psychological incapacitants [6]. CDAB concluded that it was difficult to know whether or not these studies might, in some volunteers, "set in train some irreversible effect", and suggested that the family history of volunteers should be investigated carefully to exclude from such studies any volunteer whose family had a history of psychological problems. Further, it would be unlikely that irreversible effects would be induced by studies with psychological incapacitants if volunteers were subjected to psychiatric and psychological screening tests and any who showed any tendency to mental abnormality or instability were excluded from experiments [7].

Porton consulted experts at Maudsley Hospital [8], the Royal Victoria Hospital [9] and Netley Hospital and the Director of Army Psychiatry [7] for advice on identifying psychiatric and psychological screening tests for human volunteers. Arrangements were made with the Armed Forces to obtain the services of psychiatrists to administer the tests [10, 11, 12]. Before embarking on human studies with psychological incapacitants, Porton gained experience in administering these screening tests to Service volunteers in 1960 and 1961. Details of the tests and the results of their application are summarised in Annex E.

These tests were regarded as important in establishing the safety of human experiments with psychological agents. Advice from Maudsley Hospital suggested that, as long as subjects for human studies were chosen carefully and small doses used, irreversible effects were unlikely [13]. The screening tests were implemented stringently by Porton: between 1961 and 1965 [14] and in 1967 and 1968 [15] only a third of volunteers reporting to Porton were deemed suitable.

On two occasions the committees overseeing Porton's work considered the screening tests to be too rigorous. The reasons for their concern are not recorded explicitly but they might be inferred from the minutes of the two discussions, given below.

- In 1961, an external member of the Biology Committee (BC) believed too many screening tests were being considered by Porton [16]. The shortage of volunteers was discussed at this meeting: the bulk of those who volunteered were ruled out of incapacitating agent studies.
- In 1966 the Applied Biological Committee (ABC) suggested that screening tests should be varied according to the dose envisaged for the study, rather than being applied identically for all doses [17]. This comment was made after Porton revealed that of the 80 men volunteering for a field trial with LSD only 19 were deemed by screening tests to be suitable.

It would seem that the committees regarded the progress of work with incapacitating agents as being slowed by Porton's stringent application of the screening tests. Exacerbating the problem was the decrease in the number of volunteers reporting to Porton. During the 1950s an average of 627 volunteers had reported each year but in the first three years of the 1960s the number had dropped to 340. In 1964 to 1966 it fell to 147¹. Scientifically, conclusions about the effects of incapacitating agents could be drawn only when a sufficient number of men had participated in studies. Naturally, therefore, the reduction in volunteers and Porton's stringent application of psychological and psychiatric screening tests meant that studies had to proceed slowly.

The committees' concern about the application of screening tests suggests a tension between continuing with important work and Porton's concern to make the work as safe as possible. In 1967, after years of applying the screening tests and observing the effects of incapacitants, Porton began to allow volunteers who were classed by the screening tests as "borderline" to participate in studies [18]. The screening tests were also modified, as practice showed which were redundant or as new tests were developed in the medical world [19].

11.2 Lysergic acid derivatives

11.2.1 The special study and the main investigation

Two derivatives were used in human tests at Porton: lysergic acid diethylamide (LSD) and lysergic acid ethylamide (LAE)². Only a very short series of human tests was conducted with LAE, which was thought to be about one tenth the potency of LSD [20]. LSD was used in a special study completed in 1953 and 1954, and then in human studies during the main investigation from 1961.

The effects of LSD were reported in the open literature in the early 1950s and a summary was produced by one of the panels of CDAB in March 1953 [21].

- In normal subjects LSD was known to have an effect on most people in small oral doses of 40-100 µg. Normal "patients"³ maintained consciousness under the influence of LSD; judgement and memory were not impaired but the perception of the passing of time was often disturbed. LSD usually induces marked euphoria and depression and feelings of "depersonalisation".
- The first effects of an active LSD dose appear within 30-60 minutes and peak about 2 hours after the dose has been administered. Effects persist for 3-6 hours. "Delayed effects" may be observed for one or more days but rarely for more than a week.
- Psychopathic patients can tolerate doses of LSD as high as 500 µg and react in very different ways.

Porton Down volunteers first took part in trials involving LSD in 1953 when, in the context of the Cold War, the Secret Intelligence Service (SIS) and the Department of Scientific Intelligence (DSI) sponsored a clinical investigation into the effects of LSD intoxication. Thirty seven service volunteers were tested in laboratory trials in 1953. Service volunteers who participated in these tests underwent the normal physical medical but were not screened psychologically. This only became the practice in later LSD work during the 1960s. Neither at the time of the tests, nor when a later overview of work with LSD was prepared, were any ill-effects noted.

¹ These averages have been extracted from Tables 5.3 and 5.4 in Part II.

² LSD is referred to in MOD documents as "LSD 25" or T3456. The numerical labelling of the former is obscure. LAE is sometimes referred to as "LAE 32", again for obscure reasons.

³ The use of the word "patients" in the summary of LSD produced in 1953 suggests LSD had been used by the medical profession.

Fifteen men received a single oral dose of 35-55 µg of the tartrate of LSD. The remaining 22 men received doses from 50 – 100 µg. All 22 received more than one oral dose over a period of four days. Two men had a dose of 100 µg on each day; the remainder had two or three doses over a four-day period. None of the 37 men was under stress and each man was encouraged to make notes of his experiences.

Additional tests, involving Porton staff and five Service officers, were undertaken in 1954 to establish the possible utility of LSD as a 'truth drug'. These tests showed that LSD had no such utility and so the SIS-sponsored trials involving LSD ceased. In 1961 the MOD commenced work into the potential of LSD as a possible incapacitant.

In 1956 it was recognised that LSD might have an important role to play in CW, not as an agent to be used over a wide area (like, say, nerve gases) but against "individuals, key groups or perhaps in controlling hostile crowds" [24]. The Defence Research Policy Committee (DRPC) agreed in 1956 that a small programme of work on such drugs should proceed at Porton [25]. This was a foretaste of the recommendations of the DRPC's 1960 paper. The programme of human tests with LSD started in the autumn of 1961 [26].

The programme featured human tests of LSD in the laboratory and three field trials, as shown in Figure 11.1. The field trials, given the names "Moneybags", "Recount" and "Small Change" were thought important in 1957 [1] as a means of evaluating the effect of psychological incapacitants on group activity, and the idea of conducting a field trial at Porton was raised in 1958 [27]. Since soldiers on the battlefield normally work in teams, understanding the individual response to LSD was not sufficient to understand its military value. Before the field trials with LSD, human tests were conducted in the laboratory or hospital ward at Porton.

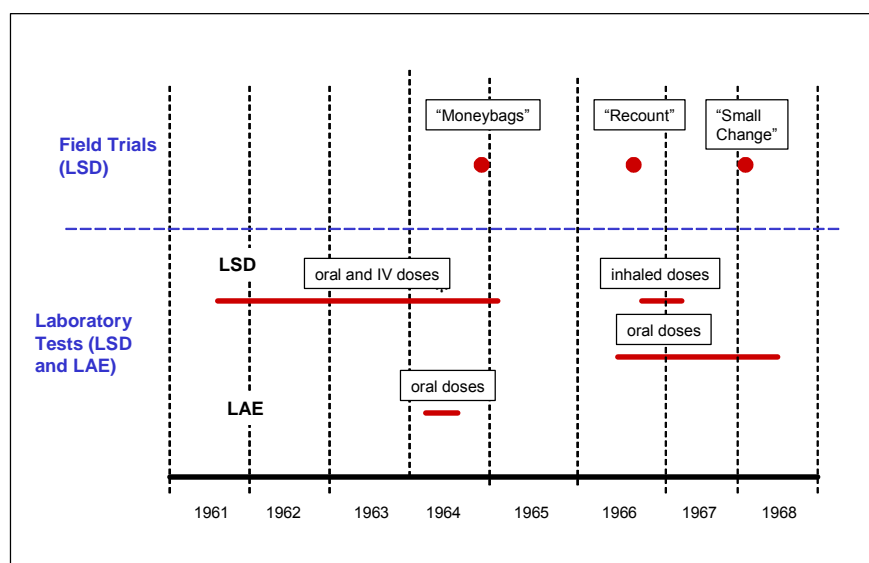


Figure 11.1. Human tests with lysergic acid derivatives

11.2.2. Laboratory tests: 1961 to 1965

Human tests in 1961 started with four members of Porton staff each receiving an IV dose of 50 µg⁴ of LSD under psychiatric supervision [26]. The dose was at the lower end of the range known to have an effect on man. No explanation has been found for deciding to administer

⁴ Doses throughout this section refer to the "tartrate" dose. Porton sometimes cited "free base" doses, which is just a different way of measuring the same dose of LSD. The free base dose is 0.8 times the tartrate dose.

the LSD through IV rather than in an oral dose. Records show that three volunteers had fairly pleasant experiences but one had an unpleasant experience and disliked recalling it 5 years later [26].

From December 1961 to January 1965, after the tests with Porton staff, 59 laboratory tests were conducted with 47 human volunteers [28]. Two staff members received a second dose of LSD during this period and 10 Service volunteers received two doses of LSD [26]. The doses used in the exposures are shown in Table 11.2.

Dose (μg)	Route	Number of exposures
50	IV	20
75	IV	12
100	IV	2
150	IV	3
50	oral	3
75	oral	3
100	oral	4
150	oral	3
200	oral	9

Table 11.2. LSD doses: December 1961 to January 1965

During the period covered by Table 11.2, the first tranche of work running from December 1961 to March 1962 involved 20 volunteers who received IV doses of 50 μg and, while under the influence of LSD, completed various psychological tasks. Twenty other men did the same tests but served as controls and were given 20 mg of sodium amytal [26]. Sodium amytal is a sedative and was used in one of the screening tests (see Annex E). Eight of the 20 men given LSD experienced moderate symptoms, such as mood changes and disturbances of perception, 4 had mild symptoms and the remaining 8 experienced little or no effect. However, all the men receiving LSD performed the psychological tasks noticeably less well than the controls and less well than they had before receiving the LSD dose.

In the work carried out between April and October 1964 men dosed with LSD performed a series of tasks, before exposure, during exposure and the day following exposure. These tasks, to assess the degradation of performance induced by LSD, included solving anagrams, reading, copying geometrical figures and a measure of reaction time. To serve as a basis for comparison, 23 men were given sodium amytal and performed the same tests. Again, the performance of the tasks by men receiving LSD was impaired but had returned to normal the day after the trial.

Information from various sources, including some cited in the DPRC 1960 paper, suggested the "possibility of LSD being used as an incapacitating agent against our troops in the field" [26]. Porton were interested, therefore, in an antidote to LSD. Typically, sedatives were used. Five men who received an oral dose of 200 μg of LSD also received a sedative, either sodium amytal or chlorpromazine, to determine if they worked as therapy to the LSD dose.

The main conclusions from the work conducted from December 1961 to January 1965 [26] were as follows.

- It did not appear that the effects experienced were directly related to LSD dose - many subjects were incapacitated by a dose of 50 μg . But it appeared necessary to give a dose of at least 100 μg to incapacitate the majority to "an obvious degree".
- An oral dose of LSD was as effective as an IV dose but the onset of effects was slower, generally taking 30 minutes or more to come on. The duration of the effects seemed longer from an oral dose.
- Recovery was usually about 12 hours and complete within 24 hours.

In early March 1964 volunteers participated in tests of LAE [28]. Oral doses up to a total of 0.5 mg were used and had little effect other than a euphoric reaction [30]. A dose of 0.5 mg equals 500 µg, which is ten times the initial dose of LSD used (50 µg) in human work and equates with the view held by Porton in 1963 that LAE was one-tenth of the potency of LSD [20]. It is not clear how many volunteers took part in this work. The summary book [29] shows 11 volunteers taking part in a "Morphine, TR2833 (sic) and LAE crossover trial" in the week beginning 7 March 64. "Crossover" indicates that all eleven had doses of each of the three substances. It is possible that these were the only volunteers exposed to LAE.

In the middle of March 1964 Porton intended to increase the LAE oral dose to 1 mg but thought it likely that LAE would not be used as an agent [30]. It is uncertain from the existing records if this dose was used or if any more LAE experiments were conducted. No reference to LAE appears in COSHE meetings held after March 1964.

11.2.3. Laboratory tests: 1966 to 1968

Some thought was given to how LSD might be used by the enemy in the field. Delivering LSD by IV injection or in an oral dose restricted the options. Oral doses might be delivered to an enemy by contaminating his water supply but if one was close enough to the enemy to inject him one would employ more straightforward methods to disable him. In 1965 and 1966 thoughts turned to delivering LSD in aerosol form [26] and the effects of inhaling it.

Up until then no satisfactory method of disseminating LSD in the air had been found at Porton. Little was known about how the effects of LSD by inhalation compared with the effects induced by ingesting LSD [26]. It was reported to CDAB in 1965 that the US believed inhaled LSD was four to five times less active than ingested LSD [31]. Giving a man two doses of LSD, one inhaled and one oral, to compare the effects was considered [26, 32] but the ABC ruled (in 1966) that initial experiments should be restricted to one dose of LSD per man [33].

The issue of repeated doses had arisen before. In 1959 a professor serving on the Chemistry Committee of CDAB noted that the effect of a few doses of psychological drugs was usually reversible but if repeated doses were given an irreversible effect might be produced. In reply, the Head of the Medical Division at Porton (under whose aegis human tests were performed) emphasised the fact that "as in previous experiments volunteers would not be given more than one dose of any compound being tested" [34]. There had in fact been exceptions to this in the past, and there continued to be in the future, as some volunteers received two doses of LSD in the laboratory work carried out between 1961 and 1965. However, following the 1966 ABC ruling, no volunteer who participated in later LSD studies received more than one dose of LSD. The COSHE produced a register of approved human experiments which cited the safety procedures and maximum doses of substances to be administered to human volunteers [35]. This register does not mention the ABC ruling of 1966 even though the ruling was adhered to.

Work with animals on the retention of particles of LSD delivered by an aerosol began in 1965 [31]. By May 1966 it was known that particles became concentrated in the lungs after LSD had been inhaled and therefore the onset of effects might be slower than after LSD had been ingested. However, while the duration of the effects might be longer judging from US work, they would be less intense. LSD inhaled, therefore, might be two to three times less effective than LSD taken orally but the ABC decided that inhalation work should begin with the same initial dose, 50 µg, that had been used at the start of oral tests [33]. Further, the ABC considered it unwise to increase this dose until some method had been found of measuring the levels of LSD in blood following an inhaled dose.

Human tests with LSD resumed in August 1966 [28]. In the next 6 months, 10 men were given LSD to compare inhalation and oral doses. The doses used, one per man, are shown in Table 11.3.

Oral dose (μg)	Inhalation dose (μg)
50	12
100	<40
100	47
150	51
	120
	120-135

Table 11.3. Doses used for LSD comparison: August 66 to March 67

The lowest inhalation dose occurred when the apparatus used to administer LSD failed: it was intended to administer a dose of 50 μg but only 12 μg was inhaled by the subject. Inhaled doses of around 50 μg had little effect. Typical LSD symptoms were observed after the inhaled dose of 120 μg and the man who received this dose performed slightly less well in psychomotor tasks after receiving the dose than he had before receiving the dose. These effects were judged to be the same as those experienced after an oral dose of 50 μg [28]. Porton had begun work on a technique to measure LSD levels in blood. This was tried after the inhalation dose of 120-135 μg . Blood samples taken from the man receiving this dose suggested 40-60 μg had been absorbed in the body [28].

Tests with men inhaling LSD were halted while the technique to measure LSD levels in the blood was refined. Over the summer of 1967, 18 men received oral doses, partly to validate the technique and partly to assess the level of incapacitation by measuring performance in psychomotor tests. One man received a dose of 50 μg , one a dose of 100 μg , six took 150 μg and ten took 200 μg . A 200 μg dose appeared to incapacitate half of the men. At this dose peak effects came on about 90 minutes after the dose had been taken and persisted for 2 hours. Residual effects in some men lasted for 11 hours.

Further work was conducted with an oral dose of 200 μg . Twelve men received this dose between September 1967 and May 1968 [37]. The results suggested that the dose to incapacitate 50% of men was greater than 200 μg , this being the dose estimated by the US to "destroy military efficiency". The ABC had approved in October 1967 human tests with an oral dose of 250 μg [38] but this dose was not used as volunteers at Porton were required for tests of greater importance⁵. Indeed, no more LSD laboratory trials were conducted. The technique to measure LSD levels in blood was validated [39].

The last element of laboratory trials involved work on antidotes to LSD. The accepted treatment for LSD intoxication is sedation but this was hardly satisfactory for soldiers on the battlefield. A drug called phenoxybenzamine alleviated LSD symptoms and, it was claimed, did so without rendering the subject incapable of military tasks as a sedative would [26]. Ten pairs of volunteers took part in a study in 1966 to explore if phenoxybenzamine impaired performance [40]. One of each pair received phenoxybenzamine and the other a placebo. Each pair performed the same psychomotor tasks. No difference in performance was detected. The men receiving phenoxybenzamine were not incapacitated and did not suffer any fall in blood pressure. Plans to test the antidotal power of phenoxybenzamine against LSD were drawn up and approved in July 1966 [40]. Again the experiment would be conducted in pairs: each of the pair would receive an oral dose of 50 μg LSD, then one would take 20 mg of phenoxybenzamine, the other a placebo. The indications from the experimental records are that this work was not carried out. According to the progress reports on LSD presented to the ABC [28] only two men received an oral dose of 50 μg after the test was approved in July 1966. No mention of phenoxybenzamine is made in the experimental records or the COSHE minutes after this date.

⁵ These more important tests were not named but a great deal of work on riot control agents was being carried out in this period for urgent operational reasons related to Northern Ireland and the Far East.

11.2.4. LSD field trials

"Moneybags", a trial to find out how a psychological agent could affect troops under simulated operational conditions, was held in late November/early December 1964 [41]. Men from 41 Commando Royal Marines (RM) took part in the trial. After one of the officers of the Plymouth RM attended the Porton Open Day in 1963, he approached Porton with an "offer in principle" to send a complete platoon [42]. Some of the RM who took part in the trial have offered their recollections to the survey through a questionnaire and remember being given a presentation at their unit by a member of Porton staff who explained why volunteers were sought.

Some of the men who volunteered from 41 Commando were found to be unsuitable for LSD through the psychiatric and psychological screening procedures. Sixteen received an oral dose of 200 µg; one man, for whom this dose was deemed too high, received 75 µg [43]. The military exercise was designed to reproduce an internal security operation similar to those the men had experienced in "Borneo, Cyprus and elsewhere". The first day was devoted to familiarisation with the exercise, the men having not worked together before. On the second day the men received LSD in water. The third day sought to evaluate the recovery of the men from the effects of LSD.

The exercise on the second day began 15 minutes after the men had received LSD. They became progressively disorganised, ill-disciplined and incapable of taking orders 70 minutes after taking LSD. Observations made on the exercise included [43] the following:

- If the drivers had been drugged (they were among the men for whom LSD was deemed unsafe) there seems "little doubt that chaos would have resulted even earlier". As it was the unit would have been "annihilated by modest enemy action" within an hour.
- Communications were chaotic because very little information was passed between the men. "By the time the recipient had been 'woken up' enough to realise that someone was talking to him, the speaker had forgotten what he was supposed to be saying".
- Military field-craft was completely forgotten. Men walked aimlessly in the open and would have been exposed to enemy fire.
- Some men were reluctant to enter the ambulance after the exercise to return to camp, but their resistance was always passive. Two men fed imaginary birds with their sandwiches, one man was climbing a tree and another attempted to chop down a tree with his trenching tool for 25 minutes. Despite the screening tests, one man had a temporary breakdown, experiencing depression for three to four hours followed by paranoia for an hour [44].
- The performance of the men on the third day was judged by the military umpire (an experienced infantry officer) to be "well-nigh perfect". This suggested that impairment was transitory.
- Overall, there was no doubt that LSD at 200 µg could render military operations impossible.

The ABC watched a film⁶ made of Moneybags at its first meeting in November 1965; one year after the exercise had been held [19]. Apparently the worst effects of the LSD dose were over within 6 hours and within 24 hours all the men in the exercise regarded themselves as back to normal. One (non-government) member of ABC thought the man who was affected

⁶ Three films of Moneybags were produced: a full version for the ABC, a version without the scenes in the station hospital for "general viewing", and one showing only selected incidents. They ran for 25 minutes, 20 minutes and 5 minutes respectively.

badly in Moneybags should have received treatment. The prevailing view was that Porton needed to find out if the man could recover on his own⁷ [33]. Thoughts turned to conducting a similar exercise but with only half the men being drugged to see how changes in their behaviour affected their unit as a whole [33]. "Recount" originated from these discussions [46].

Men from the 37th Heavy Air Defence Regiment RA participated in Recount. The men volunteered after Porton staff visited their unit and explained that the purpose of the trial was to investigate agents which might incapacitate. The name of the drug was not mentioned nor the precise symptoms that might be expected. Eighty men volunteered: 27 were rejected because their jobs were unsuitable for the trial and 34 were eliminated by the screening tests [46]. In Recount 16 men received LSD while 12 men did not. The men were split into five units: four had a mix of drugged and undrugged men whereas men in the fifth unit did not receive LSD.

Recount planning did not go smoothly. The intention in May 1966 was to use the same dose of LSD, 200 µg, as used in Moneybags [36]. By August, the Head of the Medical Division at Porton was inclined to cancel the trial [47] as the medical officers at Porton earmarked to supervise Recount had no clinical experience of a 200 µg dose. Instead a recommendation was made to the Director of Porton that the dose should be 50 µg [48]. The Director was not happy with the late change of plan. A special meeting was held: a dose of 50 µg was unlikely to produce useful results, so a dose of 100 µg was agreed [49].

Recount, held in September 1966, proved unsatisfactory as a comparison with Moneybags: [17, 18] the dose was different, the participants were not infantrymen, and their military job was to site radar and ground-to-air missiles⁸. Further, it seemed the men knew before the trial that LSD was to be used. Porton had told the senior officer of the regiment that LSD would be used and this information had filtered down to the participants. As a consequence, one officer developed elaborate plans with his men on what to do if he became incapacitated [17]. The observations made on the trial were that [46]:

- changes in behaviour were not severe and no treatment was needed, the main effects of the LSD dose were an inability to concentrate and boisterous and excessively cheerful behaviour;
- men who had not received LSD "carried" the drugged men through their duties and the performance of the unit was relatively unaffected (compared to its performance on the day before and the day after when the same tasks were performed);
- if a task had to be performed by a drugged man it could generally not be completed.

The flaws in Recount prompted consideration in April 1967 [18] of another trial, this time involving infantrymen. Volunteers were drawn from the 1st Battalion Staffordshire Regiment. The trial, called Small Change, was planned for September 1967 [50] but, with the regiment's return to the UK from overseas being delayed [51], it was held in January 1968 [52].

Small Change involved 28 men conducting simulated anti-terrorist sweeps on the Porton ranges. The men were split into a headquarters section and three other units. Half of them received an oral dose of 200 µg. A programme of 7 days of trials was scheduled. Porton believed that men in Recount had surmised (correctly) that LSD would be given on day two, and wanted to avoid such predictability in Small Change. The effects observed in the trial are given below [52]:

⁷ For the next trial, Recount, Porton decided that any man reacting as badly as the man in Moneybags would promptly be removed for treatment [36].

⁸ This heavy equipment was not used in Recount, as Moneybags showed that men under the influence of LSD had difficulty handling equipment [43]. In Recount the men surveyed different sites and then took part in a conference to report their findings and choose the best sites [46].

- Two men were withdrawn during the trial because of their symptoms and transferred to the station hospital where they were kept overnight. Both recovered 7.5 hours after receiving the LSD dose without special treatment. Another man was found to be uncommunicative, hostile and paranoid during the afternoon after the trial. He was transferred to the station hospital. Two hours later, having had no special treatment, he was more forthcoming and no longer paranoid. However, he had not completely recovered and was kept in overnight under observation. All three of these men seemed fit after an examination the following day. One said he did not return to normal until two days after receiving the dose, although he did not report this until one week after the trial.
- At no time did the "undisciplined and bizarre" behaviour seen in Moneybags develop. Further, although laboratory experiments with a dose of 160 µg suggested that half the men should have become incapable of effective action, only two were incapacitated. There was very little overall reduction in the unit's military efficiency.

The conclusions drawn from Small Change seem to mark the end of interest in LSD. Undrugged men exerted a considerable stabilising influence [52, 53] and it was concluded that LSD "is of doubtful chemical warfare value" [52]. Military members of the ABC [53] and (independently) Porton [54] considered that effort should be diverted from LSD to glycollates. Members of CDAB, at its meeting in January 1969, [55] judged LSD unsatisfactory as an operational agent because of the unpredictability of its effects and because it was expensive to produce. LSD investigations stopped by December 1968, apart from a little work with animals [56] on antidotes which continued until September 1969 [57].

11.2.5. LSD follow-up

Nine months after Moneybags, Porton saw seven of the men who had received LSD during the exercise as part of a follow-up effort [19]. All the men claimed to be back to normal two days after receiving LSD in Moneybags and were willing to take part again in a similar experiment. The officer was willing to take LSD again but not while leading troops. The psychiatric and psychological screening tests administered before Moneybags were given to the men again. Only trivial changes were found: one man was more relaxed than before Moneybags; another, who had married since the exercise, was more ambitious. In reviewing these points, the ABC considered follow-up to be crucial and it should be conducted one or two years after the dose of LSD had been received [19].

In April 1967 the ABC asked if Porton had completed a follow-up on the men who participated in Moneybags [18]. Porton had done so, as far as was possible. The only points made to the ABC were that one man had married and one had been invalided out of the Army with a back injury.

The ABC and BC held a joint meeting in December 1968 [58] and discussed behavioural studies, in particular the tests which should be used to detect any permanent effects induced by psychological incapacitants. Porton explained that no tests were conducted if there was any evidence that a drug caused permanent effects. Volunteers had been seen "various times after LSD"; one had been examined three-and-a-half years after exposure. No lasting effects had been detected. Porton staff reported that they were aware of reported chromosome damage by LSD but the evidence for that being a serious effect was uncertain⁹.

Porton devoted effort to following-up volunteers exposed to LSD. In March 1971 an attempt was underway to see all the subjects who had received LSD at Porton. To that date, 40 men had been followed-up [59]. By July 1971 Porton had followed-up, by consulting medical records, 66 of the 67 Army volunteers who had participated in LSD trials and a report was

⁹ At the time, chromosome damage may have been regarded as an indicator of carcinogenicity. Three years later the Himsforth report into the toxicity of CS (see Part V) mentions damage to the chromosomes of white blood cells in the context of carcinogenicity.

being prepared. Further reference to this report, and the report itself (if it was written), has not been found.

11.3 Glycollates

11.3.1. Background

Various glycollate compounds exist. Some have short-lasting effects, others last longer [61]. Two glycollates were used in human studies at Porton: BZ¹⁰, a long-lasting glycollate, and a shorter-lasting glycollate called "N-methyl-4-piperidyl-isopropyl-phenol glycollate" (MPIPG). The latter was referred to in Porton reports of the time as T3436, and that name will be used here. The effects of glycollates on behaviour include [62] complete disassociation from surroundings, unintelligible muttering, extreme restlessness and exploratory activity. Food, drink and sleep requirements were ignored. The onset of symptoms was usually marked by euphoria, drowsiness, a dry mouth, slurred speech, expanding pupils (called mydriasis) and uncontrolled muscle twitching.

Some comparisons with LSD can be drawn [61]. Under LSD intoxication a man is able to converse and perform simple mental and physical tasks. The disassociation induced by glycollates means that the same simple tasks cannot be attempted. LSD hallucinations tend to be confined to visual images of coloured geometrical shapes. With glycollates, auditory hallucinations are more common than with LSD and visual hallucinations tend to be of objects, animals and people.

Glycollate intoxication is often followed by amnesia, where the effects of the exposure cannot be remembered, whereas under LSD the subject retains a vivid memory of events and symptoms experienced. Some reports were received by Porton in 1968 that people exposed to glycollates showed in the weeks and months afterwards an increased capacity for work: a phenomenon not (up to then) observed following a dose of LSD.

11.3.2. Human tests with BZ

Human tests with BZ at Porton began in August 1962 [61]. A paper reviewing the knowledge available on BZ was written in 1961 [63] in which the following main points were made:

- BZ had been isolated in the US in 1950. US tests with men showed that an oral dose of 4 µg/kg body weight had no effect. As doses were increased above 6 µg/kg, subjects experienced fatigue, followed by hallucinations and disorientation.
- Effects may last a long time. Two men in US work had been given 8 µg/kg and experienced severe effects: they became delirious and noisy, had hallucinations and kept moving around continuously for a week.
- There was some evidence of a direct action on the heart which had led the US to call a temporary halt to human tests. The US had warned Porton that BZ human studies should be conducted with full medical and psychological cover, as the "subjects become zombies".
- Animal tests at Porton confirmed US results of the effect of BZ on animal behaviour.

Before embarking on human tests at Porton, staff visited the US to discuss BZ [64] and found that the effects did not vary with the route of administration. Human tests at Porton administered BZ by IV injection and orally. The doses used in the tests conducted between

¹⁰ BZ, also referred to as EA2277 and T2532 is a benzilate, but appears in a paper produced by Porton on glycollates and therein is referred to as a "long acting glycollate" [61].

August 1962 and August 1964 are shown in Table 11.4 [61, 65]. Work started with a dose of 3 µg/kg and progressed to the highest dose.

Dose (µg/kg)	Route	Number of Exposures
3 or <3	IV	3
6	oral	3
6	IV	6
7	IV	3
7	oral	5

Table 11.4. BZ doses used: August 62 to August 64

It is uncertain whether 19 or 20 exposures were made as part of this study. Table 11.4 cites 20 exposures and is drawn from a report made to COSHE in February 1965 [65]. However, the progress report on this work prepared for the ABC in March 1967 [61] refers to 19 exposures. The number of volunteers receiving these exposures is not mentioned in the report to COSHE but the report for the ABC states that 17 subjects participated. The follow-up study conducted in 1979 of volunteers who participated in BZ studies [66] notes that 21 men had been exposed to BZ doses of 6 - 7.5 µg/kg at Porton between 1962 and 1967. Excluding the 4 men who took part in the later study in the summer of 1967 (described below), this means that 17 men received doses of 6 - 7.5 µg/kg between August 1962 and August 1964. Seventeen exposures to these doses seem to have been made during this period, as shown in Table 11.4: one for each of the men cited in the follow-up study. But this begs the question of who was exposed to the 3 µg/kg doses. In any case, the follow-up study, the ABC report and the COSHE report differ. Detailed experimental records for March 1963 to October 1964 cannot be found, so the differences cannot be resolved.

The effects observed in this series are given below [61].

- No psychological effects were observed at the lowest dose. The men receiving this dose became drowsy and experienced minor changes in blood pressure and pulse. With the oral dose of 6 µg/kg, all the subjects complained of a dry mouth, dizziness and drowsiness. Mydriasis (dilation of the pupils) developed before all other symptoms and persisted the longest, up to 48 hours. All the men had raised pulses but there was no consistent change in blood pressure.
- Of the men receiving 6 µg/kg by IV injection, three had psychological symptoms. One was in a confused state for 32 hours, experiencing hallucinations and slight paranoia. All had raised pulses two hours after the dose was administered, which returned to normal 11 hours later. Changes in blood pressure varied among men but did not change by more than 20 mm Hg for more than 2 hours.
- The IV dose of 7 µg/kg induced mydriasis in all subjects and two experienced involuntary limb movements. The effects were short, none lasting more than 8 hours: pulse was raised one hour after dosing and returned to normal 7 hours later. One man's diastolic blood pressure was raised more than 20 mm Hg for over 4 hours.
- All men receiving 7.5 µg/kg orally experienced mydriasis. One subject became disorientated 9 hours after receiving the dose, became completely confused and psychotic and was not fully rational again for another 41 hours. He experienced auditory and visual hallucinations and once became aggressive. His systolic and diastolic blood pressure were both raised by more than 20 mm Hg for over 30 hours.

In reviewing these results in February 1965 [65] Porton noted that two men had showed "severe toxic delirium" for 2-4 days and three had developed "mild confusional states" for 2-3 hours. The total amnesia observed in US work during intoxication did not occur. One man remembered very well his violent reactions and was difficult to reassure. Porton doubted that more tests with BZ could be justified [65].

No more human tests with BZ were conducted until the summer of 1967 [67]. In April 1967 the results of the earlier tests were reviewed with the ABC [18]. It was mentioned that the US thought BZ was too dangerous because of its slow onset and because recovery from its effects could take up to a week.

A final short series of human tests with BZ was carried out in the summer of 1967 [50, 68]. A higher dose than 7 µg/kg was considered but discarded by Porton [68]. The aims of the tests were to examine the reasons for differences in UK and US estimations of the effective dose and to provide comparative data for a study of other glycollates (of which T3436 was to be tested first) [67].

Four men received an oral dose of 7 µg/kg, the middle of the range 6-8 µg/kg estimated at that time by the US to be the effective dose [67]. All were affected, developing elation and dizziness followed by drowsiness. Three complained of weakness of the legs but none of these three showed signs of mental incapacitation. The remaining subject suffered leg twitching that got progressively worse. Involuntary movement of the arms developed and mental deterioration was rapid. Ten hours after receiving the dose he was very restless, experienced auditory and visual hallucinations and became disassociated from his surroundings. He remained in this state for 36 hours, making a rapid recovery to normal 12 hours later. His blood pressure rose to a maximum of 150/95 (from 100/75) and his resting pulse rose from 78 to 104 beats per minute.

This series of tests marked the end of human tests with BZ, although after the series preparations were put in hand for more. Most notably, the experimental ward was thought not to be suited to housing subjects exposed to BZ [62]: smaller individual cubicles were better, so that the subject had room to walk around and did not feel observed. Subjects under the influence of BZ tended to take to pieces any equipment they came across (part of the "exploratory activity" mentioned as one of the symptoms). Individual cubicles would be stripped of clutter and personal effects could be locked away [50]. Despite these preparations, human tests with glycollates moved on to T3436.

In 1979 Porton conducted a follow-up study of the volunteers who participated in the BZ studies [66]. The study was prompted by an allegation by the Church of Scientology in the USA that exposure to BZ may be followed by long term psychological upset and personality changes. The study was based on Service medical records, as it was felt that there would be considerable difficulty in obtaining medical records of men after they had left the Services and any attempt to recall men for a routine check could cause alarm [69]. The study examined the records of 41 volunteers who attended Porton from 1962 to 1967. The 41 were selected to include 21 who had been exposed to a dose of BZ of 6 - 7.5 µg/kg and another 20 who had not participated in BZ studies. The officer at Porton who studied the Service medical records of these 41 men was not told which men had been exposed to BZ [66].

The study concluded that the incidence of illness in men who participated in BZ studies did not differ in any significant way from those who had not been exposed to BZ. Seven men who had been exposed were still serving when the follow-up study was conducted and were suffering no defects apart from minor visual acuity problems. The study suggested that no after effects could be expected from exposure to BZ.

11.3.3. Human tests with T3436

T3436 was mentioned in November 1967 as a "new" glycollate similar in action to BZ [70]. By that time work with animals had been completed which suggested the dose effective against 50% of men was about 2.8 µg/kg. The effects of T3436 were short-lived compared to

BZ. In November 1967 COSHE approved an initial oral dose of 0.5 µg/kg for human tests and decided that this dose could be increased by steps of 0.5 µg/kg until either an effect was obtained or a dose of 2 µg/kg was reached.

Human tests with T3436 began in January 1968 [71]. Between 30 January and 26 March, 10 volunteers received oral doses of T3436: five receiving 0.5 µg/kg and five receiving 1 µg/kg. No effects were observed with the lower dose [54] nor with four of the five at the higher dose [72]. The remaining man, who was given a dose of 1 µg/kg, experienced blurred vision which persisted into the following day, and mental symptoms lasting for around 2 hours. While experiencing mental symptoms he was unable to understand questions put to him. It was noted that he would not have been selected for LSD studies¹¹ because he had had a disturbed childhood although his present psychological state was "basically sound" [72]. In view of this, and the availability of treatment for T3436 intoxication, COSHE decided it was safe for work to continue but limited the next dose increase to 0.25 µg/kg [72].

Human tests with T3436 continued with no effects being observed until a dose of 6 µg/kg had been reached [71, 73]. Each increase in dose was approved by COSHE and the ABC. Details of the doses, and when they were approved, are shown in Table 11.5. Each man received only one dose.

Oral dose (µg/kg)	Number of men	Approval
1.25	5 [71]	27 Mar 1968 [72]
1.5	8 [74]	22 Apr 1968 [75]
1.75	5 [73]	23 May 1968 [74] <i>See Note 1</i>
2	5 [73]	17 Jun 1968 [76]
2.25	4 [73]	19 Sep 1968 [77]
2.5	5 [78]	22 Oct 1968 [79]
2.75	5 [78]	4 Dec 1968 [56] <i>See Note 2</i>
3	5 [78]	4 Dec 1968 [56]
5	5 [78]	13 May 1969 [80] <i>See Note 3</i>
6	5 [78]	8 Jul 1969 [81]

Notes:

1. An increase of only 0.25 µg/kg was imposed because summer was coming and it was thought possible that warmer weather might exacerbate the effects of T3436.
2. The ABC approved a maximum dose limit of 3.5 µg/kg at this meeting.
3. When approving the increase to 5 µg/kg, COSHE noted that US work suggested that the **IV** dose to incapacitate 50% of men was about 5 µg/kg, and the **inhalation** dose about 8-12 µg/kg.

Table 11.5. T3436 human tests¹²: oral doses 1.25 - 6 µg/kg

Of the five subjects who received a dose of 6 µg/kg, one was deemed to have reacted mildly [78]. He found it difficult to focus on small print and felt dizzy, later experiencing visual hallucinations and disorientation. His confusion was at its highest 5 hours after dosing. One hour later intelligent conversation was possible and, although sporadic visual hallucinations occurred, the subject could remember taking the drug and seeing imaginary animals and people. Recovery was complete 24 hours after dosing. Pulse, blood pressure and blood chemistry showed no changes from normal in any of the 5 men. EEG changes were seen in the man most affected.

In September 1969 the ABC agreed the dose of T3436 could be raised to 7 µg/kg [57]. Information received from the US around that time suggested that the oral dose which would

¹¹ The criteria of acceptance used with the psychiatric and psychological screening test results had been "eased slightly" with glycollate work as compared to with LSD [58].

¹² The table shows that 25 volunteers received doses of 2.5 - 6 µg/kg. A total of 37 men received doses of 0.5 - 2.25 µg/kg (27 men in this table and the 10 men who participated in the earlier studies). These statistics agree with those given by Porton in 1999 [82].

incapacitate 50% of men was 8-12 $\mu\text{g}/\text{kg}$ [78]. Over the 18 months to February 1971, 27 men were exposed to T3436:

- 7 $\mu\text{g}/\text{kg}$. Six men received this dose [83]: 5 felt unsteady and had difficulty concentrating. Two men experienced hallucinations [84]. COSHE approved an increase in the dose [84].
- 8 $\mu\text{g}/\text{kg}$. Ten men received this dose [83]. Eye symptoms (dilation of the pupils) persisted up to 48 hours, longer than other effects. No clear psychotic behaviour was observed in any: reports from one subject of visual hallucinations were "regarded [by Porton] with considerable scepticism" [83]. Approval was obtained to increase the dose [85].
- 9 $\mu\text{g}/\text{kg}$. Six men received this dose [83, 86]. All became drowsy and their concentration became weak [83]. One man was somewhat confused but reported no problems in perception. His pulse was depressed (to 42 beats per minute) for 90 mins: "an unusual feature" [86]. ABC approved an increase in dose to 11 $\mu\text{g}/\text{kg}$ in September 1970 [87].
- 11 $\mu\text{g}/\text{kg}$. Five men received this dose [86]. In the report to ABC [86], seven T3436 exposures are mentioned: two at 9 $\mu\text{g}/\text{kg}$ (the final two of the previous series) and five at 11 $\mu\text{g}/\text{kg}$. In the minutes of the ABC meeting [59], the five exposures are misprinted as **seven** exposures at 11 $\mu\text{g}/\text{kg}$. Four men experienced similar symptoms to those observed with a dose of 9 $\mu\text{g}/\text{kg}$ and another case of depressed pulse rate was seen. The fifth man was undoubtedly incapacitated. He became confused about time and place, suffered "frank" visual and auditory hallucinations, and was still slightly confused 13 hours after dosing. The next morning (22.5 hours after dosing) he appeared to have recovered.

This brought an end to human tests with oral doses of T3436¹³. Just as with LSD, consideration was given to conducting tests with a "realistic" dissemination method [83] - aerosol - prompting a series of inhalation tests. T3436 by inhalation was reputedly more effective than T3436 given orally: "the US had clinical charge of two cases where a retained dose of 8 - 12 $\mu\text{g}/\text{kg}$ had been administered by inhalation" [57]. The ABC agreed to inhalation work in March 1971, setting the initial dose at 25% (2 $\mu\text{g}/\text{kg}$) of the estimated incapacitating dose [57]. Human tests inhaling T3436 ran from June 1971 to July 1972. The doses used, and the number of men receiving, them are shown in Table 11.6 [88, 89, 90, 91, 92, 93]. Each man received one dose.

Dose ($\mu\text{g}/\text{kg}$)	Number of men
2	1
4	6
6	6
8	8

Table 11.6¹⁴. T3436 human inhalation tests

No effects were observed with an inhaled dose of 2 $\mu\text{g}/\text{kg}$ [88], and only "minor" effects [89, 94] with a dose of 4 $\mu\text{g}/\text{kg}$. All men receiving a dose of 6 $\mu\text{g}/\text{kg}$ showed changes in behaviour: 5 reporting visual or auditory hallucinations [90]. Minor changes in pulse and blood pressure were seen in four of the six men receiving this dose but there was no consistent pattern to them. All the men inhaling a dose of 8 $\mu\text{g}/\text{kg}$ were affected, with two possibly being incapacitated [91].

¹³ Some uncertainty about oral exposures to T3436 remains. Progress reports to ABC and COSHE while the studies were in progress (from which the statistics which appear in this section are drawn) cite 89 volunteers receiving an oral dose. A later summary report to the ABC in 1971[86] cites 91 volunteers. The statistics produced by Porton in 1999 [82] cite 90 volunteers.

¹⁴ 21 volunteers inhaled a dose of T3436. This figure differs from that (23) reported by Porton in 1999 [82].

This work appears to mark the end of human tests with T3436. No mention of T3436 studies appears in COSHE minutes, all previous exposures are cited. Ward diaries covering 1970 and 1972 [95, 96] cite studies of glycollate by inhalation. Their successors for 1973 to 1975 [97, 98, 99], although of the same format, mention no such studies. The annual report for 1973-4 [100] does not mention T3436 studies, which are noted in the next annual report [101] to be in abeyance although the hope is expressed that they would resume in 1975. However, the report for 1975-6 [102] notes that no more human work with glycollates had been conducted. The next report, 1976-7 [103], records that no more human studies with glycollates were anticipated.

11.4 Tryptamines

A survey of the open literature was conducted in 1959 and, from this, one Porton report notes [104] that, of the main types of psychological drugs known about at the time, derivatives of indole were most likely to provide new compounds of high activity. Indole is an organic compound that can be found in various sources, including flowers and coal tar. The indole nucleus was found to occur in a considerable number of compounds which produce mental effects.

Tryptamines are derivatives of indole. They were known about in 1956; academic references note that one of the tryptamines (N,N-dimethyl tryptamine¹⁵) caused hallucinations in man at doses of 1mg/kg body weight when injected intra-muscularly (IM). As a result, in 1960 [5] Porton used criminal tests to screen various tryptamines. Two forms of tryptamines were considered; "simple" tryptamines and "ring-substituted" tryptamines. Animal tests at Porton revealed ring-substituted tryptamines to be highly lethal [104] and they were not considered further.

Four simple tryptamines were examined in human tests at Porton [104]. Their numbers and the chemical names by which they were referred to at the time [105] are listed below:

- T2614 (N,N-diethyl tryptamine)
- T2619 (N,N-di-isopropyl tryptamine)
- T2627 (N-benzyl tryptamine)
- T2673 (N-ethyl tryptamine)

A summary of the effects of these compounds can be compiled from citations appearing in progress reports, which suggest that the four listed above were assessed in human studies.

- All were found to be active at doses (IM or oral) of about 1 mg/kg [104]. An IM dose of 1-2 mg/kg for both T2673 and T2614 is needed to induce psychological effects in man [106].
- T2619 appears the most potent, an oral dose of 1.33 mg/kg produced "fairly severe initial vegetative symptoms (acute dizziness and vertigo)" followed by hearing distortions which persisted for 24 hours [104].
- The effects produced by all four are only marginally incapacitating and, apart from the hearing disturbances with T2619, of short duration (less than 3 hours) [104].

¹⁵ It is not the intention to explore chemical nomenclature. However, references in some Porton documents refer to tryptamines by their T numbers, others refer to them by their chemical name. Only in a few documents are both mentioned. It helps the narrative in this case to use both.

The conclusion drawn from this work was that relatively high doses¹⁶ of simple tryptamines were required to produce only minor incapacitation [104]. This conclusion, drawn in a paper summarising work on tryptamines at Porton from 1959 to 1964, ended Porton's interest in tryptamines.

Despite the citations in progress reports, it is not clear when human tests with tryptamines took place and how many volunteers took part in the tests. Information gleaned from various sources on each is summarised below. No references to T2627 have been found.

- T2614. The annual report for 1962/3 [106] mentions human studies with T2614 but neither the summary book [29] nor the experimental log [107] has any volunteers annotated as taking part in T2614 work in that period.
- T2619. The annual report for 1962/3 [106] mentions human studies with T2619 and experimental logs and the summary book [29] both cite T2619 studies during the period 14 – 28 December 1962 [107]. The summary book states that 11 volunteers took part in "T2619 trial and controls in the station hospital". No details of dose or route of administration are given.
- T2673. The annual report for 1962/3 [106] mentions human studies with T2673 and references are made to such studies in the experimental log [107] and the summary book [29]. There are differences between the entries in the last two, as shown below in Table 11.7, although the summary book records the trials commencing a week earlier (16 November 1962) with three additional volunteers.

Week beginning	Number of volunteers annotated as taking part in T2673 trials	
	Summary Book	Experimental Log
16 November 62	3	0
23 November 62	3	3
7 December 62	6	6
Total	7	9

Table 11.7 Annotations for T2673 trials in experimental records

11.5 Nutmeg

No references to human studies with nutmeg have been found in experimental records but an entry for nutmeg appears in the COSHE summary tables produced in 1963 [20]. The COSHE register of approved human experiments [35] notes that "experiments were terminated by [CO]SHE - July 1965". Whether those annotations imply that human studies were conducted is uncertain. The tables note the following about the clinical effects of the nutmeg and the comments made by COSHE [20].

"Toxic manic depressive. [Effects are] psychosis, anxiety and nausea. 30 grams had been given in man with recovery ... Animal experimentation very difficult because the main effect is psychoactive ... Animal experiments should be done to eliminate lethal elements".

The initial dose envisaged for man in the COSHE table was 5 g, and a dose of 15 g is cited in the table as the anticipated maximum. Nutmeg was to be given orally. The COSHE register records 5 g as the maximum dose, administered orally. Despite these entries it is not clear that any human studies with nutmeg were carried out; no entries have been found in the experimental records.

¹⁶ The doses here are measured in mg/kg, in contrast to the µg/kg for LSD and glycollates.

11.6 Captagon

Captagon is a psychic energiser (form of anti-depressant). Psychic energisers were discounted in 1961 [5] as "of little use as incapacitating agents". A study was carried out in 1962 to determine whether Captagon could serve in human tests as an active placebo (a substance that induced some minor changes which were well known and could therefore be used as a control) [108].

Thirty eight subjects were given an oral dose of 50 mg of Captagon, which was, at the time, a new psychic energiser [108]. The results of this human study are not recorded. No reference to Captagon is made in Porton progress reports, annual report or experimental records covering the period.

Chapter 12. Physical incapacitating agents

12.1. Selection of candidates

12.1.1. Background

There are many ways in which a chemical agent can physically incapacitate a man. A discussion paper produced in the 1960s by Porton separated them into two categories [1]:

- Disrupting vital functions of the body. These functions include [1] the cardiovascular system which regulates the circulation of blood (through heart beat, or pulse rate, and blood pressure), the respiratory system supplying oxygen to the body, the regulation of body temperature and the composition of blood (particularly the amount of acid in it). These functions are called *homeostasis mechanisms*¹⁷.
- Upsetting a necessary, but not vital, function of the body. Here the control exerted by the nervous system over muscles (neuromuscular function) might be upset. Alternatively, physical sensors, most notably the eyes, might be attacked [1].

Riot control agents which affect the eyes would fall into the second category.

12.1.2. Hypotensive drugs

Hypotensive drugs lower blood pressure. They might be tolerated by a man for a few minutes if he was lying down, but severely low blood pressure could affect the kidneys and damage the brain [1]. Animal work suggested that if blood pressure is kept too low for too long the circulation does not recover. Unless men who were given hypotensive drugs could be guaranteed to be treated immediately, hypotensive agents were deemed by Porton to be too dangerous [1].

These points were explained to the BC in 1962 [2]. Members of the BC wondered if experiments could be conducted to find out if a rapid fall in blood pressure incapacitates. Porton considered that such experiments would mean drawing blood from the body, a procedure unlikely to be acceptable [2]. CDAB was also told, in May 1962, of Porton's view that hypotensive drugs could cause irreparable damage to the kidneys and the heart [3]. At its next meeting, in October 1962 [4], CDAB members expressed concern that hypotensive drugs had been discarded. Members wondered if they should be investigated in human tests. Porton explained that the use of these drugs in any human study was regarded as "very dangerous".

12.1.3. Hypertensive drugs

Hypertensive drugs raise blood pressure. Inducing high blood pressure to a level sufficient to incapacitate a man might cause aneurysms to burst [1], which would be fatal. A small, but uncertain, percentage of the population were known to have small congenital meningeal aneurysms [1].

Exposing men to hypertensive drugs was deemed by Porton to be dangerous. The BC [5] noted in 1964 that the US regarded hypertensive drugs as potential incapacitators. Porton explained their view that the effects of the drugs were unpredictable and some permanent effects, even death, could result.

¹⁷ In simple terms these mechanisms maintain the body in a state of health and are necessary for the continuation of life.

12.1.4. Emetic drugs

Emetics induce vomiting. Porton rejected using emetics as incapacitants [6] as very little was known about the physiology of vomiting and whether violent vomiting might change blood pressure. In any case, there was doubt that vomiting could really incapacitate (the example of sea sickness was mentioned) and it was thought volunteers would be "reluctant to participate in experiments".

12.1.5. Understanding embargos

In understanding these embargos, a distinction should be drawn between **primary mode of action** and **secondary effects**. Emetics were not investigated as incapacitating agents because, while their primary mode of action was to induce bouts of vomiting, the effect on human physiology was not known. However, that embargo did not apply to agents or substances which sometimes had a secondary effect of causing men to vomit. Nerve agents sometimes induced nausea and vomiting, as did some incapacitating agents and some riot control agents (see Part V).

Similarly, the embargos placed on hypotensive and hypertensive drugs applied to those substances whose primary mode of action was to induce a change in blood pressure. Some riot control agents sometimes had a secondary effect of increasing blood pressure. Atropine, one of the treatments developed for cases of nerve agent poisoning, sometimes induced changes in blood pressure.

These embargos did not therefore mean that no substances which might have an effect on blood pressure or might induce vomiting were to be used in human tests. The approach adopted by Porton to these secondary effects was threefold:

- a. Limits were stipulated for physiological functions. Limits on temperature, pulse rate, and blood pressure were among those defined by COSHE.
- b. Medical examinations on arrival ensured that each volunteer's physiology fell within those safe limits.
- c. During studies, physiological functions likely to be affected by the study were monitored, and the study stopped if limits were approached.

Details of these limits and the action taken where they were approached are included in Annex E.

12.2. Oripavine derivatives

12.2.1. Background

On 14 February 1961, during a visit to a pharmaceutical firm, Porton received information about a new type of powerful synthetic analgesic [7] derived from oripavine. The firm had filed patents on five oripavine derivatives and gave Porton samples of them [8]. These samples were labelled as TL 2636, 2696, 2688, 2654 and 2655. They had similar effects to morphine but were 1000 to 10000 times more powerful [9].

In low doses, the oripavine derivatives produce euphoria, nausea and vomiting and lethargy [10]. Porton used the samples in work with animals [8] and observed that:

- death occurred from respiratory depression, there was some effect observed on blood pressure but "it is not pronounced"; respiratory effects could be reversed by a known antidote called nalorphine;

- the duration of effects induced varied between animal species (short-lived in small animals but lasting as long as 18 hours in larger animals);
- the minimum effective dose of TL2636 varied from 1 µg/kg in dogs to 15 µg/kg in mice;
- the lethal dose was estimated in animals and the ratio¹⁸ between the lethal dose and the effective dose was found to be 4 in rhesus monkeys, 20 in cats, 130-200 in rats, rabbits and mice and 1000 in pigs.

There are many oripavine derivatives. Four were tested in human studies at Porton: TL2636, TL2696, TL2833 and TL3046. The majority of the work was conducted with TL2636.

12.2.2. Human tests with TL2636

The main series of human tests with TL2636 was conducted in 1961 and 1962 [8]. The first exposure in man was accidental. A member of Porton staff, misled by the apparent inactivity of an oral dose in animal work, retained on his tongue after a tasting test a quantity of TL2636, later estimated as less than 3 µg/kg. Less than 30 minutes later he became disturbed and light-headed, experiencing vertigo, nausea and vomiting when he moved. He was incapacitated for several hours. He recovered after about 8 hours, following a short sleep.

Eleven pilot trials were conducted with 4 members of Porton's medical staff. Doses of 1-1.5 µg/kg were taken orally and "slightly larger" doses were inhaled [8]. One member of staff took TL 2636 five times [11]. The effects experienced were substantially similar to those observed after the accidental exposure. Human tests with oral doses of TL 2636 were then conducted with volunteers. Table 12.1 shows the doses used [8].

Oral dose (µg/kg)	Number of men
1	3
1.5	6
3	11
4	3
5.5	6
6	7
8	8
10	4

Table 12.1. Oral TL2636 human tests: 1961 to 1962

The three men given an oral dose of 1 µg/kg received two doses on separate occasions. All other men participating in oral tests received only one dose of TL2636. The human tests were split into two series. The first, using doses up to and including 4 µg/kg, sought to investigate the general symptoms induced by TL2636. The second series "in which the safety of higher doses was being assessed" [8] used the higher doses shown in Table 12.1.

Observations from the first series of oral tests [8] included the following:

- in the subjects affected the symptoms usually came on within half-an-hour and complaints were generally of muzziness or light-headedness (as after drinking "moderate" amounts of alcohol);
- a third of the subjects experienced moderate to severe nausea, most of them vomited and both of these effects were made worse by movement or activity;

¹⁸ This ratio is a measure of the safety of a compound. If the dose required to induce any effect is very close to the dose that kills, the ratio will be small.

- men recovered within 6 hours, they usually "sank into a near sleep and then woke feeling wan but otherwise all right";
- nearly half showed clinical in-coordination; reading became difficult for some of the men.

Psychomotor tests (see Annex E) were used in the first series but not in the second. It was apparent from the first series that symptoms were exacerbated by activity. Therefore all men participating in the second series lay down to rest during the tests [8]. The 13 men receiving oral doses of 5.5 µg/kg and 6 µg/kg all experienced severe nausea and incoordination. Symptoms lasted for 12 hours or longer. No changes were seen in the ECG and blood pressure of these men but their temperature (taken orally) fell. Given that changes in body temperature had not been observed in animals receiving up to 5 µg/kg, it was considered that the fall in body temperature was a consequence of the men experiencing nausea and vomiting.

One of the men receiving a dose of 10 µg/kg suffered prolonged nausea and dizziness and did not recover until 30-36 hours after taking the dose. His blood pressure fell to 85/50 mm Hg two hours after receiving the dose and his systolic pressure remained below 100 mm Hg for 5.5 hours. The man was examined 4 months later and found to be completely fit and well (he apparently volunteered for further trials) [8]. Accounts of this man's experience differed slightly.

- "This man's cardiovascular condition would have given cause for concern had the depression [of the blood pressure] continued. However, no treatment was thought necessary and he made a complete and spontaneous recovery" cites the Porton report of the TL2636 tests published in January 1963 [8].
- One man was "not himself after 36 hours"; evidently he decided not to vomit for 15 hours and "this may have been his undoing", the depression of the blood pressure "did give some cause for concern" reads the minutes of the BC meeting held in November 1962 [11].

Human tests with this and higher oral doses of TL2636 were stopped after this man's experience [12]. Other human tests were conducted with TL2636 by IV injection and inhalation.

IV tests. Twenty seven men received IV doses of TL2636 of 0.1-0.3 µg/kg, 22 of them receiving a dose of 0.25 µg/kg or 0.3 µg/kg [8]. All of the men were affected but individual reactions varied. Some subjects given the lowest dose experienced "severe discomfort". A third of the 22 men given the higher doses showed noticeable but transient falls in pulse rate and one man showed a short-lived drop of 30 mm Hg in his systolic blood pressure. It was concluded that 0.3 µg/kg by IV injection had "slightly less effect" than 3 µg/kg given orally [8].

Inhalation tests. Work had been carried out in 1959 outside Porton using cigarettes for inhalation trials which were found to be more convenient than aerosols. The method involved injecting TL2636 into a normal cigarette which the subject then smoked. Reports indicate that Porton calculated that 3-4 mg (per man) could probably be safely given through the cigarette method. Interestingly this calculation¹⁹ was based on an assumption that 10 µg/kg was suggested by oral experiments as "safe by that route" [8]. The inhalation tests were split into two parts:

¹⁹ No Porton document has been found which explains the method of the calculation explicitly, although the following assumption is possible. The report introducing the cigarette inhalation method [8] notes that, in cigarette inhalation work conducted outside Porton, about 20% of the drug injected into a cigarette generally appears in smoke and nearly all of that is retained by the smoker. Porton's assumption that 10 µg/kg was safe (although this was an oral dose) translates into a total dose of 700 µg (or 0.7 mg) for a man of average weight (70 kg). If only a fifth of the drug injected into a cigarette was inhaled, 3.5 mg (5 times 0.7 mg) could be injected in the cigarette and the smoker would be expected to inhale a total dose of 700 µg.

- Preliminary trials, where the dose injected into the cigarette varied between 1 mg and 2.5 mg. 35 men participated in these trials. Individual variation was considerable with some men experiencing "fairly severe discomfort" from the lowest dose.
- A formal trial in which 4 men each received a cigarette dosed with 3 mg and 9 men each smoked a cigarette dosed with 4 mg. All subjects experienced severe dizziness and had difficulty reading. If they attempted to concentrate their feelings of nausea worsened and they usually vomited. Five of the 9 men smoking a cigarette with 4 mg vomited repeatedly during the trial.

The conclusions drawn from these human tests with TL2636 during 1961 and 1962 were that [8]:

- TL2636 incapacitates in low doses, as little as 1 µg/kg orally: the estimated effective oral dose is 4 µg/kg;
- TL2636 seems to be more effective when inhaled than when ingested: it is estimated to be 8 times more effective inhaled than oral;
- no mental effects were observed;
- the safety margin of TL2636 (the ratio of lethal to incapacitating dose) may be as low as 5 and it would be unwise to assume it is higher than 10 in man.

TL2636 was discussed at the CDAB meeting held in February 1964 [13], a month after the report containing these conclusions was produced. TL2636 was produced by using natural substances of rather limited supply. This, combined with the low safety ratio of lethal to incapacitating dose, suggested TL2636 was of doubtful value as an incapacitating agent [13].

Another series of human tests with TL2636 was carried out in 1967 and 1968 [14, 15, and 16]. The motivation for this series was to find out if the effective incapacitating dose of TL2636 was reduced by activity and exercise [10]. The earlier work, in 1961 and 1962, had suggested the effects of TL2636 were exacerbated by activity. If this were true, a much lower dose than the 4 µg/kg estimated in 1963 might be enough to incapacitate²⁰. Then, the safety margin would be increased.

The human tests conducted in 1967 and 1968 involved 20 volunteers taking oral doses of TL2636. The posture of the men was changed (for example, they were asked to stand up from a lying position) and the men were asked to exercise by stepping up onto and down from an 18" high stool thirty times in one minute. Various physiological features (including blood pressure and pulse) were monitored. No man was asked to exercise if he felt too ill [10]. The oral doses used and the effects are summarised below [10]:

- 2 µg/kg. Six men received this dose. Five were affected by euphoria and dizziness which was most marked when the men stood up. The euphoria passed off quickly and was replaced by nausea. Exercise seemed to have little effect.
- 3 µg/kg (four men) and 4 µg/kg (ten men). Symptoms were similar to those at 2 µg/kg, but vomiting was more common (three men vomited repeatedly) and dizziness was accompanied in some cases by faintness. Unsteadiness was characteristic and exaggerated by changes in posture and exercise.
- Measurements of pulse and blood pressure confirmed a depression of the cardiovascular system which generally reached a maximum 90-120 minutes after

²⁰ In reality, few soldiers on a battlefield under attack by an enemy could be expected to be resting in a horizontal position.

the dose was taken. Falls in systolic blood pressure were usually less than 10 mm Hg.

The conclusion drawn from these tests was that exercise did not produce any additional symptoms, but sometimes exaggerated the symptoms that were present. Exercise had no effect on those men with only mild symptoms. It was decided to test these conclusions during a field exercise, in which men would be undertaking their normal operational duties.

The opportunity offered by the LSD trial "Small Change", held in January 1968, was taken. This trial, explained in the previous chapter, took place over 4 days, with LSD being used on Day 4. On Day 3 seven men were given oral doses of 150 μg ²¹ of TL2636. These seven men were chosen because they had been excluded by psychiatric screening tests from receiving a dose of LSD [17]. None of the seven men were told that they were given TL2636. Like the other men taking part in Small Change they were before the trial 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" [17]. The report of this adjunct to the LSD trial refers to TL2636 as an "active placebo" [17].

One of the seven men was severely affected and had to be removed from the trial. He became nauseous and dizzy about an hour after taking TL2636, suffered from blurred vision and felt that his feet and eyelids were heavy. He could not raise his rifle to a firing position. He was taken by ambulance to the Porton hospital, vomited twice, fell asleep and woke up an hour later completely recovered.

A military umpire was used in Small Change to assess the military effectiveness of the men. He assessed that men who were conducting simulated anti-terrorist sweeps performed only about half as efficiently, when under the influence of the TL2636 dose, than when they were drug-free. Men working in the simulated headquarters performed only marginally less well after a dose of TL 2636.

These tests in 1967 and 1968 marked the end of work with TL2636. It was evident that exercise did not have a serious influence on the effect of TL2636 and therefore there was no reason to change the conclusions drawn from the 1961 and 1962 work [10]. Indeed, in the field trial the effects of TL2636 were less marked than were observed with the same doses in the laboratory. Clearly, men (with the exception of one) were able to resist the effects and complete their duties. A dose of TL2636 sufficiently large to guarantee certain incapacitation in the field would carry an "unacceptably high risk of fatal outcome" [10].

12.2.3. Human tests with TL2696

Some pilot tests with TL2696 were conducted in 1961. The pilot trial included insufficient tests to justify any report by the end of 1962 and apparently showed TL2696 to have the same general effects as TL2636. The number of volunteers who took part in TL2696 studies is a little unclear.

- A Porton progress note explains that "half a dozen subjects had been given" TL2696 by June 1962 [18].
- Four volunteers are annotated in one of the experimental logs [19] to have participated in a TL2696 trial in mid-November 1961.
- The COSHE meeting held in February 1965 [12] discussed TL2696 exposures. Two men had received a dose of 0.25 $\mu\text{g}/\text{kg}$ administered by IV injection and they developed mild dizziness and nausea for around 5 hours. Three other men took an oral dose of 2 $\mu\text{g}/\text{kg}$. Two of them suffered only a little nausea and "fuzziness" for about 30 minutes. One man experienced no symptoms at all.

²¹ For a man of an average weight of 70 kg, this dose represents a little over 2 $\mu\text{g}/\text{kg}$. Based on the actual weight of the seven men who participated, the actual dose was "no more than 3 $\mu\text{g}/\text{kg}$ " [10].

- In the COSHE summary tables produced in September 1965 [20], which tabulate symptoms, effects and time to onset, and approximate effective dose, a sparse entry for TL2696 refers to "2 human cases".

From these conflicting data, it would seem most likely that five volunteers took part in TL2696 studies, as outlined by the COSHE meeting, and that the studies were carried out in the winter of 1961. The experimental logs cite only four volunteers taking part in TL2696 studies in the week beginning 4th November, but the surrounding weeks have one or two volunteers against whose name appears the annotation "trials in the station hospital". Possibly one of these was the fifth man.

12.2.4 Human tests with TL2833

TL2833 is a short-acting oripavine derivative, similar in action to TL2636 [21]. The nature and progress of human studies is unclear. Preliminary studies had "just begun" in September 1963 and the results from them suggested TL2833 had a "rapid knock down" action when administered subcutaneously, but was not active orally [21]. It is not clear if these preliminary studies involved men. The "knock down" action of TL2833 and its impotence when ingested could have been discovered through animal work.

Entries in experimental logs show the earliest date that volunteers participated in human tests with TL2833 as August 1963 [22], so these preliminary studies may have involved volunteers. References in experimental records [22] to volunteers taking part in TL2833 trials are summarised in Table 12. 2.

Week beginning	TL2833 trials	
	No. of volunteers	Comment
30 Aug 63	6	TL2833 and TL3046 trial
2 Nov 63	5	TL2833 and TL2636 trial
17 Jan 64	6	TL2833/morphine crossover
7 Mar 64	4	TL2833/LAE/morphine crossover
18 Apr 64	4	TL2833/morphine crossover
25 Apr 64	2	TL2833/morphine crossover
2 May 64	4	TL2833/morphine crossover
Total	29	The two men from 25 Apr appear again in the five for the 2 May.

Table 12.2 Annotations for TL2833 trials in experimental records

Details of the doses used have not been found in the experimental records, but references to doses have been found elsewhere:

- The COSHE summary tables produced in December 1963 [23] list the doses and route of administration for incapacitating agents. Whether the doses listed had been used or were anticipated is not clear. Against the TL2833 entry four doses are listed: 250 µg oral, 60 µg and 100 µg subcutaneously, and 300 µg inhalation. The maximum human dose is cited as 300 µg inhalation, and the "starting point" (this might be the initial dose) as 100 µg subcutaneously.
- The COSHE register of approved human experiments [24] notes that "100 µg [of TL2833] has been given" and cites subcutaneous and IV routes of administration.
- The future programme for TL2833 which appears in the COSHE summary tables notes "subcutaneous administration on cross-over trial with 10 mg of morphine to compare emetic effect". [23] So perhaps the TL2833/morphine trials listed in Table 12.2 featured 100 µg of TL2833 subcutaneously and 10 mg of morphine.

Certainly some of the tests involved TL2833 being injected subcutaneously, as the experiences of one of the subjects was reviewed by the COSHE in February 1965. This man,

injected subcutaneously with 100 µg of TL2833 in March 1964 became catatonic for two to three minutes [12, 25]. The reaction was terminated by the administration of nalorphine [25]. The COSHE meeting in February 1965 which reviewed this case noted that experiments with TL2833 were stopped after this incident [12], although the experimental records indicate that volunteers participated in trials after March 1964 (see Table 12.2).

Some volunteers had received the same dose of TL2833 by IV injection. The records of two volunteers receiving this dose were reviewed in 1965 [12]: the data suggested that their cardiovascular system had been depressed by the 100 µg dose of TL2833 and may have persisted in that depressed state for 3-4 days. One volunteer who had taken part in a TL2833/morphine trial had had a systolic blood pressure of 80-90 mm Hg for 6-8 hours [12].

It would seem, therefore, that the COSHE register is accurate in recording 100 µg doses of TL2833 having been given subcutaneously and by IV. In February 1965, after reviewing the cases outlined above, COSHE decided that no further tests should be carried out with TL2833 because of the danger of possible cerebral hypoxia (a deficiency of oxygen to the brain) due to the reductions in blood pressure. TL2833 does not appear in any document seen by the survey after this date.

12.2.5 Human tests with TL3046

TL3046 is a short-acting oripavine derivative. It was reported in the open literature to be an emetic in man but this was not confirmed by trials conducted in the Toxicology Section before September 1963 [21]. Preliminary human trials with TL3046 had been started by September 1963 and suggested that the derivative was no more active than TL2636 [21].

Experimental logs [22] note TL3046 being used in human tests with volunteers on two occasions: a joint trial with TL2833 (shown in Table 12.2) in August 1963 with six volunteers, and a joint trial with TL2636 in October 1963 with five volunteers.

No details of the doses of TL3046 used in these tests have been found. There are no entries in the December 1963 COSHE summary tables or the COSHE register. The COSHE summary tables produced in September 1965 have an entry for TL3046 but merely state, in the column labelled Symptoms and Signs: "Dizziness. No other effects observed" [20]. Perhaps this means that the human studies in 1963 quickly revealed that TL3046 induced few effects and it was then discarded.

12.3. Pyrexal

Pyrexal induces the signs and symptoms usually associated with fever: headache, shivering, sweating, and aching of limbs and the back. Reports of its being used in the UK, either as therapy or in scientific investigations, appeared from 1956 onwards [26]. These reports suggested that an IV dose of less than 1µg induced feverish symptoms in man. Some reports indicated pyrexal was effective when inhaled.

Further, human tests with pyrexal were conducted at Porton in 1959 and 1960 [19, 27, 28, 29, 30]. Details of the doses used are given in Table 12.3 [26].

Dose (μg)	Route	Number of men
0.3	IV	26
0.3	IV	20
0.5	IV	20
0.3	IV	5
0.5	IV	10
0.02	nasal spray	5
0.062	nasal spray	5
0.2	nasal spray	5
0.4	nasal spray	10
0.6	nasal spray	5
0.8	nasal spray	4

Note: the 26 men receiving the dose of 0.3 μg were not asked to perform any tasks while under the influence. The other men receiving an IV dose sorted cards or picked up balls with tweezers.

Table 12.3. Pyrexal doses in human tests: 1959 to 1960

No symptoms or changes to blood pressure and body temperature were observed during the tests with the nasal spray. With the IV tests, headaches were the predominant symptom (normally starting an hour after injection, getting worse for the next 40 minutes). Recovery was usually complete after 5 hours. Thirty six of the 51 men given 0.3 μg said they would have reported sick but 22 of the 36 believed they could have carried on working, albeit less efficiently than normal. Twenty one of the 30 men given 0.5 μg would have reported sick; only 5 of the 21 thought they could have carried on working. Temperature and blood pressure were "both elevated considerably", more so with the higher dose. Body temperature remained above 100°F on average for 4 hours, returning to normal after an average of 9 hours [26].

Porton staff discussed pyrexal with professors and doctors at Oxford in 1960 and 1961 [31, 32] towards the end of the human tests at Porton and afterwards. Work with pyrexal at Oxford had induced body temperatures as high as 108°F, although with doses a little higher than those used at Porton [32]. The highest body temperatures observed during the Porton tests had been 102.6°F with the 0.3 μg dose and 104°F with the 0.5 μg dose. The Oxford studies further reported that pyrexal set up an immune reaction to itself very quickly. If a man did not receive a sufficient dose to affect him, subsequent doses needed to be very large to induce an effect.

The conclusion drawn by Porton in 1961 [26, 33] was that pyrexal only harassed, with the main effect being a headache which, while severe, was not enough to prevent tasks being completed. Moreover, the effects induced by pyrexal were transient. No more work with pyrexal was conducted at Porton.

12.4. Tremoram

Interest in tremoram as a possible incapacitating agent was provoked by an external paper published in 1956 [34]. Tremoram is obtained by incubating tremorine with a substance from the liver. Tremoram had been produced in this way by external workers in 1961 [35] and tested on animals. IV injections of tremoram produced muscle tremors, muscular weakness and general incapacitation in a number of species [35].

Work was conducted at Porton in 1962 with animals having tremoram (referred to as T2785) administered by parenteral injection [36]. The lowest effective dose was around 30 $\mu\text{g}/\text{kg}$. Marked tremor was usually present but at lower doses tremoram almost always induced profuse salivation and diarrhoea. From this work the signs of tremoram poisoning in man were expected to be salivation, diarrhoea and possibly Parkinson-like tremor [36]. Human tests with tremoram were conducted at Porton, but the details are obscure. Relevant citations are listed below:

- The COSHE summary table produced in December 1963 [23] noted that "one exposure, in man" had been completed. That is in accord with discussions at the Chemistry Committee meeting of December 1963 [37] of "a recent IV administration to a human of 30 µg (approximately 0.5 µg/kg) of tremoram" and "as predicted there was a marked fall in blood pressure, a slight incoordination of finger movements and, after 40 minutes, complete recovery".
- Members of the Chemistry Committee thought that the hypotensive effect made tremoram "useless" as an incapacitating agent [37]. This view is mirrored by an entry in the COSHE summary table of December 1963 which records "the slow rate [of] IV needed to prevent hypotension makes this route impracticable... No IV work should be done on volunteers. The oral/inhalation route should be tried" [23].

From the second citation it might be inferred that the person exposed to tremoram by IV in December 1963 was not a service volunteer but probably a member of Porton staff. Subsequent references to human tests with tremoram found by the survey are as follows.

- At the CDAB meeting of February 1964 it was reported that testing with humans had "just started" [13].
- COSHE, at its meeting in June 1964, records that a member of the medical staff had conducted a self-experiment with tremoram. No details of the dose are recorded but the effects induced were not as expected from animal work [38].

Both of these may refer to the IV exposure carried out in December 1963. No other references to tremoram occur in later documents, or in the COSHE register of approved human experiments. No mention of it (or T2785) has been found in experimental logs. From the information available, it appears that tremoram studies (in which there may have been only one exposure) involved only members of Porton staff.

12.5 Aldactone

One reference has been found to human tests with Aldactone [30]. Aldactone, a synthetic steroid with a proprietary name of "Spirolactone" used to treat certain cases of hypertension, was thought to have the potential to interfere with a man's ability to tolerate heat, thus inducing heat exhaustion or cramps [30].

In 1960/61 four men exercised daily for 90 mins in a temperature of 93°F for two weeks. They acclimatised normally. On the 8th day they were given 200 mg of Aldactone by mouth at 2130 and on the following morning at 0830 another 100 mg. No obvious decrement in performance was observed but the loss of electrolytes in sweat increased [30]. It was intended to conduct studies with longer exposures and harder work [30], but no further references to Aldactone have been found by the survey.

Chapter 13. Suspension of human tests

On February 2nd 1965 COSHE discussions turned to the advisability of giving volunteers the doses necessary to induce full incapacitation [1]. It was at this meeting that COSHE reviewed the instance of cardiovascular depression induced by T2636, the catatonic episode produced by T2833 and the cases of toxic delirium in the BZ tests. Various points followed the review of these cases [1]:

- While the body might be able to take a 5% fall in function in organs like the liver and kidney, the possibility of a permanent fall-off in brain function was an unacceptable risk.
- Cases of toxic delirium lasting 2-3 days might produce irreversible changes in cortical function and personality. It was impossible to say what influence on future actions even subconscious memories of delirium would have. In the case of LSD the depersonalisation "which is such a frightening feature of the effects of the drug" clearly might affect a man's adjustment to himself and to his environment.
- There was a real danger of permanent damage resulting from cerebral hypoxia (lack of oxygen to the brain) after drugs which produced a marked depression of the cardiovascular system.

The head of the Medical Division at Porton thought that while incapacitating agents were reputed to be safe there appeared to be "strong reasons" for doubting this. If tests were dangerous, even if the effects appeared to be innocuous, it was considered unethical and unjustified to conduct human tests with these agents in peacetime [1]. COSHE agreed that very serious consideration be given as to whether any more work with these agents should be conducted on man.

Evidently members of the Medical Division shared concerns about certain aspects of the incapacitating programme [2]. One member, who played an important part in the programme, fell sick in January 1965 and was admitted to hospital suffering from depression. His assistant was "very near breaking point" by mid-February 1965 [3] and resigned a few days later [4]. Two other members had resigned in November 1964 and December 1964.

Soon after the COSHE meeting in February 1965, the head of the Medical Division discussed the situation with an expert of Maudsley Hospital, who had originally advised on setting up the psychiatric and psychological screening tests. After this discussion, the head of the Medical Division on the 12th February banned all further tests with hallucinogenic drugs [5]. He wrote to the Edinburgh Medical School and asked "is there any justification whatsoever for putting a healthy man in even remote danger of permanent damage either to body or mind?" [3]. In March the ban was extended to oripavine derivatives [6].

The Director of Porton was concerned with this "question of medical conscience". His view was that the ban had caused considerable embarrassment to senior officials in London [7]. The Director convened a meeting of medically qualified members of the most senior defence scientific committee, so that the head of the Medical Division could [8]:

- tell medical colleagues about some of the problems besetting Porton in the testing of incapacitating agents, both physical and mental, on man;
- to define the level of incapacitation that may be ethically induced in volunteers;
- to be assured that the incapacitating agent programme would not go beyond what "our medical colleagues outside Porton would consider justifiable".

The meeting of senior medical men, with the head of Porton's Medical Division, was held at University College Hospital in August 1965 [9]. Most of the discussion centred on the

question of the extent to which Porton medical officers were justified in "deliberately dosing healthy men with drugs specifically designed to induce some malfunction, either physiological or psychological?" The medical men were content that this could be done ethically if Porton were seeking to develop therapies against the agents which enemies might use against the Armed Services. At this point the head of Porton's Medical Division intervened, as recorded in his notes of the meeting:

"I had therefore to disclose after warning those present that this was a highly secret matter that we were in fact looking for an agent which we could use under certain circumstances" [9].

This admission "changed the complexion very considerably" [9] and it was thought that Porton were being asked to do things that "went far beyond the Medical Research Council rules for human experiments" [9]. On the other hand the medical experts debated whether such work might be covered by Nuremberg rules governing experiments for the "good of society" [9].

Evidently the debate reassured the head of the Medical Division at Porton that the work of Porton was acceptable to medical colleagues outside Porton [10]. The meeting went on to discuss the formation of the ABC which should serve as a "Father Confessor" for Porton staff and "damn the proposals [for experiments] of those who were trying to go too far and too fast" [9].

After the meeting the impetus to set up the ABC was continued. It was acknowledged that some of the newer incapacitants work went "very far into the realms of the unknown" when it came to assessing the safety of experiments. The ABC should be set up to guide and support the Medical Division at Porton [10]. The proposal was put to the Army Board in October 1965 [11], which generated the terms of reference for the ABC in November [12].

The meeting with external medical colleagues and the decision to set up the ABC seem to have reassured Porton that the work on incapacitating agents was ethically acceptable and so work on the incapacitating agent programme restarted, although the consequences of losing staff from the Medical Division were felt. In total, three members had left and the member admitted to hospital for depression recovered but did not rejoin the Porton staff [2]. One practical consequence of losing such expertise was the decision to use only a reduced dose of LSD in Recount.

References

Chapter 11

1. WO195/14166. Conclusions and recommendations of 12th Tripartite Conference - Medical. AC14171 BioC 294 Ptn/IT4205/4477/57 22 Oct 57.
2. WO195/15925. CDAB 57th meeting 8 Oct 64.
3. WO189/1078. Porton Technical Paper 765. Biological Testing of Incapacitating agents Part I Review of existing testing methods. 9 Jan 61.
4. WO189/1079. Porton Technical Paper 766. Biological Testing of Incapacitating agents Part II Results of tests using drugs with known effects on man. 12 Jan 61.
5. WO189/1104. Porton Technical Paper 793. Biological Testing of Incapacitating agents Part III Results of screening tests on new compounds. 31 Aug 61.
6. WO195/14757. CDAB 41st meeting 4 Jun 59.
7. **Med/IL 1040/860/60 21 Apr 60 ADM to D Army Psychiatry, War Office. [U]**
8. **Consultation Report. Psychotomimetic tests. Ptn/TG1009/5244/61 11 Oct 61 TG1009. Policy regarding tests on human subjects. [U]**
9. WO195/15077. BC 25th meeting 9 Nov 60.
10. **Incapacitating Agents. Med/TG1009 & IT4204/1715-7/61. 15 Aug 61 TG1009. Policy regarding tests on human subjects. [U]**
11. **Consultation Report. Psychological Incapacitants TG1009 3 Nov 61 TG1009. Policy regarding tests on human subjects. [U]**
12. **Yearly report by Senior RAMC officer to Under Sec of State July 61-Jun 62. Med./IL 1040/1563/62 16 Jul 62. [S]**
13. WO195/15391. CDAB 50th meeting. 24 May 62.
14. WO195/16136. PN119A. The Service Volunteer Observer Scheme from 1959 to 1965. 28 Oct 65.
15. WO195/16686. Statement on Volunteer Observer Scheme at the CDEE. PTA/40/02/2399/68 7 May 68. For BC 13 Jun 68.
16. WO195/15154. BC 26th meeting 24 Feb 61.
17. WO195/16371. ABC 3rd meeting 7 Oct 66.
18. WO195/16462. ABC 4th meeting 26 Apr 67.
19. WO195/16161. ABC 1st meeting 24 Nov 65.
20. **COSHE Summary Tables: Poisoning due to incapacitating compounds, symptoms, signs and therapy. 4 Dec 63. [R]**
21. **LSD Enzyme panel of CDAB. AC12247 27 Mar 53. [U]**
22. **COSHE 24th meeting 10 Jun 66.**
23. **Ladell's 1966 report.**
24. **Programme of research into LSD 25. Ptn/TA2800/420/56 27 Jan 56. [R]**
25. **Abreactive Drugs. Extract from minutes of DRPC 27 Mar 56 [DRP/M(56)5]. HQ/TA3500/8987 22 May 56. [U]**
26. **Summary of work on LSD at Porton in the last five years. Med/TA2100/835/66 29 Mar 66. [R]**
27. **Psychochemical agents OAD/TA2800/257/58 14 Apr 58. [U]**
28. **Summary of work on LSD at Porton in the last five years. Med/TA2100/835/66 29 Mar 66. [R]**
29. **Experimental records MPG 47: Summary book 31 Aug 59 - 31 Dec 84.**
30. **COSHE 4th meeting 18 Mar 64. [C]**
31. WO195/16154. CDAB 60th 8 Oct 65.
32. **COSHE 22nd meeting 17 Mar 66. [C]**
33. WO195/16273. ABC 2nd meeting 20 Apr 66.
34. WO195/14637. Chemistry Committee 32nd meeting 5 Mar 59.
35. **COSHE Register of Approved Human Experiments. Med IT4010/550/76 Jan 76. [R]**
36. **Progress Report on laboratory experiments with T3456 (LSD). Ptn/TA2100/6229/67 14 Sep 67. [R]**
37. **Progress report on lab experiments with T3456. Ptn/TA2100/2437/68 13 Jun 68. [U]**
38. WO195/16579. ABC 5th meeting 19 Oct 67.
39. **Technical Note 5. The determination of T3456 (LSD) in human plasma following oral administration. 1 May 69. [U]**
40. **COSHE 25th meeting 8 Jul 66. [C]**
41. **Experimental Log MPG 64 12 Oct 64 - 15 Oct 65.**
42. **Porton Annual Report 1 July 1963 to 30 June 1964. [S]**
43. WO189/444. Porton Technical Paper 936. A field experiment using LSD 25 on trained troops. 24 Aug 65.
44. **COSHE 11th meeting 9 Dec 64. [C]**
45. **COSHE 17th meeting 24 Sep 65. [C]**
46. WO189/482. Porton Technical Paper 979. "Recount" a second field experiment to assess the effects of T3456 (LSD) on trained troops. 18 Sep 67.
47. **COSHE 26th meeting 12 Aug 66. [C]**
48. **COSHE Proceedings: dose to be used in Recount. Med/IT4010/2062/66 15 Aug 66. [C]**
49. **COSHE 27th meeting 17 Aug 66. [C]**
50. **COSHE 35th meeting 3 Jul 67. [C]**
51. **COSHE 37th meeting 13 Sep 67. [C]**
52. **Technical Paper 3. The effects on military efficiency of dosing half an infantry platoon with T3456. Jan 69. [C]**
53. WO195/16743. ABC 6th meeting 13 Jun 68.
54. **COSHE 41st meeting 14 Feb 68. [C]**
55. **CDAB 69th meeting. 10 Jan 69 CDAB Proceedings 1968 onwards. [S]**
56. WO195/16855. ABC 7th meeting 4 Dec 68.

57. ABC meeting 24 Sep 69 (CDAB 418/69.) [C]
58. WO195/16887. Joint meeting of ABC and BC 4 Dec 68. Seminar on "Behavioural Studies".
59. ABC meeting 25 Mar 71 CDAB 14/71. [C]
60. ABC meeting 14 July 71. CDAB 25/71. [C]
61. Early exploratory work with BZ in the UK. Ptn/TA2501/1503/67 10 Mar 67. [R]
62. The behavioural effects of drugs on man as illustrated by the glycollates. Ptn/TA2700/5930/68 dated 6 Nov 68. [R]
63. Present knowledge on EA2277 (BZ). Ptn/TA3700/5487/61 7 Nov 61. [R]
64. WO195/15477. BC 31st meeting 15 Nov 62.
65. COSHE 12th meeting 2 Feb 65. [C]
66. MC Proceedings. A follow-up of volunteers after exposure to BZ. Med C 5/79. [R]
67. Preliminary report on human laboratory tests of BZ. Ptn/TG3003/6220/67 11 Sep 67. [R]
68. COSHE Special Meeting 12 Jun 67. [C]
69. MC meeting 12 Oct 79. [R]
70. COSHE 39th meeting 29 Nov 67. [C]
71. Progress on human studies of the pharmacological action of glycollates. Ptn/TG3003/2439/68. [R]
72. COSHE 42nd meeting 27 Mar 68. [C]
73. Progress on Human studies of the glycollates T3436. Ptn/TA2700/6073/68 20 Nov 68. [R]
74. COSHE 44th meeting 23 May 68. [C]
75. COSHE 43rd meeting 22 Apr 68. [C]
76. COSHE 45th meeting 17 Jun 68. [C]
77. COSHE 48th meeting 19 Sep 68. [C]
78. Progress report on human studies with T3436. Ptn/TA2700/4803/69 21 Aug 69. [R]
79. COSHE 49th meeting 22 Oct 68. [C]
80. COSHE 56th meeting 13 May 69. [C]
81. COSHE 58th meeting 8 Jul 69. [C]
82. Overview of research carried out on glycollates and related compounds at CBD Porton Down. DERA/CBD/CR990418 Sep 99.
83. Current position on clinical pharmacology of glycollates. Ptn/IT 4208/5225/70 28 Aug 70. [R]
84. COSHE 62nd meeting 4 Feb 70. [C]
85. COSHE 63rd meeting 12 May 70. [C]
86. T3436 Current Position Report Med.B/IT4208/409/71. [C]
87. ABC meeting 17 Sep 70 CDAB 19/70. [C]
88. COSHE 74th meeting 4 Oct 71. [C]
89. COSHE 77th meeting 20 Dec 71. [C]
90. COSHE Proceedings. T3436 Summary of effects produced by nominal effect of 6 mug/kg by inhalation. Med/TA2501/1166/72. 20 Mar 72. [C]
91. COSHE 79th meeting 24 Apr 72. [C]
92. COSHE 80th meeting 31 May 72. [C]
93. COSHE 81st meeting 17 Jul 72. [C]
94. COSHE 76th meeting 1 Nov 71. [C]
95. Experimental log MPG 68.
96. Experimental Log MPG 73.
97. Experimental Log MPG 69.
98. Experimental Log MPG 70.
99. Experimental Log MPG 71.
100. Porton research and development report for 1973-4 and programme for 1974-5. [S]
101. Porton research and development report for 1974-5 and programme for 1975-6. [S]
102. Porton research and development report for 1975-6 and programme for 1976-7. [S]
103. Porton research and development report for 1976-7 and programme for 1977-8. [S]
104. WO195/15933 Synthesis and pharmacological activity of indole derivatives - a review of investigations at CDEE Porton 1959-1964. (for Chemistry Committee meeting 18 Feb 65).
105. WO189/344. Porton Technical Paper 822. Synthesis and biological testing of a series of tryptamine derivatives. Aug 62.
106. Porton Annual Report 1962/63. [S]
107. Experimental Log MPG 63 26 Oct 59 - 1 Feb 63.
108. Human testing of behaviour affecting drugs. Ptn/TA2800/3112/62 13 Jun 62. [U]

Chapter 12

1. **Military criteria for incapacitation - UK paper for Quadripartite working group Jun 65. [R]**
2. WO195/15402. BC 30th meeting 27 Jun 62.
3. WO195/15391. CDAB 50th meeting. 24 May 62.
4. WO195/15461. CDAB 51st meeting. 4 Oct 62.
5. WO195/15900. BC 34th meeting. 23 Jul 64.
6. **COSHE 98th meeting 17 Feb 75. [C]**
7. WO195/15498. Chemistry Committee 43rd meeting. 22 Nov 62.
8. WO189/357. Porton Technical Paper 835. An Oripavine derivative (TL2636) as a potential incapacitating agent. 9 Jan 63.
9. WO195/16154. CDAB 60th 8 Oct 65.
10. **Technical Paper 68. The effects of small oral doses of an oripavine derivative on human subjects under both laboratory and field conditions. Feb 72. [C]**
11. WO195/15477. BC 31st meeting 15 Nov 62.
12. **COSHE 12th meeting 2 Feb 65. [C]**
13. WO195/15794. CDAB 55th meeting 13 Feb 64.
14. **Experimental Log MPG 66. 19 Jun 67 - 22 Dec 67.**
15. **Experimental Log MPG 67. Jan 68 - Dec 69.**
16. **Porton Annual Report 1967/68. [S]**
17. **Technical Paper 3. The effects on military efficiency of dosing half an infantry platoon with T3456. Jan 69. [C]**
18. **Human Testing of behaviour affecting drugs. Ptn/TA2800/3112/62 13 Jun 62. [C]**
19. **Experimental Log MPG 63 26 Oct 59 - 1 Feb 63.**
20. **COSHE Summary Tables Med/IT4010/2338/65 20 Sep 65. [R]**
21. WO195/15697. BC 33rd meeting 26 Sep 63.
22. **Experimental records MPG 47: Summary book 31 Aug 59 - 31 Dec 84.**
23. **COSHE Summary Tables: Poisoning due to incapacitating compounds, symptoms, signs and therapy 4 Dec 63. [R]**
24. **COSHE Register of approved human experiments Med/IT4010/550/76 Jan 76. [R]**
25. **COSHE 6th meeting (undated - Summer 1964). [C]**
26. WO189/363. Porton Technical Paper 841. Effects of Pyrexal on man Feb 1963.
27. **Experimental Log MPG 62. 9 Jan 56 - 19 Oct 59.**
28. **Porton Progress Report No. 33. Jan - Jun 59. [S]**
29. **Porton Progress Report No. 35. Jan - Jun 60. [S]**
30. **Porton Annual Report 1960/61. [S]**
31. **Incapacitation. Med/TA 3501/1952/60 9 Sep 60. [U]**
32. **Discussions on Pyrexal. Med/TA3501/579/61 10 Mar 61. [U]**
33. WO195/15217. BC 27th meeting 18 Jul 61.
34. WO195/15687. Porton Technical Paper 871. Pharmacological studies of tremorine, tremoram and related compounds. 1964.
35. WO195/15901. Metabolism of tremorine by mouse liver. Ptn/TA2501/5678/64. 19 Oct 64.
36. **Tremoran (T2785) Med/IL 1026/2075/62 3 Oct 62. [U]**
37. WO195/15735. Chemistry Committee 47th meeting. 10 Dec 63.
38. **COSHE 7th meeting 15 Jun 64. [C]**

Chapter 13

1. **COSHE 12th meeting 2 Feb 65. [C]**
2. **Director, Porton to Chairman of SAC 3 Mar 65. TG1009 Policy regarding tests on human subjects. [U]**
3. **Head of Medical Division to University of Edinburgh Medical School 8 & 12 Feb 65. TG1009 Policy regarding tests on human subjects. [U]**
4. **Deputy Chief Scientist (Army) to University of Edinburgh Medical School 17 Feb 65 NZ/33/2/65. TG1009 Policy regarding tests on human subjects. [U]**
5. **COSHE Proceedings. Med/IT 4010/387/65 dated 12 Feb 65. [C]**
6. **COSHE 13th meeting 19 Mar 65. [C]**
7. **Head of Medical Division to Director Porton and Deputy Chief Scientist (Army) 17 Feb 65. TG1009 Policy regarding tests on human subjects. [U]**
8. **Head of Medical Division to Director Porton. Med/TG1009/457/65 19 Feb 65. TG1009 Policy regarding tests on human subjects. [U]**
9. **COSHE Proceedings. Ad Hoc meeting on Human Experiments. Head of Medical Division to Director 11 Aug 65. [R]**
10. **SAC chairman to Chief Scientist (Army) JMB/GH/1178/65 dated 10 Aug 65. TG1009 Policy regarding tests on human subjects. [U]**
11. **Director Porton to Chief Scientist (Army) Ptn/TG1009/5725/65 25 Oct 65. TG1009 Policy regarding tests on human subjects. [U]**
12. WO195/16134. Terms of reference of the ABC. 4 Nov 65.