



DEPARTMENT OF HEALTH

**GOVERNMENT RESPONSE
TO THE HOUSE OF LORDS SELECT
COMMITTEE ON SCIENCE AND
TECHNOLOGY'S REPORT ON
THERAPEUTIC USES OF CANNABIS**

*Presented to Parliament by the Secretary of State for Health
By Command of Her Majesty
December 2001*

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GOVERNMENT RESPONSE TO THE HOUSE OF LORDS SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY'S REPORT ON THE THERAPEUTIC USES OF CANNABIS (2nd Report, HL Paper 50, Session 2000-01)

INTRODUCTION

The Government welcomes this further contribution to the debate on the therapeutic use of cannabis. The report was published on 14 March 2001 as a follow up to the earlier inquiry, "Cannabis: The Scientific and Medical Evidence" (November 1998)¹ and identifies some important issues related to the development of cannabis-based medicines.

Based on the scientific evidence presented, the Committee recognised in its earlier report that there is not enough rigorous scientific evidence to prove conclusively that cannabis itself has or indeed has not medical value of any kind². The Government therefore would wish to encourage research in this area among those who are looking to develop cannabis as a medicine and welcomes the initiation of clinical trials to provide that evidence.

This document reproduces each of the Report's concluding concerns and recommendations in turn and provides the Government's response to them.

1. Conclusion: The Committee expresses concern at the slow progress made by the two MRC-funded trials.

The Government wishes to emphasise that the development and peer-review of high-quality clinical trials are processes which cannot be rushed, irrespective of the need, otherwise there would be a danger that an inadequate trial design would result in a flawed clinical study.

Nevertheless, in recognition of the importance of this area, the Medical Research Council (MRC) and the Department of Health participated in the Royal Pharmaceutical Society's working party on therapeutic uses of cannabis. In addition, a MRC "Trial Development Group" advised applicants on the development of trial designs of the high scientific quality that would be highly competitive in obtaining funding. In addition, the MRC fast-tracked the two trial applications through their decision-making process.

The Government recognises that only after a decision to fund a trial is made can the researchers put in place procedures to manage the detailed practical aspects of the trial. As with all such trials, these two proposals went before the appropriate ethical committees and the researchers sought approval from the Medicines Control Agency (MCA). Then they had to recruit staff, purchase equipment and the trial capsules, recruit hospitals to participate in the study, develop administrative arrangements, print patient information leaflets and finally recruit patients who met the eligibility criteria to join the trial.

¹ 9th Report Session 1997-98, HL Paper 151

² Cannabis: The Scientific and Medical Evidence, November 1998, p41 para 8.1

Both studies were able to start recruiting participants very soon after the MCA authorised them in September 2000. At present, both studies are actively recruiting participants. The results of both studies will be published in high-quality peer-reviewed journals, in the normal way, at their conclusion.

2. Conclusion: The Committee expresses concern that the current requirement to obtain Home Office licences, and the stigma attached to cannabis, is effectively inhibiting research in this area.

This was one of a number of views expressed to the Committee during its original inquiry¹ (paragraphs 7.18 to 7.26), as to the possible reason for the lack of research. The Government believes that the evidence does not provide the grounds to support such an assertion. In his evidence to the original inquiry, the then Home Office Minister, George Howarth, gave evidence on the time taken to process the last six licence applications (Q663). This ranged from two weeks to four months, with most applications being dealt within a month.

The Government has consistently made it clear that it welcomes clinical trials into the therapeutic use of cannabis. As noted above, this remains the position. The Home Secretary, in his evidence to the Home Affairs Committee on 23 October 2001, made it clear, that subject to the satisfactory outcome of the current trials, he would approve a change to the misuses of drugs legislation to enable the prescription of a cannabis-based medicine.

With regard to the licensing requirements, the Home Office continues to work closely with those proposing research and it is encouraging to note the evidence given by both Dr Zajicek and GW Pharmaceuticals that the Home Office has been helpful to them in planning their trials. The Home Office continues to deal with licence applications as expeditiously as possible; the most recent application from, Dr Holdcroft, was dealt with in two months.

3. Conclusion: The Committee considers that it is undesirable to prosecute genuine therapeutic users of cannabis who possess or grow cannabis for their own use.

The Government understands this concern and set out its position in some detail in evidence to this follow-up inquiry (Q47 to 50). But there are two points perhaps that are worth underlining.

Firstly, the number of such prosecutions is very small. It would be unwise, on the basis of the available data, to draw firm conclusions about the consistency with which the law is applied across the country. Clearly every case is distinguished by its circumstances, and inevitably there will be those cases where a false or an unsubstantiated claim of a therapeutic need is made.

It is also important to remember that at each stage of the prosecution process, from the initial contact with the Police through to consideration by the courts, the scope for the exercise of discretion exists. While the law can make no distinction on the criminality of the possession of cannabis for recreational or therapeutic reasons, while the efficacy and safety of the latter remain unproved, the Government believes that the criminal justice system does allow for a sympathetic approach to the genuine therapeutic user.

4. Recommendation: The MCA should reconsider their position on the licensing of medicines containing cannabidiol (CBD).

The Committee has expressed concerns that the MCA has taken an over-cautious approach, leading to delays in any eventual approval of applications for a product licence. The Government has great sympathy for those whose conditions are not helped by existing medication. But it sees no case for setting aside the standards and regulations which exist to protect patients who volunteer for clinical trials and allowing them to be exposed to experimental medicines that have not been properly evaluated. There are well-established procedures derived from national and European legislation and EU guidelines which prospective medicines have to go through to minimise any risk in clinical trials. The Government believes that the MCA has handled its regulatory responsibilities properly on this issue in the interest of patient safety.

Underlying the Committee's concerns about delay is the issue of whether CBD and cannabis oil should be evaluated as new medicines. The Government considers that the new cannabis-based products under development are not long established herbal extracts and that these products should be classified as new medicinal products for the following reasons. Their compositions present new issues for which there is no current evidence. The older evidence was considered, but it was not possible to extrapolate from the anecdotal human experience with those older products, with unknown levels of cannabinoids, to the toxicity of Cannador. The pharmaceutical standard for tincture of cannabis in the British Pharmaceutical Codex of 1949, to which the Committee refers, does not state the levels of CBD present. The tincture therefore could not be considered equivalent to Cannador that contains up to 30% CBD or the GW Pharmaceutical product which contains over 50% CBD. The 1949 Pharmaceutical Codex Revision Committee referred to the uses of cannabis as follows, "Cannabis is too unreliable in action to be of value in therapeutics as a cerebral sedative or narcotic and its former use in mania and nervous disorders has been abandoned". They appear to have had some concerns about its safe use as a medicine.

The Committee criticised MCA's decision that there was need for further data on the toxicity of cannabinoids under evaluation. This decision was made in line with normal procedures and international guidelines. The MCA subsequently invited four independent experts from the Committee on Safety of Medicines (CSM) to audit the Agency's decision in relation to the

“Cannabinoids in Multiple Sclerosis” (CAMS) trial proposed by Dr Zajicek. Each expert concluded that the MCA’s approach was justified and that without sufficient data on CBD it was not wise to allow patients to be exposed to Cannador for more than the 15-week initial phase of the trial.

The Government reaffirms the position taken by the MCA at the time the decision was taken to ask for more data, that the evidence provided for the trial products fell short of the requirements of the European guidelines for pre-clinical toxicity studies to support trials of 15 weeks duration. Furthermore, additional data would have been needed to support trials of a year or more. For example, the applicants did not provide evidence from their products to show that they were not mutagens or would not cause embryo/fetal abnormalities. MCA had to refer to studies in the literature, which were old and not conducted to modern standards. These provided some reassurance about the delta-9-tetrahydrocannabinol (THC) component of the products, but there were very few studies to provide any evidence of lack of toxicity of CBD. There was virtually no data on lack of mutagenicity of CBD and studies with inhaled marijuana showed it to be toxic to the embryo without distinguishing whether THC, CBD or other active compounds were responsible. The toxic effects identified were not only inhibition of spermatogenesis, as suggested by the Committee, but also related to the uterus, ovaries, testis, thyroid, bone marrow, spleen and adrenals.

The Committee correctly notes that the doses used to produce these toxic effects were high. However, the studies did not use the clinical trial products and did not establish a dose at which there was no effect. It is not safe therefore, to conclude that these effects only occur at high doses. Because of the possibility that toxic effects may occur at much smaller doses, new studies are needed to determine the dose at which no effect is seen.

The Government takes the view that it would not have been responsible for the MCA to have set these safety concerns aside, leaving the patient to reach a view without adequate advice on potential side effects. Moreover, without more robust scientific evidence it would also have been improper to ask doctors to take responsibility for their patient’s safety when using these products.

There have been further developments on this issue. Three months after the authorisation of the CAMS study, additional scientific evidence on the toxicity of CBD was submitted to the MCA. The Agency sought the advice of the CSM on this additional toxicity data and its implications for exposure in man both for clinical trials and a marketing authorisation application, as follows:

- firstly, based on the evidence submitted, would the CSM be prepared to permit the administration of cannabis-based medicine extracts in the CAMS and GW Pharmaceuticals clinical trials beyond 15 weeks and if so what extension period would be justified and supported by the data?

- secondly, on the available pre-clinical and clinical evidence, what additional data would the CSM recommend to support a marketing authorisation application (MAA) of a cannabis extract for chronic use in patients with a chronic illness such as Multiple Sclerosis?

On the basis of the additional data on CBD and the advice of the CSM, in February 2001 the MCA authorised an extension of 12 months to the CAMS trial and the GW Pharmaceuticals trial provided there was appropriate safety monitoring. MCA also met GW Pharmaceuticals and advised them what additional data they would require to support a marketing authorisation (licence). The CSM advised that the carcinogenic potential of CBD would need to be investigated unless a good justification for not doing such a study was provided and that the mutagenic potential of CBD would need to be fully studied.

The Committee also commented on the MCA's reluctance to discuss the position taken by the Canadian regulatory authorities. The Government takes the view that it would not have been appropriate for the Agency to make public comment about the Canadian Government's regulatory actions unless it had notification of the regulatory authority's official position. The MCA's oral evidence informed the Committee that at that stage the Agency had received only unofficial communications from the Canadian Authorities³. In a subsequent official statement, Health Canada indicated that it was unable to comment on GW Pharmaceuticals statement because the information is considered proprietary and confidential. However the authority provided the following general statement: "An assessment of sufficient pre-clinical toxicity data for the approval of a product can only be established once a sponsor has submitted a New Drug Submission for Marketing Approval. To date, Health Canada has not received a New Drug Submission for cannabis-based medicinal extract".

Overall, the Government accepts that it should be impartial in its approach to licensing cannabis-based medicines, as suggested by the Committee. Development of cannabis-based medicines poses a number of very difficult scientific and regulatory problems⁴. The MCA is treating these products in the same way as any other drug, taking account of all the information available on the balance of risks and benefits including relevant human exposure, in making their decisions. Whilst acting within the appropriate constraints of regulations that protect clinical trials subjects, the MCA is working closely with those developing these products to identify solutions to the specific problems. In doing so the MCA has contributed significantly to the progress of the development of these medicines.

³ 2nd Report Session 2000-01, HL Paper 50, p14 para 5.

⁴ Gathering the evidence on medical marijuana. *Nature*, 2001, 401:613



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