Therapeutic uses of cannabis : with evidence / Select Committee on Science and Technology.

Contributors

Great Britain. Parliament. House of Lords. Science and Technology Committee.

Publication/Creation

London : Stationery Office, 2001.

Persistent URL

https://wellcomecollection.org/works/muv6qsja

HOUSE OF LORDS

SESSION 2000–01
2nd REPORT

SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

THERAPEUTIC USES OF CANNABIS

WITH EVIDENCE

Ordered to be printed 14 March 2001

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SECOND REPORT

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By the Select Committee appointed to consider Science and Technology.

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THERAPEUTIC USES OF CANNABIS

Background

1. In this short Inquiry we wanted to follow up issues relating to our earlier Inquiry, *Cannabis: The Scientific and Medical Evidence* (November 1998).[1] In that Report, we recommended that doctors should be permitted to prescribe an appropriate preparation of cannabis if they saw fit, albeit as an unlicensed medicine and on a named-patient basis. In a departure from the usual convention, the Government rejected this recommendation on the morning the Report was published. The Government's written reply was no more encouraging.[2] In March 1999, therefore, the Committee wrote:

> "we regret that the mind of the Government appears to be closed on this issue, and hope that the results of new research now under way may cause them to revisit our recommendations at an early date."[3]

2. This Inquiry was convened to examine the current state of research into the therapeutic uses of cannabis, the roles of the Home Office and the Medicines Control Agency in the licensing of cannabis-based medicines, and more recent issues relating to the prosecution of therapeutic cannabis users.

3. One hearing was held. We took evidence from: Charles Clarke MP, Minister of State in the Home Office; Dr Brian Davis, from the Medicines Control Agency Licensing Division; and Ms Judy Sanderson from the Health Services Directorate in the Department of Health. The transcript of that session is appended to this Report.

4. In addition to receiving written memoranda by these witnesses, we also solicited written material from the Alliance for Cannabis Therapeutics (ACT); G. W. Pharmaceuticals, a private company engaged in the development of cannabis-based medicines; and the Medical Research Council. These too are appended to this Report. We extend our thanks to those who took the time to contribute evidence to this Inquiry.

5. In 1998, we recommended that cannabis and its derivatives should continue to be controlled drugs. We still hold that view. We consider that any debate on the legalisation of cannabis and cannabis-based medicines should maintain a clear distinction between therapeutic and non-therapeutic use. This report is concerned solely with the therapeutic use of cannabis and cannabis-based medicines.

The State of Research

6. The Medical Research Council (MRC) recently approved awards totalling over £1.5 million involving two new trials:

(i) Dr John Zajicek, a neurologist at Derriford Hospital, Plymouth, is conducting a three year study to assess the efficacy of cannabis extract and tetrahydrocannabinol (THC) in the treatment of spasticity in people suffering from multiple sclerosis. The title of the trial is "Cannabinoids in Multiple Sclerosis" ("CAMS");

(ii) Dr Anita Holdcroft at Hammersmith Hospital, Imperial College School of Medicine, London, is conducting a two year study to assess the efficacy of cannabis extract and THC as

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1 9th Report Session 1997–98, HL Paper 151.

2 Published as Appendix 2 of our 2nd Report Session 1998–99, HL Paper 39.

3 2nd Report Session 1998–99, HL Paper 39, p. 5.

postoperative analgesics. This trial is entitled "A clinical trial as proof of principle of the analgesic effectiveness of cannabinoids on postoperative pain" ("CANPOP").

In addition, the MRC has awarded over £600,000 to fund basic cannabinoid research.[4]

7. Progress on the implementation of these trials, however, has not been rapid. Dr Zajicek's trial has only just started to recruit its projected 600 patients, while the precise operational details of Dr Holdcroft's trial have yet to be finalised.

8. The two MRC-funded trials are "proof of principle" trials, rather than trials of a specific medical preparation. While we welcome good quality research into the therapeutic effects of cannabis, we are concerned that the timescale for developing usable therapeutic preparations from these trials is extremely long.

9. A private company, however, G. W. Pharmaceuticals, has also conducted extensive research into the development of a cannabis-based medicine. From written evidence submitted to us, we are pleased to note that the company is making some progress, both in establishing the efficacy of a cannabis-based medicine in the treatment of patients with multiple sclerosis as well as spinal cord injuries, and in developing suitable medical preparations. It is planning to move to Phase III clinical trials shortly.[5]

10. G. W. Pharmaceuticals has also made progress in improving the mode of delivery of cannabis-based medicines. It has developed a sub-lingual spray which seems to avoid the dangers inherent in smoking herbal cannabis, and the difficulties of controlling the dose during oral administration.[6]

The Government Position on Cannabis-Based Medicines

11. We are pleased to note that the Government now display a more encouraging *attitude* towards the licensing of therapeutic preparations of cannabis than we have previously detected. The Minister was quick to deny suggestions that the Government were hiding behind scientific opinion. Should the quality, safety and efficacy of an appropriate preparation of cannabis be established, we were assured that the Government would reschedule cannabis from Schedule 1 to Schedule 2 of the Misuse of Drugs Regulations 1985.[7] In effect, the Minister assured us that once a safe, effective, cannabis-based medicine had been licensed by the Medicines Control Agency, the Government would actively co-operate in permitting it to be prescribed.

12. The Government's *policy* has not in fact changed since their response to our *Cannabis* report in 1998. Up until now we have sensed that the authorities have been dragging their feet, at least partly because they may have feared that permitting therapeutic preparations of cannabis to be prescribed would be interpreted by the public as a move towards allowing recreational use. The Minister told us, however, that:

> "there is now a much sharper awareness of the distinction between medicinal use of cannabis and recreational use of cannabis in the public debate" (Q. 49).

We are pleased, too, that the Minister now shares our view that, were the law relaxed on the therapeutic use of cannabis, the Government's hand in suppressing illegal, recreational use would be strengthened (Q. 51).

13. In our original inquiry we were told that research into cannabis was hampered by the "stigma" attached to cannabis and the burden of obtaining Home Office research licences.[8] Since that Report, the Royal Pharmaceutical Society has produced protocols for the conduct of the two MRC-funded "proof of principle" trials of cannabis. In addition, both Dr Zajicek and G. W. Pharmaceuticals have told us that the Home Office has been helpful to them in planning their trials. While we stand by our original recommendation that cannabis should be rescheduled in order to facilitate research,[9] we are at least encouraged that the Home Office is co-operating well with researchers within the current regulations.

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4 For fuller details of these trials and research projects, see the memorandum by the Medical Research Council (p. 33).

5 See the memorandum by G. W. Pharmaceuticals (p. 27) for an explanation of the phases of clinical trials.

6 An oral preparation of synthetic delta-9-tetrahydrocannabinol in sesame oil is already available as "Marinol". However, the absorption into the blood stream via oral administration tends to be variable, such that patients either underdose themselves and do not obtain benefit from the drug, or risk unwelcome euphoria.

7 See Recommendation 8.6, paras 7.6–7.8, and Box 3 (p. 19) of our earlier Report, *Cannabis: the Scientific and Medical Evidence*.

8 See paras 7.18–7.26.

9 See our earlier Report, *Cannabis*, Recommendation 8.6 and Box 8.

Therapeutic Cannabis Users and the Law

14. There have recently been a number of high-profile cases involving the prosecution of therapeutic users of cannabis: the memorandum by the Alliance for Cannabis Therapeutics (ACT) (p. 26) has highlighted a number of them. The decision to prosecute, taken by the Crown Prosecution Service (CPS), does not seem to be consistent from region to region. Moreover, in some cases, juries have acquitted therapeutic users who do not deny the offence, but plead therapeutic use in mitigation; in other cases, defendants have been found guilty and sentenced.

15. The Minister sought to deny that therapeutic cannabis users were subject to "postcode prosecuting". He stressed that the number of therapeutic users who were prosecuted was extremely small when compared to the total of 89,000 cases involving cannabis in 1998.[10] He also said that the variation in the outcome of cases for therapeutic users was less than for other offences, including the recreational use of cannabis. The number of cases of therapeutic users of cannabis being prosecuted is certainly small. Exact statistics are difficult to obtain, however, as the Home Office does not maintain a record of those prosecuted for cannabis use who claim therapeutic use as a defence.

16. The Minister further said that he had no intention of changing the current position, whereby the decision whether or not to prosecute for cannabis-related offences is made locally by the Police and the CPS. He did, however, emphasise that discretion could be exercised at three levels of the prosecution process: by the Police; by the CPS; and by the Courts. Guidelines issued by the Association of Chief Police Officers (ACPO) on dealing with cannabis offences specifically refer to therapeutic use, and recommend that a caution is usually appropriate; the CPS guidelines require that any prosecution should be in the public interest; and the Court of Appeal issues guidance that the possession of small amounts of cannabis for personal use can often be met by a fine.

17. We accept that recreational users, if arrested, may claim to be therapeutic users. We have no wish to dissuade the Police and the CPS from prosecuting those whom they believe to be making such claims falsely.

18. We recognise that the Government do not consider it appropriate to override the authority of the Police and the CPS. We also understand that the present system allows discretion to be used at many levels. We consider, however, that the acquittal of cannabis users by juries on compassionate grounds brings the law into disrepute. In the absence of a viable alternative medicine, moreover, and though we would not encourage *smoking* of cannabis,[11] we consider it undesirable to prosecute genuine therapeutic users of cannabis who possess or grow cannabis for their own use. This unsatisfactory situation underlines the need to legalise cannabis preparations for therapeutic use.

The Medicines Control Agency and the toxicity of Cannabidiol

19. While we are encouraged at the recent change of attitude shown by the Home Office, we consider that decisions taken by the Medicines Control Agency (MCA) appear to be inconsistent. We did not feel that the MCA adequately answered our questions about the proposed use of cannabidiol in cannabis-based medicines. We were also disappointed that the witness from the MCA seemed unprepared even to consider discussing the basis on which the MCA's decisions were made.

20. Raw cannabis (*cannabis sativa*) contains more than 60 cannabinoids and more than 400 chemical compounds. The two most abundant cannabinoids, which are currently subject to the most detailed investigation, are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Both these cannabinoids are present in raw cannabis. They are also both present in the cannabis oil capsules ("Cannador") which Dr Zajicek is proposing to use in his CAMS trial,[12] and in the cannabis extracts used by G. W. Pharmaceuticals.

21. THC has long been established in the pharmacopoeia. The MCA are satisfied that there is adequate information on the toxicological profile of THC to justify long-term exposure to THC in the CAMS trial (p. 31). An oral preparation of synthetic THC in sesame oil ("Marinol") can already be prescribed by doctors.[13]

22. By contrast, the MCA are unhappy with the toxicology data on CBD. They said that there is some evidence that CBD inhibits spermatogenesis in animals, and that overall there is a lack of adequate data. The MCA have therefore not permitted Dr Zajicek to proceed with his trial of Cannador

[10] The most recent year for which figures are available. See Home Office Statistical Bulletin (2000), "Drug Seizure and Offender Statistics, United Kingdom, 1998".

[11] For reasons explained in our earlier *Cannabis* report, paras 4.17–4.18, 5.54–5.57, and para. 8.4.

[12] The primary active ingredients in "Cannador" capsules consist of 70% THC and 30% CBD.

[13] "Marinol", however, is an unlicensed drug and can only be prescribed on a named-patient basis. It is not generally available and has to be imported from the USA.

(cannabis oil) capsules beyond 15 weeks. Moreover, the MCA's decision to insist on further toxicology data on CBD could delay the production of a cannabis-based medicine by G. W. Pharmaceuticals by as much as 2 to 3 years. Were the MCA not to require further extensive toxicological studies on CBD, G. W. Pharmaceuticals claim that they could have a cannabis-based prescription medicine available for patients in 2003.

23. We note that, according to G. W. Pharmaceuticals, the Canadian regulatory authorities have stated that they do not require additional animal toxicology studies for CBD. We put this to the MCA, who refused to comment (Q. 5); we found this refusal highly unsatisfactory.

24. We consider that the decision of the MCA is flawed for three reasons which are discussed in turn below:

(a) the MCA persist in treating CBD and cannabis oil as "new medicines",[14] though cannabis oil, which contains both CBD and THC, has a long history of human use and appeared in the British Pharmacopoeia Codex until 1948;[15]

(b) the studies which the MCA took to indicate an inhibition of spermatogenesis involved doses of CBD at least 100 times higher than the doses contemplated by either Dr Zajicek or G. W. Pharmaceuticals; and

(c) the potential side-effects of CBD about which the MCA are concerned might be regarded as trivial by those patients, such as those suffering from multiple sclerosis, who stand to benefit from medicines incorporating CBD. These concerns could be dealt with by issuing a warning to physicians who prescribe cannabis-based medicines. The attitude of the MCA in not allowing patients to make their own decisions could be regarded as overprotective.

25. Both the MCA and the Home Office persist in treating cannabis-based medicines as new medicines. Cannabis, however, has a history of medical use in man stretching back hundreds of years. For much of the nineteenth century and the first half of the twentieth century, moreover, it was administered in Britain as a tincture (cannabis oil in alcohol): thus the oral administration of cannabis extracts which contain significant quantities of CBD has a long history of medicinal use. In choosing to ignore the long history of safe therapeutic cannabis use, and in classifying cannabis extract (and CBD) as a "new medicine", the Government and the MCA are treating a long-established herbal extract as if it were just another new synthetic chemical, and are thus not making an informed scientific judgement.

26. Campaigners against cannabis have long argued that it may have adverse effects on human fertility. Despite 30 years of trials, however, this has never been adequately proven. The trial to which the MCA refer in their oral evidence (Q. 2) was based on tests in small numbers of animals, and the results were equivocal, even though the administered doses of CBD were 100–1000 times higher than those proposed for any human medicine. In short, we regard the raising of this unsubstantiated issue as further evidence that the MCA have not adopted a positive approach towards the licensing of a cannabis-based medicine.

27. We are concerned that the MCA's approach to the licensing of cannabis-based medicines, and their insistence on the provision of new toxicological data which could delay the approval of such medicines, place the requirements of safety and the needs of patients in an unacceptable balance. Patients with severe conditions such as multiple sclerosis are being denied the right to make informed choices about their medication. There is always some risk in taking any medication; patients and their doctors should certainly be informed about the toxicological concerns that the MCA have raised, but these concerns should not prevent them from having access to what promises to be the only effective medication available to them.

28. Overall, we consider that the MCA's attitude means that cannabis-based medicines are not being dealt with in the same impartial manner as other medicines.

29. We believe that a thorough and impartial reappraisal of the published scientific literature on the safety of CBD and cannabis extracts should lead the MCA to reconsider their present overly cautious stance. We are at least encouraged that the MCA state that they are conducting a more detailed review of existing literature reports on cannabis and CBD.

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[14] Dr Davis calls them "new products" (Q. 22); the Home Office, in their written memorandum (p. 28), state that before any cannabis-based medicine could be prescribed, it would have to go through the same procedures as "all prospective new medicines".

[15] See our earlier Report, *Cannabis*, Chapter 2.

Summary of Conclusions

1. We are concerned at the slow progress made by the two MRC-funded trials. We consider that the current requirement to obtain Home Office licences, and the stigma attached to cannabis, is effectively inhibiting research in this area.

2. We are pleased that the Home Office is showing the first signs of adopting a genuinely pragmatic and expeditious approach to the issue of cannabis-based medicines.

3. The Minister considered that the attitude of the police, the Crown Prosecution Service and the courts, reflects "an understanding that where cannabis is used for medicinal purposes, that is to be considered in a somewhat different light to purely recreational use" (Q. 49). Noting the inconsistency with which the law is presently applied across the United Kingdom, we endorse this view, and further consider it undesirable to prosecute genuine therapeutic users of cannabis who possess or grow cannabis for their own use.

4. We consider that the Medicines Control Agency are not approaching the question of licensing cannabis-based medicines in a properly balanced way, especially given the long-established history of cannabis use, and the needs of patients for whom there is no medicinal alternative. To end the delay in the development of an effective cannabis-based medicine, we recommend that the MCA should reconsider their position on the licensing of medicines containing cannabidiol.

Since the MCA gave oral evidence to our inquiry, we understand that they have conducted a review of their decisions regarding cannabis and cannabidiol, and that they are considering modifications to their position set out in this report.

APPENDIX 1

Members of the Select Committee

Lord Flowers (*co-opted*)
Lord Haskel
Lord Howie of Troon
Lord Jenkin of Roding
Lord Lewis of Newnham
Lord McColl of Dulwich
Lord Methuen
Lord Oxburgh
Lord Patel
Lord Perry of Walton (*Chairman for this Inquiry*)
Baroness Platt of Writtle
Lord Quirk
Lord Rea
Lord Wade of Chorlton
Baroness Walmsley
Lord Walton of Detchant
Baroness Warwick of Undercliffe
Baroness Wilcox
Lord Winston (*Chairman of the Select Committee*)

The Committee appointed as its Specialist Adviser:

Professor Leslie Iversen FRS, Visiting Professor of Pharmacology, University of Oxford

Declarations of interest

Lord Rea—Trustee (unpaid) of the Medicinal Cannabis Research Foundation, set up by G. W. Pharmaceuticals

Lord Walton of Detchant—Former President: British Medical Association, Royal Society of Medicine, General Medical Council, Association of British Neurologists, World Federation of Neurology. Former member: Medical Research Council

Lord Winston—Director of NHS Research and Development, Hammersmith Hospital NHS Trust, London

APPENDIX 2

Witnesses

The following witnesses gave evidence. Those marked * gave oral evidence.

Alliance for Cannabis Therapeutics

* Charles Clarke MP, Minister of State, Home Office

* Dr Brian Davis, Medicines Control Agency, Licensing Division

G. W. Pharmaceuticals Ltd

Medical Research Council

* Medicines Control Agency

* Ms Judy Sanderson, Health Services Directorate, Department of Health

MINUTES OF EVIDENCE

WEDNESDAY 7 FEBRUARY 2001

Present:

Dixon-Smith, L.
Haskel, L.
Howie of Troon, L.
Jenkin of Roding, L.
Perry of Walton, L. (Chairman)
Platt of Writtle, B.
Porter of Luddenham, L.
Quirk, L.
Rea, L.
Wade of Chorlton, L.
Walmsley, B.
Winston, L.

Examination of Witnesses

DR BRIAN DAVIS, Medicines Control Agency Licensing Division, MR DAVID SNOWDON, Toxicology Assessor, Medicines Control Agency, MR CHARLES CLARKE, Member of the House of Commons, Minister of State, Home Office, and MS JUDY SANDERSON, Health Services Directorate, Department of Health, were examined.

Chairman

1. I thought that, before welcoming our witnesses and starting questions, it would be worthwhile saying that this meeting follows on from the House of Lords report of 1998, which recommended that cannabis should be made available for therapeutic purposes, although not for recreational purposes. Apparently there are three clinical trials going on, two funded by the Medical Research Council and one by a private company, GW Pharmaceuticals. We wish to establish where they have got to and how the fruits of that research can be made available to patients as a medicine as soon as possible. The results seem to be, in this very limited way, promising. The Committee would also like to ascertain what legal obstacles to research and development of cannabis-based medicine still remain. They are also interested in the current policy of the prosecution of therapeutic users of cannabis. Having said that, can I welcome you, Minister, and your colleagues. I should say that we have had written evidence from the Medicines Control Agency (MCA) and we have also had written evidence from the Home Office, but they both arrived too late to be circulated and they are simply tabled this morning. We will be asking questions that you may well have answered already but we will have them answered, if we may, orally this morning. May I begin by asking question 1, which is a preliminary statement that cannabidiol (CBD) is present in significant amounts in natural cannabis which has been used as a herbal remedy in many different forms of human medicine for hundreds of years. According to information we have had from GW Pharmaceuticals, the Canadian Health Authorities have pronounced themselves to be satisfied with the toxicology data currently available on CBD, and do not require any further studies prior to the approval of a cannabis-based medicine. The question is: are you satisfied that cannabidiol does not require any further toxicity testing? If you are not satisfied, what further toxicity data is needed?

(*Mr Clarke*) Can I first, Lord Perry, thank you for the hearing this morning. We are very glad to participate in this public debate. May I apologise to you for the apparent late arrival of the evidence that you have only just received. I am not sure why that is the case but I do apologise. It is a discourtesy which should not have happened. May I introduce my colleagues: Dr Brian Davis, from the Medicines Control Agency Licensing Division and Judy Sanderson from the Department of Health, Health Services Directorate. On your first set of questions about the Department of Health Medicines Control Agency, I am going to rely, with your permission, principally on Dr Davis and Ms Sanderson to help. On the Home Office questions, which you will come to later, I will deal with those as they come through, if that is acceptable to you. I would like to ask Dr Davis to deal with the first question you have just asked.

(*Dr Davis*) If I may, I would like to introduce a number of the team that I have brought with me, with your permission, as I may refer some of your later questions to them: Dr Ian Hudson, who is the Director of the Licensing Division at the MCA; Dr Linda Anderson, who is a pharmaceutical assessor; and Dr David Snodin, who is a toxicology assessor. Could I take your first question where you ask: "Are the MCA satisfied that CBD does not require any further toxicity testing?" The Agency is satisfied that patients may safely be exposed to CBD for a limited duration. The Agency had concerns about the exposure of patients to CBD for a long period and therefore it did not allow a proposed extended exposure of one year. The literature on the toxicity of CBD is very limited. The agency were sufficiently reassured by this to allow patients to be exposed for short periods but considered that additional data would be required before patients were exposed to CBD for long periods. There is a considerable literature on the toxicity of the other component of cannabis, THC (tetrahydrocannabinol). The MCA was reassured by this and therefore allowed patients to be exposed to THC for long periods. The further question is: "If you are not satisfied, what further toxicity data is needed?" The MCA has received additional data on the toxicity of CBD. The Agency will present this additional evidence, with all the other evidence available, to the Committee on Safety of Medicines this month and ask their advice on whether any further toxicity testing is required for clinical trials. We will also ask them to advise on any additional, non-clinical safety studies that they

Chairman *contd.*]

consider necessary to support the marketing authorisation. To the last part of your question, my Lord Chairman, the MCA makes decisions in the light of UK and European legislation and guidelines, taking into account the need to protect patients from exposure to medicines that have not been adequately tested for their toxicity. The MCA do not wish to comment on GW Pharmaceuticals' statements about the Canadian health authority.

2. I have read, of course, the document that you submitted. You raise concerns about published results, suggesting that high doses of cannabidiol may impair male fertility in monkeys. In view of the fact that these findings were inconclusive, and the studies employ doses of cannabidiol very much higher than those that occurred in clinical trials, might these concerns be met by the provision of a warning statement into the position in connection with the approval of a new, future, cannabis-based medicine?

(*Dr Davis*) Could I refer your question to our toxicology assessor?

(*Dr Snodin*) The monkey study to which you referred did show effects on testes on spermatogenesis, even at the lowest dose tested. Therefore, we do not have evidence of a "no effect" level for these effects on the testes. Thus, we feel that this needs to be investigated further before we can go forward with extensive clinical trials.

3. The lowest dose tested was still bigger than the dose that is being administered, was it not?

(*Mr Snodin*) The lowest dose was higher, yes, but it still showed an effect. We do not know at what dose in the monkey there is no effect. That is the problem.

Lord Winston

4. There is a large number of drugs which depress spermatogenesis which are in use. Were there reasons for concern that this particular effect was greater than with the other drugs which were in common practice in the pharmacopoeia?

(*Mr Snodin*) Added to this monkey study, there was a general concern over the lack of other toxicity data, which was related in part to the fact that the longest animal study we had available was only of 90 days' duration. Our usual standard for animal study requirements to support clinical trials is that the duration of the animal study should be at least as long as the proposed duration of the clinical study because one could have cumulative and other effects that might be apparent only on prolonged dosing, which were not apparent during these short studies. We have that general concern, as well as this specific concern over testicular effects. As you say, the testicular effects may eventually not be considered significant provided appropriate warnings are given to patients but we feel that this this issue may just be part of the picture. We do not really know at the moment.

Chairman

5. You are not moved at all by the Canadian decision?

(*Dr Davis*) We do not wish to comment on the Canadian position.

6. I did not ask you to comment. I said: are you not moved by it?

(*Dr Davis*) We only have unofficial communications from the Canadian authority and it would be inappropriate for us to comment.

7. Can I move on to ask you what your response would be if the planned phase III trials that are going to be carried out by GW Pharmaceuticals are positive?

(*Dr Davis*) This is a very difficult question. We assume that "positive" means that the benefits outweighed the risks and that the company would like to pursue a marketing authorisation. The MCA would not be able to give an opinion without seeing the proposed development programme for the confirmatory phase III trials and the results of the confirmatory trials. However, the Agency would also need to consider all the data on the quality and safety related to the product. The Agency is happy to meet with GW Pharmaceuticals to discuss their development programme. In fact, the Agency has met with GW Pharmaceuticals on several occasions to advise them on the information that they will require to allowed them to conduct their proposed clinical trials. At the last meeting five weeks ago, the Clinical Trials Unit advised them that they should seek a meeting with the licensing assessors. It would be at this meeting that the MCA would advise the company on the additional data that would be required to support a marketing authorisation. GW Pharmaceuticals would need to decide which procedure, either national or European, they wish to follow to obtain a marketing authorisation and prepare the appropriate application with evidence to support the quality, safety and efficacy of their product for the proposed indication.

8. If the result is positive and is published, there will inevitably be a very large demand from the public for access to this preparation, will there not?

(*Dr Davis*) Again, this comes back to our interpretation of "positive". The role of the MCA is to ensure that products that go on to the market and are widely distributed meet the standards of quality, safety and efficacy, and that would have to be met before we could issue a licence, that is before either a the European or national licence could be issued.

Baroness Platt of Writtle

9. Do you consider that the timetable put forward by GW Pharmaceuticals that a commercially available preparation will be available by 2003 is realistic? What obstacles do you consider might delay that deadline?

(*Dr Davis*) The Agency would need to see the results of the exploratory phase II trials and the development plan of the confirmatory phase III trial before giving an opinion on GW Pharmaceuticals' timetable. GW Pharmaceuticals are responsible for the rate of progress of their development plan and for

Baroness Platt of Writtle *contd.*]

setting the timetable of activities leading to an application for a marketing authorisation. You ask: "What obstacles do you consider might delay that deadline?" GW Pharmaceuticals have identified long-term toxicity studies as an unknown factor in their timetable. It may be that reports of non-clinical safety studies from the literature or in the public domain would provide adequate data to support extended clinical trials, and possibly even an application for a marketing authorisation for the THC component of their product. This is obviously subject to the review by the MCA and the advice of the Committee on the Safety of Medicines (CSM). The toxicological data relating to the CBD are far less extensive. The Agency will submit all the available information to the CSM and ask for them to advise what further, non-clinical safety studies would be required to support extended clinical trials and a marketing authorisation, with a product containing high levels of CBD. The Agency has suggested to GW Pharmaceuticals that they meet with the licensing assessors after the CSM have given their advice to discuss their development plans. It would be at that meeting that the Agency would advise on any obstacles that might delay the proposed timetable.

Lord Winston

10. Can we come on now to the three-arm study of the Medical Research Council (MRC), which I hope you would agree is a well-designed cannabinoid study. If the MRC trials prove positive, would the MCA be prepared to issue a certificate to allow appropriate cannabinoid preparations to be made available?

(*Dr Davis*) This is also a difficult question. We are not sure what the Committee means by "issuing a certificate". If by that they mean a marketing authorisation, then an applicant would need to provide evidence of quality, safety and efficacy. This would include evidence that the product could be manufactured reproducibly and to have consistent effects one batch to another. The MCA is happy to meet with those responsible for the MRC trials to review the data from the present trials and advise them on what additional evidence they would need to support a marketing authorisation.

11. Presumably the trials, if they were positive, would prove efficacy at least and they might go some way towards establishing safety as well, at least in the short term, might they not?

(*Dr Davis*) These trials were designed as proof of principle trials and they are exploratory trials. The normal package to prove efficacy for a marketing authorisation would require what would be confirmatory trials using an appropriate dose in a somewhat wider group of patients.

12. So you would expect to see further trials as the next step?

(*Dr Davis*) We would have to look at the results and then give advice based on the results of the phase II exploratory trials.

13. What do you think the timetable for the development of these preparations might be if they look to be efficacious?

(*Dr Davis*) The MCA would advise those responsible for setting the timetable on the extent of clinical data required to demonstrate that the product was safe and efficacious. In fact, Dr Zajicek has recently written to the Agency to ask what information would be required to obtain a market authorisation. The Clinical Trials Unit advised him to request a meeting with the licensing assessors, who will be able to answer his questions.

14. Do you see these trials assisting in the development of a cannabis-based medicine?

(*Dr Davis*) These trials were designed as proof of principle studies to show if the trial design could demonstrate the efficacy and safety of an orally-administered cannabis product and of a pure THC medicine when given to patients with MS-related spasticity or patients with post-operative pain. The investigators anticipate that if Marinol, that is the pure THC medicine, is found to me more efficacious, the manufacturer could be persuaded to apply for a marketing authorisation to make it widely available for the new indication. On the other hand, if Cannador, that is the medicine that contains THC and CBD, is found to be more efficacious, then anyone wishing to develop Cannador would need to prepare a development plan. The MCA would be pleased to review the data and advise on their development plan.

Lord Rea

15. Could I go back a little bit to the toxicity testing on monkeys and the finding of reduced spermatogenesis? Is it going to be possible to do some trials on humans and to measure the spermatogenesis effect at present or do we have to wait until more trials on animals are done before we can go ahead?

(*Dr Davis*) At the present time, we have allowed trials with the CBD and THC for short duration and we have advised the investigators that they should in fact monitor and look for changes in the testes.

Lord Winston

16. To come back to the MRC trial specifically for a moment, what would be the MCA's response if it was found that the plant-based extract was hugely more efficacious?

(*Dr Davis*) Our response would be that we would have to look at the data from the trials, evaluate the data and then advise those responsible for the trials on a development plan for that medicine.

17. It might be likely, might it not, that under those circumstances patient groups and other people who are suffering from these diseases might become quite vociferous about the failure to implement the further possibility of that drug being used. Would that be a problem?

(*Dr Davis*) There have been some important advances in the research since your Committee made their report. I emphasise that this is a very difficult area of research and clinical investigation. It was

Lord Winston *contd.*]

important to identify the products that were suitable for conducting this research in the first place. It was then important to identify the appropriate route of administration for the product and to devise protocols in order that we could test these products. From the MCA's point of view, given all of those difficulties, we feel that this research is in fact progressing remarkable rapidly. We feel that we would have to see the results but, given that promise, that we would want to continue to follow the scientific evidence that was becoming available.

Chairman

18. The oral preparation was available in the British Pharmacopoeia right up until 1948. It had been used for a very long time.

(*Dr Davis*) My understanding is that at the time of the review of the licence of the preparation that you refer to, it was considered that there was no appropriate medical use for it and the licence was not renewed at that time.

Chairman: That was why it was taken out. It was taken out with almost every other herbal preparation in the pharmacopoeia. That does not mean that it has not been tried in patients over a very long period.

Lord Winston

19. You can understand our frustration at this time, I hope, in that in the pharmacopoeia, in common practice as we stated in our report, there is a wide number of drugs which have hugely varying effects. One typical drug product is salicylic acid in aspirin, which has all sorts of effects. I agree that you might not want to give it a licence now if it was launched on the market at the moment but the fact is that it is widely used and widely efficacious. Presumably the issue is one of safety, is it not?

(*Dr Davis*) I would submit that there is no robust evidence to show whether cannabis-based medicine is or is not effective.

20. I am posing a hypothetical question, that there might be robust evidence to show that this is efficacious. It is on that assumption that I am asking the question. The MRC trial might show that, might it not?

(*Dr Davis*) It is the Agency's role to facilitate those trials in order that we can collect that robust evidence and provide a scientific base for the decisions that we make.

Baroness Walmsley

21. I would like to press you a little further on timing because there are those that do not agree that work is progressing speedily. I am sure you are aware that among the population there are a lot of people who would like to get the show on the road and get good quality information as soon as possible. In fact, some people consider that time is running out. Can I have your comment on why the MRC trial has taken so long to get under way and what could the Government do to ensure that future trials are not subject to the same delays?

(*Dr Davis*) The Agency would like to emphasise that this is a complex area of clinical investigation and drug development. Drug development normally takes a long time. The MCA is not surprised at the preparation for a clinical trial, involving an unusual medicinal product with adverse psycho-active effects in a disease with natural remissions, has taken a long time. The challenge is to derive robust scientific evidence from the studies. Dr Zajicek has kept in close contact with the Agency as he prepared for this trial. The Agency has advised him on a number of aspects of his trial and met with him to discuss the details of his proposal and answer his questions. During the preparations, the investigators changed the design of the trial to take account of practical problems, and we understand that they have had some difficulties in obtaining suitable preparations of some of the medicines. Both trials were approved in September 2000. Dr Zajicek wrote to the MCA in January to confirm that patients are now being randomised at the first centre in Portsmouth. To take the second part of your question, what could the Government do to ensure that future trials are not subject to the same delays, the Agency can reassure you that any perceived delay has not arisen from unnecessary bureaucracy. The Agency has devoted a lot of time to considering the scientific aspects of these studies, with a view to advising the investigators on the best approaches to their research and how to avoid regulatory pitfalls. All of this dialogue is intended to help achieve the objective of collecting robust, scientific evidence on the effects of cannabinoids on pain and on MS-related spasticities, or on other disease conditions.

22. As my colleagues have mentioned, this is not a drug on which we have started from square one. It is a drug about which a great deal has been known. Has all that knowledge and information been fed in?

(*Dr Davis*) To take that in two parts, at the Medicines Control Agency when we use the word "drug" we are talking about a specific product because we are aiming to license a product. These in fact are new products. They are not things that have been around since time immemorial. These are products with their own specific characteristics and they set their own difficulties for the research that is involved. We are aware of all the evidence that has been produced on previous formulations of cannabis and have taken that into account.

Lord Jenkin of Roding

23. The oral preparation of THC in sesame oil is already available. Due to the inflexibility of the titrated dose, however, adverse effects frequently occur and that means that this particular form of medication has turned out to be pretty unpopular. The MRC-funded trials also use oral forms of cannabis. My question therefore is: are you quite satisfied with the protocols under which the MRC trials are taking place and what would your response be if the trials in fact produced positive results?

(*Dr Davis*) A working group of the Royal Pharmaceutical Society under the chairmanship of Sir William Asher, past Chairman of the CSM, designed the MRC trials to prove the principle that a

Lord Jenkin of Roding *contd.*]

cannabis-based medicine can be tested in clinical trials to determine if it is safe and efficacious. To answer the question as to what our response would be should the trials have a positive result, the question of a positive result is a difficult one. A positive result for the MRC trials would indicate that they had shown that it was possible to investigate the efficacy and safety of a cannabis-based medicine using the chosen trial design and selective route of administration. It may also indicate that there were encouraging signs that the drug was safe and efficacious. The MCA would be happy to meet with those responsible for the trials to review the data and advise them on their future development plans. If those responsible decided to try to develop a cannabis-based medicine for marketing, the Agency would be happy to discuss the whole development plan with the applicant, including the quality aspects of the product and the anticipated requirements for evidence to demonstrate safety and efficacy. More extensive trials may be required. The applicant may even wish to consider an alternative route of administration or a different dosage form. In fact, Dr Zajicek recently wrote to the Agency to ask what information would be needed to support an application for a market authorisation. The Clinical Trials Unit advised him to seek a meeting with the licensing assessors and offered to arrange such a meeting. At that meeting the Agency would discuss the scientific evidence needed to support the quality, safety and efficacy aspects of such an application. You also asked what our response would be, should they have negative results. On the question of negative results, the negative result for the MRC trial would be disappointing. It might show that it was not possible or practicable to use the proposed trial design to demonstrate safety and efficacy in the proposed indications. Alternatively, it might show that the product was either not safe or not efficacious in that particular indication. In these circumstances, the Agency would be very willing to meet with the investigators or others responsible for the trials if they wished to test a different trial design or a different medicinal product or an alternative route of administration. At that meeting, the MCA would advise them on any new research proposals.

24. May I go on to ask the last part of the question? This all assumes that there will be an oral mode of delivery. One can understand that that may not produce the results which are required. May I say straight away that I am not a toxicologist and I know nothing of the science of this, but one could understand that. Would your Agency be prepared to discuss with the promoters of the trial other forms of administration which might produce more consistent results?

(*Dr Davis*) Yes, the Agency would be very happy to discuss alternative routes of administration. In fact, we have had discussions with the investigators on just this very point.

Lord Howie of Troon

25. My question is directed towards the Home Office. I say good morning to the Minister. As I see it, the Government will maintain its position on the therapeutic use of cannabis until appropriate, and I assume successful, trials have taken place. Looking at it from the Minister's point of view, this question goes beyond science and has political characteristics which may well be thought in some way to be sensitive. My question is really this: should the trial show that cannabis has beneficial therapeutic effects, how might the Government react?

(*Mr Clarke*) We would react very positively. I hear what you say, Lord Howie, about the political environment but our tests are principally scientific. Perhaps I should say, in the light of the interest expressed earlier on, that as a constituency Member of Parliament I am subjected to pressure, particularly from MS sufferers in my own constituency, and they come and see me in my regular surgery. There is a very nice man who comes regularly and he last came last Friday to put exactly the points about time scale which Lord Winston and Baroness Walmsley were raising. I understand the points. That is why our test is scientific. If the clinical trials into cannabis are successful and they do lead to a medical preparation which is approved by the Medicines Control Agency, the Government is absolutely clear that we are willing to amend the Misuse of Drugs Regulations to allow the prescribing of such medicine. I would like to emphasise again that the key determinant factor for us is the issue of the marketing authorisation for cannabis-based medicine by the MCA following completion of successful clinical results. That is the test and not the more general political environment which, as you rightly say, is around. It is a scientific test as far as we are concerned.

26. It seems rather encouraging to me, although sometimes governments do sit on their hands. Can I take it that that is not likely to be your attitude?

(*Mr Clarke*) I do not recognise the initial remark! It is certainly not our attitude. Joking aside, I am well aware of the implication of the question and the explicit statement in the question. Certainly the attitude of the Home Office, and I think in the Department of Health as well, is very, very clear, that once the trials' outcomes are clear in the way that Dr Davis has been trying to describe in his evidence to you this morning, we will act very expeditiously to ensure that any approved treatment can be brought into general circulation.

Lord Porter of Luddenham

27. The question I have to ask will not take very long because we have almost covered it. I would like to ask it rather bluntly, because it is a very important question, to make sure it is being asked firmly. If the Medical Research Council trials do get a certificate of approval from the Medicines Control Agency, will the Government then remove its ban on the therapeutic use of cannabis?

(*Mr Clarke*) The short answer to that question, my Lord, is yes. That is an answer to a blunt question. Following the issuing of a marketing authorisation or a product licence by the MCA and by the process already described by Dr Davis this morning, the Government will set in hand the necessary changes to the misuse of drugs legislation. It is the case that the Advisory Council on the Misuse of Drugs would

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have to be consulted formally before any changes could be made, in accordance with sections 7 and 31 of the 1971 Act. It is the case that any changes could be made very swiftly by way of secondary legislation and subject to a negative resolution and therefore we would not be bidding for primary legislation. Specific changes would be required to two statutory instruments: first, the removal of cannabis from Part I of the Schedule to the Misuse of Drugs (Designation) Order 1986, which specifies the controlled drugs which are designated as drugs to which section 7(4) of the Misuse of Drugs Act 1971 applies. That is the first one, removing cannabis from Part I of the Schedule to the Misuse of Drugs (Designation) Order 1986. The second such instrument which would need to be changed is the transfer of "cannabis" from Schedule 1 to Schedule 2 (or 3) of the Misuse of Drugs Regulations 1985. As I say, both of those can be made by means of secondary legislation because they are orders and are subject to the negative resolution. The only delay from our point of view is, firstly, the profound delay which we have been discussing this morning about the MCA being satisfied that the marketing authorisation can be issued, which for us is a very serious point; it is not a trivial point for the reasons Dr Davis has been setting out. We need to be sure that there are no deleterious effects of the drugs. Secondly, the formal process of consulting the Advisory Council on the Misuse of Drugs: I think that would be relatively rapid and the actual legislative change is a straightforward and, I think, quick process.

Lord Wade of Chorlton

28. Were a licensed cannabis preparation available, do you consider that illegal therapeutic cannabis use by other means of administration would be affected by that?

(*Mr Clarke*) I am not entirely clear what is meant by the question but let me try and answer it as clearly as I can. The process that I have described, the Misuse of Drugs Regulations 1985, which would have to be amended, authorises patients to possess controlled drugs which have been prescribed for them by a doctor; i.e. fit the particular criterion which would be set out by the Medicines Control Agency. The use of cannabis for self-medication purposes would fall outside that definition if it was not prescribed by a doctor and would thus remain unlawful. It would be the particular medication which would be lawful, based on the testing process that we have described. It may be helpful to the Committee to draw an analogy with the prescribing of heroin. Heroin may be prescribed by doctors at the moment to treat a number of medical conditions and is available in various medicinal forms, for example, tablets and injections. However, its possession by a person other than on a doctor's prescription written for that person is unlawful. It is the doctor who is the key to the whole process, whether that heroin is in medicinal form or non-medicinal form, whichever way it arises. It is the medicine which would be made legal rather than general use of cannabis, even by those who are affected by particular conditions which they are seeking to resolve.

29. Would you imagine that if such a licensed product were available to the people who are now suffering and they could get it on prescription and it is known to be available, that is not going to have an impact on the users of what might still be officially illegal cannabis? In other words, are you going to find it a more difficult issue to control in the event that it is a legal product on the marketplace?

(*Mr Clarke*) That is a very interesting question. At the moment much of the debate about cannabis at all is about the difficulty of enforcing the legislation which currently exists, particularly amongst young people, but that is a very serious issue for us to address and it is a major factor in the general public debate about these issues. I am sure you are right, that if a specific preparation were found to be efficacious and was therefore authorised and safe and authorised by the MCA, that debate would take a further step forward. I do not think it would be a qualitatively different position to what exists at the moment. In fact, it might even help the situation because, were we able to say that there is a preparation here which, properly authorised, properly licensed and properly prescribed by a GP could help a condition, then that would be a much more defined nature of the debate than what exists at the moment.

30. Could I ask a further supplementary? In the discussions that we have had from the beginning of this evidence you have been defining the rules and regulations for making new products coming on to the marketplace, but what we are dealing with here is a product that can have very particular benefits to a group of people who can gain benefit in no other way. In making your decision on whether you would agree to this licence or not, do you take that into consideration or do you insist on the same level of certainty that you would deal with for a product that might be in general use? I make that point with personal experience. You mentioned heroin that is now being used. I had a shot of heroin when I was in very intense pain once and I thought it was marvellous. Under those circumstances I would not have given a damn what the side-effects might have been. It did its job. For these people who are using these products, they are clearly in that position. I wondered whether you take that into account?

(*Mr Clarke*) Firstly, I acknowledge the accuracy of your point. There is a large number of people, and I am thinking particularly of MS sufferers, and there may be others, who absolutely genuinely believe that cannabis assists their situation and are prepared therefore to take it, whatever the legality of the situation. That is a fact at the moment as we speak. However, the presumption of your question that it is beneficial and it is efficacious is not something that certainly I as a politician could judge. I do not think this is ducking the question but we do have to turn to the authorised bodies, the expertise which is available, and in this case it is for the Medicines Control Agency to make the judgment about the beneficial or other nature of any particular product. That is what we do. I do not think any government minister could operate on the basis that a number of

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people feel that it is OK for them. We have to operate on the basis of being as near as we can get to some kind of objective scientific test and that is what the Agency is trying to assess. I heard frustration raised in earlier questions about the time it has taken to get to that objective test. For the reasons I mentioned earlier from my own constituency, I understand the frustration but for me that does not change the central proposition, that to get to a position of change in the law on this, we need to have a proper scientific judgment which stands up on the basis of proper research. I think that if any government minister were to vary his position from that central proposition, that would be a very rocky ground on the basis of some hunch or view of that kind. We need to rely on that kind of testing which Dr Davis described earlier.

31. You would agree that there is a matter of degree there and it is one thing to say you have a hunch but quite another to say a considerable amount of research, but there are still areas where there might be slight doubt.

(*Mr Clarke*) I agree, but those are precisely the issues, as I understand it, which will be addressed by the MCA on the question of marketing authorisation. Of course that is true but I am not a doctor. There are many distinguished doctors in this room and in the country who can advise on these things. But, as I understand it, every judgment about a drug is about the balance of the issues involved in precisely the way you have described, both from the MCA's point of view in deciding whether to authorise the marketing of a drug but then, from the individual GP's view, in deciding in relation to the particular individual whether the drug should or should not be prescribed. Both of those are serious professional issues, which I think politicians and others sweep aside really at their peril. It is a question of resting upon that structure which is there.

Lord Winston

32. I wonder if we might bring in Ms Judy Sanderson from the Department of Health on this very issue. Lord Wade has raised a very key drug. He has talked about the use of heroin in the management of pain. We all know that heroin is one of the most efficacious drugs for pain relief. It has huge consequences potentially and it is a drug that is less and less given in the Health Service in consequence, but it is still given very often to patients who are quite debilitated. Many of these patients for whom we are seeking perhaps cannabis to be used really do not care terribly much about the pathogenesis because it is a side effect which has been known for at least two or three decades anyway. I wonder whether you feel how the patient's perspective might be particularly within the NHS. You might like to comment on the same points really.

(*Ms Sanderson*) From the Department of Health's perspective, we have to stick to the MCA routine and to test things properly and thoroughly. I appreciate that people with MS often feel very strongly about cannabis. We get some very difficult letters sometimes from people about how difficult their situation is. But we also get lots of difficult letters from other people with other neurological conditions who do not even have the hope that cannabis may one day bring for MS. I appreciate the point that people are in pain and have difficulties but I still think we ought to be going through the proper routine with this and that we should not be deviating just because it is cannabis. These rules are here for a purpose. The purpose in the long term is to protect the patient thoroughly. Often things which are seen as wonder drugs appear and when they are tested out in real life they do not turn out to be quite so wonderful as everybody had hoped at first.

33. One might make the observation of course: I would not be allowed as a doctor nowadays in the NHS to be paternalistic towards my patients. I wonder whether you might not be being a little bit over-protective when we have patients who are seriously ill with diseases and who are quite likely to die in the near future. Would you comment on that?

(*Ms Sanderson*) I am afraid I did not hear that very clearly.

34. I understand your concerns and the need to protect patients of course is paramount but you will be aware that we as doctors increasingly are coming under fire for being over-paternalistic, almost authoritarian it is said in the press at the moment. I wonder whether there is not perhaps a risk of being over-protective to patients who are very debilitated, who possibly have no alternative recourse and who really are suffering from a disease which is so serious that they are not likely to recover and the trivial side effects, because in the main to them they are trivial side effects, are not that serious. I wonder whether you would comment on that, the issue of paternalism in regulating.

(*Ms Sanderson*) I am not a doctor.

35. Of course, but you are a representative of the Department of Health and you are involved with the care of patients.

(*Ms Sanderson*) Yes. The issue of paternalism and doctors goes back a long way. It is coming to the fore at the moment but it is something that has been a cause in concern for some patients for a very long time, the fact that they are not considered to be a partner in their care and treatment. Making somebody a partner in care in their treatment does not necessarily involve giving them medicine which is not at this moment in time prescribable.

(*Mr Clarke*) May I add a point on behalf of the Health Minister? I recognise that Lord Winston's point is obviously true. It applies to all professions, in my opinion, if you have an increasingly educated population. The thing that people are looking for with doctors, as with other professions, is high quality information to themselves to help them make their own judgments and they are looking to the professionals, in this case the doctors, to guide them in those judgments. It seems to me precisely the problem we have in this particular debate is: what is the content of that high quality information? If it is that cannabis is a good thing or even hearsay evidence saying "for me cannabis was a good thing, how does it go?", the question that seems to me to arise for doctors, and indeed for government generally, is: is that sufficient as a basis of

Lord Winston *contd.*]

information for the doctor to give to his or her patient and to give guidance to the patient to deal with the paternalism points that you rightly raise? That is precisely the dilemma we are in at the moment. What is the quality of information which we can give about the use of cannabis or the use of a particular preparation in relation to solving the problems that people experience even, as I acknowledge to you correctly, if it may be for a short time scale, with some of the down-sides not being perceived as an immediate down-side to those particular individuals? I have understood that there is no clarity at the moment about what information a doctor can give to his or her patients on these issues.

Chairman

36. There must be a balance, surely, between the need to have complete security on toxicity and the need to treat patients. The question is whether this balance that has been stated by the MCA is exactly the right one.

(*Mr Clarke*) Dr Davis can say a word about the MCA's responsibilities in this matter but may I make a prior remark? The MCA does have its responsibilities in the matter which Dr Davis has tried to clarify. I will say something in a second about that. Then the question of professional guidance arises in this situation, which is a matter for the professions as to how they operate. I think that is a very interesting question to explore in the light of Lord Winston's remarks about the relationship to the professional and the citizen .

Lord Howie of Troon: I would like to reflect very briefly—I am not asking for a big answer—on this question of partnership because I am not terribly sure about it. By profession I am an engineer. I know how to keep buildings up and I know what makes bridges wobble and possibly how to stop them wobbling, but I do not know anything about medicine. When I go to the doctor, which I do infrequently, I do not really pose as a partner. I am really looking for him to lay hands upon me and cure whatever infirmity I have got. I think perhaps we are being a little bit cautions about this partnership business.

Lord Dixon-Smith

37. May I make an observation on the last few minutes of this particular discussion and that is that is seems to me we are in danger of losing the distinction between specific cannabis products and cannabis itself. I thought I was clear when we began the discussion and the investigation that the MCA were looking specifically at cannabis products. The discussion recently has become slightly more lax, shall we say. That may be partly because of the way the questions have been drafted. I do think we need to keep that distinction very clear in our minds.

(*Mr Clarke*) Perhaps I can apologise if I introduced that into the discussion and simply reaffirm the point that Lord Dixon-Smith has made, that the issue that we as a government are currently considering is that of whether there is a product which can be authorised appropriately by the MCA to deal with these particular issues.

Chairman: We are talking altogether about hypothetical products because these clinical trials have not got underway properly yet. We are trying to look at the situation which will come about when the clinical trials are reported and they are on products undoubtedly.

Lord Haskel

38. May I make the point, Minister? Would you agree that your attitude, from the point of view of the patient, is one in which you might be accused of hiding behind scientific opinion? After all, these scientific matters we now know are never black and white. For people who are suffering and who know that cannabis may and will relieve their suffering, do you not think that from the point of view of the patient, the patient would accuse you of hiding behind scientific opinion so that you yourself do not have to make a decision?

(*Mr Clarke*) That is not an accusation which has been made to me on this matter. Were it made, I would reject it because I think that when one looks at the quality of public decisions, ministerial decisions or whatever, it is exceptionally important to take account of scientific advice. I am a supporter of science. I know there is a tendency around now—I am not suggesting that you, Lord Haskel, are making that point—to denigrate science and to say we know nothing. I do not think that is true. We know a lot of things about many matters and I want to elevate science rather than decry it in its role in informing public decisions, whether in this country or elsewhere. Of course, people look for certainty and some of the most substantial research, including that in the university in my constituency, the University of East Anglia, the Institute of Food Research, is about risk assessment in these matters. There are risks involved. It is only on the basis of good scientific advice and an assessment of the risks that, in my opinion, politicians and everybody else ought to take decisions. I want to see more and better quality and better researched scientific advice rather than to undermine it.

Lord Rea

39. Can I put this in a slightly different way to the Minister? Even if medication containing the components of cannabis is found to be safe, valued and useful, there will be some patients who think that the old-fashioned way of actually smoking the entire herb, or whatever you call it, is better, even though an authenticated product would be available and perhaps prescribable. Will the Home Office's attitude towards those who continue to buy cannabis plant products and smoke them be any different?

(*Mr Clarke*) No, as I answered, I think it was Lord Wade, earlier on.

40. I know it is purely a legal point of view. Might the attitude and the vigour with which prosecutions are carried through be affected?

(*Mr Clarke*) I have to say no to that as well. One of the joys of my position, if I am at risk of being

Lord Rea *contd.*]

accused of hiding behind others again, is that the question of enforcement of the law is a matter of the operational responsibility of chief constables in deciding how to approach the matter. Of course, the question of prosecution is a matter for the Crown Prosecution Service and that they do. Quite rightly, that is not susceptible to ministerial or political involvement. If it were suggested that we ought, as the Home Office or the Special Constabulary or the Association of Chief Police Officers, to issue guidance saying that the law should not be enforced in relation to a particular area, I think that would be a very, very slippery slope indeed for us to go down. I certainly would not be prepared to take that course myself.

Lord Jenkin of Roding

41. May I say that I would not disagree with a word the Minister has just said about the role of the police in prosecuting and so on. I am sure that he and his colleagues will have recognised the note of some impatience on the part of the members of this Committee. The report was produced in 1998. We get the very strong feeling of the authorities dragging their feet. It has been a long time, as Lady Walmsley said, for the MRC trials to get under way. Does this not in fact reflect in some way the astonishingly rapid and negative response by the Home Secretary himself within 24 hours of the report being published and have people taken the tone from that so that it is all taking much longer than it really need have done?

(*Mr Clarke*) There are two questions there. Firstly, on the general question of dragging feet, I have heard the tone of the Committee this morning. I certainly do not feel that the Home Secretary has been delinquent in these issues. In fact, he has made clear from the outset that, as far as the medical issue is concerned, we are very open to that. Dr Davis gave evidence earlier on to you about the time scale issue of the MCA and MRC research. He said that he did not think red tape had been a factor in the time process that occurred but it was a question of how to get into what is a complex situation some authoritative advice. On the second question you raise about the response to Lady Runciman's report, the Police Foundation report, to which a further response will be published either today or tomorrow, it is the case—and not just said by the Home Secretary but myself as well on the media at that time—that the Government's position is that cannabis generally should not be legalised. The reason for that in summary is that we think it is likely that the legalisation of cannabis will increase consumption of cannabis and that that would be deleterious to the public good in a variety of different ways. We could have said, "We are not saying our position will wait as the considerations are too important". I think that would have been wrong because it would have led to uncertainty about what the Government's position on this was. I certainly felt it important, as the Minister responsible, to make our position clear at that time and then to go through the great detail which we have to respond the other 67 detailed recommendations of the report, many of which we agree with and many of which we support on this central issue of the legalisation of cannabis. I think it would have been absolutely mistaken to send any messages or signals that the Government was considering modifying its position.

42. With the greatest respect, that was not what Lord Perry's sub-committee recommended.

(*Mr Clarke*) I do beg your pardon. I misunderstood completely. I thought that Lord Jenkin was referring to Lady Runciman's report.

43. No. I am referring to the report that we are following up here.

(*Mr Clarke*) The last half of that answer is based entirely on a misapprehension.

44. We accept that. This report, Lord Perry's sub-committee's report, recommended very firmly that cannabis and its derivatives should continue to be controlled drugs. The point I think I made earlier was that a lot of the official response to this took its tone from the very swift and negative response of the Home Secretary. He gave the impression that he perhaps had not understood the limited nature of the recommendations that were being made in this report. I wonder whether you could comment on that?

(*Mr Clarke*) Firstly, I beg your pardon for the misapprehension, and I apologise for that. The report was published on 11 November 1998. In fact the same reason I gave earlier led the Home Secretary to take the view that he did, that to allow speculation to develop around this area would be mistaken. We have tried to be as clear as possible around the issues and the evidence that I have just given over a consistent period of time, that we are more than ready to legislate in this area once we are clear that a medicinal product can be developed and is authorised by independent and properly researched advice. I think it would have been mistaken, although as I say I was not in the Department at the time and was not the Minister, if we had kept that issue open for a very long period, which would have been necessary as we were waiting for the outcome here. It is important to set out our position. It certainly was not intended, I am sure, by the Home Secretary to be offensive to the Committee. I am sure he would want me on his behalf to apologise to the Committee if that was how it was taken. There is always an issue, Lord Jenkin, and your Lordship is a very experienced senior government minister, about when documents come out from various sources, whether one simply lets the issues run without comment or tries to set out as clearly as possible what the Government's position is on the issue. The Home Secretary made the judgment he did at that for that reason.

Lord Jenkin of Roding: My Lord Chairman, I will let the matter rest there.

Lord Haskel

45. Dr Davis made the point that he would not like to comment on the decision made in Canada. I accept that point. To what extent are you taking notice of developments in other countries? For instance, do you regard the medical programmes on marijuana to be advisable?

Lord Haskel *contd.*]

(*Mr Clarke*) The broad issue is that Government is very much interested in and does take notice of scientific research and development made in other countries such as the licensing of Marinol, a medicinal form of dronabinol, the main active ingredient of cannabis, in the USA. But evaluation and detailed consideration of such developments is a matter for the Department of Health and the Medicines Control Agency. We are also aware that there is growing interest in the possible medicinal uses of cannabis in a number of other countries. You mention Canada in your question. Dr Davis has answered about Canada earlier. We understand that the Canadian Therapeutics Products Programme is currently examining the steps required for the cultivation and distribution of a cannabis-based medicine. The Committee may be interested to know that representatives of this programme have met with Home Office officials to learn more about the UK's policy on this issue and about the licensing of cannabis research in the UK. That is for the general reason that we are in favour of interchange of information on these issues as much as possible. We are also aware of the so-called "medical marijuana" programmes in several of the US states. Alaska, Colorado, the District of Columbia, Nevada, Oregon and Washington State have voted to allow the cultivation and use of cannabis by individuals for medicinal purposes. However, whilst a few individual states permit the medicinal use of the drug, the US Federal Government is opposed to the use of cannabis for medicinal purposes in the absence of a scientifically proven medicinal form of the drug; i.e. broadly speaking the position I have been arguing before this Committee. The US Government has made clear that it opposes such initiatives for the following reasons. Firstly, that they undermine the medico-scientific process for establishing what is a safe and effective medicine. That is precisely the issue for your Committee. Secondly, that they contradict federal drugs regulations and laws. We have indicated for our part that, in the event we get a clear process, we are prepared to amend our laws. Thirdly, that they might be vehicles for the legalisation of cannabis for recreational use. I have tried to answer that in relation to Lord Howie's question and then Lord Porter's question. We regard the scientific question here as pre-eminent. As far as the other European Union states are concerned, we understand that in Holland the use of cannabis for both medicinal and recreational purposes remains unlawful. However, whilst the possession of cannabis remains illegal, the laws are not in practice enforced in Holland. Dutch drugs policy has facilitated the sale and possession of cannabis for personal use through the system of coffee shops and cannabis cafes. Under existing guidelines, the Dutch authorities take no action against those in possession of small quantities of cannabis for personal use, whether it is for medicinal or recreational use. As a question of actual policy, the medicinal or recreational point is not a matter which they take into account. Elsewhere in the EU, we understand that three other countries, Italy, Spain and most recently Portugal, have decriminalised or want to decriminalise the consumption and possession of small quantities of drugs, including cannabis. Their drugs laws therefore facilitate the use of cannabis for both medicinal and recreational purposes. So again a distinction as between medicinal and recreational is, as I understand it, not drawn. I am sorry to have given such a lengthy answer but I thought I had better get on the record the extent of our awareness of what is happening elsewhere. The short answer is that we do try very hard to take account of what is happening in other countries. We are very much focused on the medical issues and what is happening in developments there.

46. Thank you very much for putting that on the record. From what you have just told us, it is quite obvious that in many countries where people from Britain travel to or from on holiday or for work the attitude is rather more tolerant than the attitude of the Government. Do you think that this is going to help bring about maybe a swifter decision or perhaps a more tolerant attitude of Government towards the medical use of cannabis?

(*Mr Clarke*) There are general issues involved in the use of cannabis where I think you are certainly right. Experience in other countries will inform the public debate in this country and indeed people travelling to other countries draw their own conclusions about that process. But we distinguish, and have tried in this Committee this morning, between the general use of cannabis—about which there is a debate and discussion but which the Government strongly opposes, for the reasons that have been set out and in particular we believe the likelihood that consumption will increase which we consider will be generally deleterious to the public interest—and medicinal use where we have a much more, I hope the Committee will agree, constructive approach. That is to be very positive about changing the law in the event that the medicinal evidence stacks up in the way that we judge by the MCA view.

Baroness Walmsley

47. I would like to return to the issue of the prosecution of therapeutic cannabis users to which you referred briefly earlier. We have received evidence that there is enormous inconsistency in the outcome, particulary of some of these prosecutions, ranging from acquittal to custodial sentences. We know from what you said earlier that of course any decision to prosecute is not taken by the Home Office but by the CPS. There is a concern that the prosecution of therapeutic users of cannabis is currently very inconsistent. We wonder what can be done about it. Do you think that the postcode prosecuting of therapeutic cannabis users is fair? Perhaps this is where the Home Office could come in: should there be national guidelines for the CPS in these cases and, if so, who should lay them down?

(*Mr Clarke*) Firstly, two contextual points, if I might: I would not accept the phrase "postcode prosecuting". I am aware that "postcode" is now put in front of just about any decision where there is local discussion in the country to emphasise a point. As I am not in favour of moving to a Stalinist state, where everything is decided locally essentially on every issue that comes along, I have to reject the phrase. There are serious issues about prosecution practice and

Baroness Walmsley *contd.*]

sentencing practice across the country in this area, as in many other areas, and that is one of the matters that is currently being considered by Lord Justice Robin Auld in his Review of the Criminal Justice System because the question you raise in this area is highly relevant to other areas of law, too. The question of what form of guidance and how we can move forward is a very live issue. I am not going to prejudge the outcome of Lord Auld's report, which will be published in the next few weeks. I certainly acknowledge on the record that the concern you raise is one that does exist and exists right across a range of different offences in the decisions that are taken. The second general contextual point is that in 1998 there were 89,000 cases involving possession of cannabis. 1998 is the last year for which we have publised statistics. While we do not keep data on any offences by reference to the defence offered by the accused, all the available evidence suggests that the prosecution of persons using cannabis for therapeutic reasons, as opposed to cannabis more generally, is rare. I say this noting, as your question does, that such cases tend to attract a high media profile and so it is unlikely that there are many more prosecutions of medicinal users of cannabis than those of which we are aware. In view of the relatively small number of such cases per year, I do not think there is sufficient data to support the allegation of a serious distortion of practice across the country in this particular area. In cannabis use more generally, there may be more of an anomaly in particular areas, that is true. As I said earlier, prosecution is a matter for the CPS and the Attorney General and I cannot comment on those things. As far as the police are concerned, I would like to make some comments and about the actions of the CPS based on our dealings with them. Firstly, we have to be clear that possession of cannabis is a criminal offence, whether it is for recreational or therapeutic purposes. However, in relation to both therapeutic and recreational uses of cannabis, our criminal justice system, in my view rightly, provides for the exercise of discretion at various stages. Firstly, it is for the police to decide what action to take. The use of cautions by the police is widespread for minor drugs offences but the extent of their use does vary between police force. In order to address this and improve consistency between forces, the Association of Chief Police Officers (ACPO) issued guidance on the use of cautioning in early 1999, for exactly the reason implied. That ACPO guidance includes a range of scenarios, one involving a genuine case of the medicinal use of cannabis. It advises that police officers verify, where possible, the medical condition of the offender and that, depending on other factors such as any previous offences, a caution may be appropriate. It is obviously early days in respect of the ACPO Cautioning Guidelines that I have just mentioned but already provisional 1999 cautioning data has shown a slight narrowing in the cautioning range, indicating that the guidelines are beginning to have an effect on the practice and conduct on the use of discretion by different police forces. I believe that the specific reference in the ACPO guidelines shows that the police are sympathetic to those with genuine medical conditions who are not helped by existing therapies in deciding how they use their discretion in enforcing the law. However, there will inevitably be some cannabis users who make false claims of medical need. In cases where the police are minded to prosecute, the final decision rests with the CPS. CPS lawyers, and this is the second point, are guided by the Code for Crown Prosecutors, which constitutes national guidelines. In relation to drugs offences, I understand that the Code says that possession of small amounts of drugs may not always require a prosecution. That is what the current guidance issued by the CPS says. The Code also requires prosecutors to weigh public interest factors. Such an assessment, based on the individual circumstances, is right and proper. The Attorney General has previously stated that it would be contrary to our legal principles to go further towards a structured use of prosecutor discretion. That is one of the issues being considered by Lord Auld in his review. The final discretion is of course by the court. Where a case is prosecuted and a conviction results, the court has discretion to take account of the circumstances of the offender and the offence before passing sentence. At the three levels of discretion, (a) police discretion; (b) the CPS discretion; and (c) the court's discretion in deciding what to do, on the first there are guidelines issued by ACPO which try to narrow the differences. On the second, the CPS, there are Crown Prosecution Service guidelines which address these areas. Then of course the courts are a law unto themselves.

48. Would you therefore agree that, if we are relying on three levels of discretion, we will still have these high profile inconsistencies, which could very well serve to undermine the confidence of the public in the law and therefore to be regretted?

(*Mr Clarke*) As I said in the early part of my answer, the central thesis that you make clear is one I accept, that wide variations in practice across many different types of law can undermine confidence. That is why that is one of the issues being addressed by Lord Auld in his review. The Prime Minister gave great attention to that matter in establishing the review. On the particular question you raise about prosecutions for the medicinal use of cannabis, I do not accept the fundamental proposition. I think the variations issue is much less sharp than it is either for cannabis misuse as a whole across the country or indeed for some other offences.

Lord Quirk

49. Granted, as you say, that prosecutions of medicinal users of cannabis are really rather rare, where they do occur, the media seize on them. The second part of this question is the real nub of what I would like to raise. The general public seems to agree with the courts being very lenient in such cases when they are prosecuted. But in the three years since Lord Perry's sub-committee reported in November 1998, do you feel that there has been a change in the public perception of cannabis offences, whether for therapeutic or for recreational purposes, and that the distinction between the two has become a bit blurred? In your answer to an earlier question, you said that if we were to proceed to approve the medical use of certain cannabis products, nonetheless it would remain illegal, even for therapeutic purposes, to take something that had not been approved. Do you not

Lord Quirk *contd.*]

feel that there will have to be more a serious look at the whole issue of the illegal use of cannabis, with some help and guidance given to the police forces which have to administer at the moment a law which many of them feel does not have public support?

(*Mr Clarke*) Firstly, I am speaking without the benefit of public opinion research in terms of answering your particular question as to how public attitudes have changed over the last three years, so I am speaking impressionistically. I think the effect of Lord Perry's report, and indeed the general debate, has actually been the reverse of what you imply, in the sense that I think there is now a much sharper awareness of the distinction between medicinal use of cannabis and recreational use of cannabis in the public debate. As I have heard it since I have had this responsibility in this job, for 18 months, I believe that the debate is quite different around the medicinal use of cannabis to that around the recreational use of cannabis. I think that distinction is much sharper than I certainly recall it being before. To what extent Lord Perry's report can take credit for that, I am not certain, but I certainly think that debate has sharpened in what I regard as a generally helpful way. Certainly the way the Government has tried to respond is to try to draw distinctions in the way that we approach this as to medicinal and non-medicinal use of cannabis. I should have said, in answer to the previous question on guidance to the courts, that, obviously while no actual guidance is given by the Government to the courts, the Court of Appeal has issued sentencing guidance covering drug offences, including the possession of cannabis. That Court of Appeal guidance says that when only small amounts are involved being for personal use, the offence can often be met by a fine. I understand that sentencing data confirmes in that this guidance is being followed. I should add that in response to the earlier position. That sets out a set of attitudes which I have tried to go through—the police, the CPS and the court—which I think reflects, shall I say, an understanding that where cannabis is used for medicinal purposes, that is to be considered in a somewhat different light to purely recreational use and certainly to the use of much more serious drugs and drug dealing across the whole range. I still believe, and I think the Government's position is absolutely right and defensible, that we should focus on medicinal issues, which are in fact the issues that Lord Perry's committee rightly focused on, and rest upon the medical authority for scientific evidence which is developed through the MCA.

50. You made a very good point earlier about the medical use of heroin as distinct from, so to say, the recreational use of heroin. Is it your belief that such a clear distinction, which is apparently widely accepted throughout our society, can be maintained in the case of cannabis, if cannabis products do become medically acceptable?

(*Mr Clarke*) My answer is provisional on your final clause. In the event that MCA did come to the view that authorisation ought to be offered, then I think the distinction can be drawn in that way. There is a hypothetical question: in the event that that happened, to what extent would, for example, MS sufferers want to use cannabis as opposed to the medicinal preparation? That really is absolutely unknown until such a preparation were on the market. I take the point and I do not think any speculation would be constructive because, by hypothesis, if the MCA come to the view that it was efficacious and its marketing ought to be authorised, then MS users who were benefiting, in their perception, from cannabis would expect to benefit from this product if it were available to them. Working on the assumption that it would not work for them but cannabis raw, as it were, does is not a fruitful area until we have some idea what the MCA position actually is.

Lord Jenkin of Roding

51. Very briefly, I hope the Minister is indeed right, that there is now a much greater understanding of the distinction between the recreational and the therapeutic uses of cannabis. You will remember that some of the views that the Committee had were very critical of the legalise pot movement. There were processions through the streets with MS suffers in wheelchairs, as if it was all part of the same argument. We heard the argument that Lord Quirk has made about heroin and the example earlier from Lord Wade. I do not believe for a moment that the fact that doctors can prescribe heroin for cases of serious pain has in any way undermined the legal authorities' position in treating heroin as a very dangerous drug, which has to be available only on prescription. Is not the lesson that if the Government can move towards facilitating the therapeutic use of cannabis, that actually could strengthen their hand against the widespread use for recreational purposes?

(*Mr Clarke*) I agree with that, always again subject to the proviso that medicinal use is an effective way of operating. I can say to Lord Jenkin that as a practising politician who opened a major retail centre in the middle of my constituency in Norwich some years ago, one of my opponents in the last general election was a drug dealing candidate. Harold Marks was a convicted drug dealer and he was standing in the legalising of cannabis campaign. It was a serious aspect in the election and was brought into my particular election generally. I do believe that Lord Jenkin is completely right, that if we could sort out, (a) the cynicism of some of those campaigning for that position, and (b) if we could get them to support issues clearly, that would help facilitate the debate on the wider use.

Chairman

52. May I ask a final question? We know that heroin is a far more dangerous drug than cannabis. We also know that most of the new drugs that are licensed by the MCA have much more serious side-effects than cannabis. Can we be assured that the insistence on the work in the use of the normal programme of testing that is used by the MCA for new drugs is not based on the fact that cannabis is used recreationally?

(*Mr Clarke*) I can give that assurance and I have tried to say throughout, and I am happy to have the opportunity in closing to reassert the point, that our

Chairman *contd.*]

policy concerns in this issue are entirely scientific and medical and not more general, political, cultural, crime-related or whatever. It is that medical and scientific basis upon which the Government will take its decision whether to change the law. Again, to reassert it, we will not do it without some substantive medical judgment being made on these matters in the appropriate way, which I think is through the Medicines Control Agency.

Chairman: Thank you very much.

WRITTEN EVIDENCE

Memorandum by the Alliance for Cannabis Therapeutics: A Patients' Organisation

OBSERVATIONS BASED ON CORRESPONDENCE TO ACT

It seems that more people with MS and other seriously ill people are trying cannabis, judging from the correspondence to the ACT over the past two years. We have received over a hundred letters from patients asking if we can supply cannabis. An interesting development is that the doctors who are treating these patients have begun to suggest they try cannabis, even though it is illegal and unlicensed.

Another development is that there are now several supply networks set up by patients to supply each other. The founder of one such network, Colin Davies who has severe back injuries, was tried at Manchester Crown Court in July 1999 charged with cultivation and possession with intent to supply. He did not deny that he was supplying people with MS, but claimed medical necessity. He was acquitted on all charges.

SUGGESTIONS FOR ACTION

Immediately directives should be given from Government as to how the police should proceed in cases where the defendant has a serious medical condition.

We susggest that if a patient has a written recommendation from their doctor, they are allowed to grow up to eight plants at home for their own use.

Court cases which have come to public attention concerning medical use of cannabis since the publication of the House of Lords Select Committee's report on Cannabis in 1998: this list has been compiled from press cuttings:

September 2000

Lezley Gibson, MS Sufferer. Charged with possession. Carlisle Crown Court. Aquitted.

March 2000

Thomas Yates from Lowestoft, Suffolk. MS Sufferer. Charged with possession and cultivation. Acquitted.

2000

Neil McLaughlin-Winters, MS Sufferer. Shetland Sheriff Court. Fine.

July 1999

Colin Davis, Severe Spinal Injuries. Charged with cultivation and possession with intent to supply. Manchester Crown Court. Acquitted.

July 1999

Albert James, Rheumatic Pain. Charged with possession. Old Bailey. Conditional discharge.

February 1999

Eric Mann, Sufferer of Arthritis. Charged with cultivation and possession. Swansea Crown Court. One-year custodial sentence.

December 1998

Brian Gilday. Possession with intent to supply to his mother who is in pain. Edinburgh High Court. 200 hours community work.

Clare Hodges

1 December 2000

Memorandum by GW Pharmaceuticals Ltd

GW Pharmaceuticals Limited (GW) is a private UK pharmaceutical company working under Home Office licences to develop non-smoked prescription medicines derived from cannabis. GW's medicines consist of extracts of specific cannabis plant varieties incorporated into advanced drug delivery technologies, such as sprays and inhalers. These products undergo full scale pharmaceutical development programmes with a view to obtaining approvals as prescription medicines from medical regulatory authorities such as the Medicines Control Agency (MCA).

The beneficial therapeutic effects reported by patients who use cannabis result from the interaction of certain cannabinoid molecules in the plant. GW's products are all sourced from specific cannabis plant varieties which the company has bred so as to exhibit a pre-determined ratio of selected cannabinoids. GW's clinical trials have demonstrated that different ratios of cannabinoids have important different therapeutic benefits. Indeed, cannabinoids have been shown to have analgesic, anti-spasmodic, anti-convulsant, anti-tremor, anti-psychotic, anti-inflammatory, anti-oxidant, anti-emetic and appetite-stimulant properties. Research is also ongoing into the neuroprotective and immunomodulatory effects of cannabinoids. To date, GW has focused on two principal cannabinoids: Delta 9 Tetrahydrocannabinol (THC) and Cannabidiol (CBD).

Since the company's inception in 1998, GW has developed a system of cannabis cultivation to produce commercial quantities of selected cannabis chemovars (defined by chemical content of cannabinoids) suitable for extraction to pharmaceutical grade preparations. Preparations of various defined cannaboid ratios have been analysed and formulated into a range of non-smoked drug delivery systems. The most advanced set of products at this time are those being delivered using the sub-lingual (under the tongue) route of administration, by means of a spray or rapidly dissolving tablet.

In order to obtain regulatory approval for a prescription medicine, each new medicine is required to undergo extensive pre-clinical testing as well as Phase I, II and III clinical trials.

- Phase I—Conducted in healthy volunteers to provide evidence of safety. The trial also examines the pharmacokinetic profile of the drug—the absorption, distribution, metabolism and excretion of the drug by the human body and its biological effects on humans.
- Phase II—Requires detailed submission to MCA on quality and safety of test medicines before commencement and approval to proceed from MCA. Conducted in limited number of patients to assess short-term safety and preliminary efficacy. Appropriate dose ranges and regimens for Phase III trials are also determined.
- Phase III—Requires more detailed submissions on quality, safety and efficacy to MCA. Comprehensive evaluation of safety and efficacy in large numbers of patients.

Following initial volunteer Phase I studies (September 1999) to establish safe dosage regimen, tolerability and clinical pharmacology, GW has been able to satisfy the MCA with regard to quality and safety of its cannabis-based medicines in order to gain approval to proceed on to Phase II trials designed to explore efficacy in patients. This approval (known as a Clinical Trial Exemption certificate or "CTX") forms an essential step in the pivotal regualatory development programme for a prescription medicine and was a critical milestone for the company.

In addition to these CTX trials, independent physicians undertaking trials under their own responsibility are using GW materials under DDX approvals (Doctors and Dentists Exemption certificate). However, it should be noted that DDX trials on their own are insufficient to support regulatory applications. Nevertheless, they are helpful to GW in that they serve to provide important additional information on its test medicines.

The MCA has to date issued to GW CTX trials approvals covering:

- Relief of pain of neurological origin and defects of neurological function in Multiple Sclerosis, Spinal Cord Injury, Peripheral nerve injury, Neuro-invasive cancer, and Dystonias.
- Relief of pain and inflammation in Rheumatoid Arthritis.

Over 40 patients, principally suffering from Multiple Sclerosis or Spinal Cord Injury, have entered the exploratory efficacy trials so far. Thirty-seven patients have progressed to long-term safety assessments of whom virtually all have experienced significant alleviation of at least one key symptom and in some cases the improvement has been sufficient to transform lives. These improvements are particularly notable in that they have occurred in a group of patients whose symptoms have been considered intractable in the face of all available standard therapy.

Among the positive effects recorded are: relief of neuropathic pain, spasms, spasticity and bladder-related symptoms; partial relief of tremor; improvements in quality and length of sleep; improvements in mood and measures of overall well-being.

Adverse effects have also been reported, and most of these seem to occur early in the treatment periods and diminish as a suitable dose is arrived at by self-titration. Almost all of these effects have been transient, of only mild or moderate intensity, and generally well tolerated by the patients. In GW's trials, most patients

have been able to self-titrate (adjust) to a dose which achieves useful symptom relief without the handicap of unwanted psychoactive effects which would interfere with ordinary daily activities.

In addition to its clinical trials programme, work continues with other research and development activities including: improved cultivation and harvesting techniques; evaluation of alternative extraction methods; introduction of Good Manufacturing Practice for extraction, formulation and finished product manufacture; refinement of analytical methodologies and Quality Control procedures; preparation of internal standards; full Good Laboratory Practice stability programmes; pre-clinical pharmacology and toxicology; development of Anti-Diversionary Packaging; remote patient monitoring and systems integration.

GW has supplied cannabis extracts for pre-clinical research as well as clinical trials to academic researchers and clinical investigators (undertaking DDX trials) both in the UK and abroad. GW has supplied all extracts to third parties free of charge.

GW recently achieved approval from the Canadian regulatory authorities to commence Phase II trials in Canada. Although the Canadian regulatory authorities have stated that they do not require additional animal toxicology studies, consideration is currently being given by the MCA in the UK as to whether long-term (two years) carcinogenicity studies in animals would be required to support the use of CBD in chronic conditions such as Multiple Sclerosis.

Subject to confirmation from the MCA of no further toxicology requirements in addition to those already undertaken by GW to date, and satisfactory Phase III results, the initial cannabis-based medicine product delivered by means of a sublingual spray could be available for prescription in the UK by 2003. In the event that long-term animal toxicity studies are required by the MCA for Multiple Sclerosis and other chronic conditions, then the time to approval in the UK for those conditions may be considerably longer.

GW has worked closely with officials from the Home Office in order to ensure compliance with all regulatory and legal issues surrounding this research and development programme. The company is very grateful for the Home Office's valuable support and advice. In addition, we are grateful to the MCA which has provided helpful advice and comment on our overall plans for research.

In conclusion, GW is focused on bringing prescription cannabis-based medicines to patients in the shortest time possible. The company's programme has proceeded at a considerable pace and, indeed, for GW to have reached Phase III clinical trials in less than 30 months from initial planting of the very first cannabis plants represents remarkable progress by any pharmaceutical industry standard. At the time of the publication of House of Lords Science & Technology report on cannabis in November 1998, GW stated that it hoped to have a prescription medicine available for patients in 2003 and, subject to the MCA not requiring long-term animal toxicity studies to support use in chronic conditions, the company's programme remains on target. GW believes that this represents the best solution for patients for whom cannabis may provide substantial medical benefit.

G W Pharmaceuticals

25 January 2001

Memorandum by the Home Office

The Government's policy on the medicinal use of cannabis remains as set out in its response to the Committee's 1998 report, namely, that it believes it would be premature to amend the misuse of drugs legislation to allow the prescribing of cannabis before the quality, safety and efficacy of a medicinal form of the drug has been scientifically established and a marketing authorisation has been issued by the Medicines Control Agency. As the Committee is aware, this is the procedure that all prospective new medicines have to go through in order to protect public health.

If the clinical trials into cannabis are successful and lead to a medical preparation which is approved by the Medicines Control Agency, the Government has made it clear that it would be willing to amend the misuse of drugs regulations to allow the prescribing of such a medicine.

It should be emphasised that the key determining factor is the issuing of a marketing authorisation for a cannabis-based medicine by the MCA, following the completion of successful clinical trials.

Following the issuing of a marketing authorisation (product licence) by the MCA, the Government would set in hand the necessary changes to the misuse of drugs legislation. The Advisory Council on the Misuse of Drugs would have to be consulted before any changes could be made—in accordance with sections 7 and 31 of the 1971 Act.

The changes could then be made swiftly, by way of secondary legislation subject to negative resolution, and would not be constrained by our obligations under the UN Convention.

Changes would be required to two statutory instruments:

— the removal of "cannabis" from Part I of the Schedule to the Misuse of Drugs (Designation) Order 1986 (which specifies the controlled drugs which are designated as drugs to which section 7(4)of the Misuse of Drugs Act applies); and

— the transfer of "cannabis" from Schedule 1 to Schedule 2 (or 3) of the Misuse of Drugs Regulations 1985.

The medicinal use of cannabis is sometimes used as a stalking horse by those who favour legalisation for recreational purposes. However, much of the correspondence the Home Office receives from members of the public suggests an encouraging level of understanding that the two issues—medicinal and recreational use—are quite separate.

Memorandum by the Medicines Control Agency

The Committee asked the Medicines Control Agency (MCA) to comment on why the Agency refused to extend administration of treatment beyond 15 weeks in Dr Zajicek's proposed clinical trial of Cannador (cannabis oil capsules), Marinol (Δ9 tetrahydrocannabinol (THC)) and placebo capsules in 660 patients with multiple sclerosis (MS) related spasticity (ie the CAMS study).

1. Introduction

The Agency did not grant an extension of treatment because of a concern about the safety of Cannador capsules. In particular, Cannador capsules contain 5-30 per cent cannabidiol (CBD) and the Agency has a concern about the toxicity of CBD.

In response to the Select Committee's request, the Agency sets out below:

— the scientific basis for the decision;

— the means the Agency has used to audit that decision;

— the results of that audit.

This response also outlines the Agency's plans to evaluate additional information about the toxicity of CBD that was received by the MCA in late December 2000.

2. Dr Zajicek's Trial (The CAMS Study)

2.1 *Clinical Trial Design*

The CAMS study has been designed as a multi-centre, three-arm, randomised, placebo-controlled trial of Cannador (cannabis oil), Marinol (THC) and placebo. The primary trial objective is to assess and compare the efficacy and safety of the products in the treatment of spasticity arising from multiple sclerosis (MS) in 660 adult patients. Because it is uncertain which cannabis preparation may be most suitable for therapeutic use, the CAMS trial will investigate whether Cannador (70 per cent THC plus 30 per cent CBD) is better than Marino (100 per cent THC) in alleviating spasticity.

3. MCA Clinical Trial Evaluation Procedures

3.1 *Legislation and Guidance for Clinical Trials*

The MCA is charged with protecting public health. In the case of clinical trials, the Agency is required to protect trial subjects from exposure to investigational products that have not been adequately tested for toxicity and/or are not of a suitable quality. Furthermore, the Agency must ensure that there is a scientific basis for the proposed trial and that the risks have been properly weighed. These duties are carried out under the powers of the Medicines Act and its secondary legislation.

The Agency provides written guidance to applicants for Clinical Trial Certificates (CTC) and Clinical Trial Exemptions (CTX) in Medicines Act Leaflet 4 (MAL 4).

The Agency provides written and oral guidance for applicants for DDX by correspondence or by phone.

The Agency evaluates applications for CTCs, CTXs and DDXs differently.

For a CTC, professional assessors, from the Agency's Clinical Trials Unit, prepare a report from the detailed original scientific evidence provided by the applicant to demonstrate the quality of the product and support the product's safety based on pre-clinical and clinical data. The application and the Agency's assessment are considered by the Committee on Safety of Medicines (CSM). The CSM advises the Licensing Authority about whether to grant or refuse a CTC.

For a CTX, professional assessors, from the Agency's Clinical Trials Unit, prepare a report based on similar evidence to that required for a CTC that has been summarised by the applicant and certified by a doctor. The professional assessors evaluate the notification looking for evidence of safety concerns arising from the data provided by the applicant or from the lack of key data considered essential by the assessors to provide reassurance about patient safety.

For a DDX, the notification normally includes very limited information about the trial and the product. This is because firstly, doctors and dentists have the clinical freedom under the Medicines Act to conduct any

clinical trial and, secondly, many of the proposed trials are with licensed products but for new indications. The relevant professional staff within the Agency review the DDX notification. If the Agency has a safety concern based on either the information provided or on "in-house" information that the applicant may not be aware of, the Agency may refuse the exemption and, either ask for additional information, or inform them of their right to submit an application for a CTC which will be considered by the CSM. On the other hand, if the Agency has a safety concern but is reassured by "in-house" information, the Agency may use that information to allow a trial notified under a DDX to proceed.

4. MCA's Evaluation of Dr Zajicek's DDX Notification

The Agency worked with Dr Zajicek and advised him about the pharmaceutical, pre-clinical, and clinical information needed to support his DDX notification.

Because Cannador is an unlicensed product, more information was sought about its production and the controls applied during the manufacture. The Agency asked Dr Zajicek if he was able to provide any further evidence about the toxicity of Cannador or CBD because independently the MCA had also previously requested reassurance from another applicant for a clinical trial exemption about the toxicity of CBD. In response Dr Zajicek provided an excerpt from the Investigator's Brochure of Cannador about the toxiocology of cannabis extract and a brief report on the effects of CBD. The Agency evaluated this information and advised Dr Zajicek about its concern about the lack of pre-clinical data to support the risk evaluation for the long-term exposure of patients to CBD.

The Agency approved Dr Zajicek's DDX notification in September 2000. This approval permitted exposure to Marinol (THC) for the initial 15-week phase of the CAMS trial and for a further year for patients who experienced clinical benefit. The Agency decided that the duration of exposure to Cannador (70 per cent THC + 30 per cent CBD) should be limited to the initial 15-week phase of the CAMS trial. The Agency advised Dr. Zajicek that the decision to limit the duration of exposure to Cannador would be reviewed when further safety data became available that provided reassurance about the toxicity of CBD.

5. MCA's Safety Concerns

5.1 *Guidelines*

There are European guidelines[1] on the pre-clinical toxicity studies needed to support the use of a medicine in a clinical trial. According to those guidelines repeat-dose toxicity studies in two species (one non-rodent), of duration equal or greater than that proposed in the clinical trial up to a maximum of six months in rats and nine months in dogs are required on the intended test material before a trial can be considered. In addition, the guidelines require reproductive toxicity studies to assess the effects on embryo-foetal development and mutagenicity data to evaluate the potential for genotoxicity, but they do not require carcinogenicity studies.

5.2 *Toxicity of CBD*

The Agency's major safety concern about the CAMS trial in September 2000 was the lack of data on the general toxicity, mutagenicity and reproductive toxicology of CBD.

Dr Zajicek did not provide any novel or robust pre-clinical data on exposure of rodents or non-rodent species to CBD.

The Agency had to rely on "in-house" data from published literature on animals exposed to inhaled smoke from marijuana. There were virtually no data on the mutagenicity of CBD.

The preclinical studies with inhaled marijuana showed it to be toxic to the embryo but they did not distinguish whether THC, CBD or other active compounds were responsible.

The Agency considered that, because of the chemical differences between THC and CBD, it could not extrapolate the findings from THC to CBD.

5.3 *Toxicity of THC*

Information provided in Dr Zajicek's DDX notification in September 2000 provided reassurance that exposure to THC for the initial 15-week phase of the CAMS trial and the proposed extension of treatment in responding patients for a further year was acceptable.

The studies showed some toxicity. Oral THC was toxic in the rat affecting the uterus, ovaries and testes. Stopping the exposure for eight weeks did not reverse the testicular effects. Whilst exposure for two years in the rat produced no evidence of increased cancer risk, exposure for two years in the mouse increased the

[1] Note for Guidance on non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals. CPMP/ICH/286/95.

incidence of thyroid gland neoplasms and thyroid cell enlargement at all doses. Literature reports of mutagenicity studies incidated that THC was not genotoxic.

Overall the Agency concluded that there was adequate information on the toxicological profile of THC to justify the proposed long-term exposure to THC in the CAMS trial.

5.4 *Toxicity of other Cannabinoids*

Studies of crude extract of cannabis are difficult to interpret because they do not distinguish which active component of the extract is responsible for the findings. Also there is the possibility of interaction between components that may mask or enhance a toxic effect.

After repeated-dose oral administration in the rat of a crude extract at up to 1,500 mg/kg/day for 119 days, slight histopathological changes were noted in bone marrow, spleen, adrenals and testes. Reports of reproductive toxicology studies indicated that marijuana was toxic to the embryo. The evidence for teratogenicity was considered equivocal. However, it was considered debatable that THC was a teratogen at the exposures achievable in man. Exposure of dogs (the only non-rodent species tested) to marijuana smoke produced changes in the airways as expected.

6. MCA's Decision on Dr Zajicek's Application

Dr Zajicek provided adequate preclinical evidence to support the exposure of patients to THC for the 15-week initial phase of the CAMS trial and for the one-year extension phase. Thus patients could be exposed to Marinol for the extension phase.

Dr Zajicek submitted extremely limited pre-clinical data on CBD. The only "in-house" safety information on CBD was based on exposure to inhaled marijuana smoke, where the precise content of CBD was unknown. However, the Agency considered that there was likely to have been some exposure of animals and humans to CBD in inhaled marijuana smoke. But, the dose was unknown and unlikely to be as high as that from the 30 per cent CBD in Cannador. The Agency decided to allow 15 weeks' exposure to CBD (Cannador) in the initial phase of the CAMS trial but not to allow the proposed extension of this exposure by a further year until the Agency received more robust pre-clinical data from Dr Zajicek or other sources.

7. Audit of MCA's Decision

The Agency responded to the Committee's request to comment on its decision on the CAMS trial by undertaking an audit as follows:

- An Agency pre-clinical professional assessor made an independent evaluation of Dr Zajicek's DDX notification;
- Four expert toxicologists drawn from the members of the Committee of Safety of Medicines were independently invited to review a summary of the pre-clinical data about THC and CBD available to the Agency in September 2000. Also, to review the Agency's decision to limit exposure to CBD (Cannador) in the initial 15-week phase of the CAMS trial.

The Agency's assessor and each of the CSM experts concluded that Dr Zajicek had provided insufficient information on the toxicity of CBD to allow patients to be exposed to Cannador for more than the 15-week initial phase of the CAMS trial.

They considered that the Agency's decision was justified and that without sufficient data on CBD it was wise not to allow the extension phase of the CAMS trial.

They agreed that the pre-clinical data in Dr Zajicek's notification taken in conjunction with "in-house" data was sufficient to allow exposure to Marinol for the 15-week initial phase and the one-year extension phase of the CAMS trial.

8. Additional Information on CBD

Other sources, including a literature search, revealed information on the general toxicity of CBD in late December. These data include 90-day repeat oral dosing toxicity studies in both rodents and a non-rodent species with CBD (99 per cent pure) at a range of doses in both species that were likely to expose the animals to higher doses than the maximum human dose. A preliminary review of the data suggests that CBD had toxic effects on the testes including inhibition of spermatogenesis. There are no data demonstrating that these changes are reversible. There were a number of other effects including reduced haemoglobin in some animals and changed hormone profiles in others. The data also showed changes in relative weight of organs; they increased for kidney and liver and decreased for testis, uterus, ovary, thyroid and thymus after 90 days. No morphological changes were associated with these organ-weight changes. Overall, these studies appear to suggest that the main toxicity of CBD is the testes. However, it is not possible to determine from the data to

what extent other organs were investigated, nor what possible metabolic or other changes caused the increased organ weight. Therefore, these studies are not considered to provide a complete reassurance regarding the safety of CBD.

9. MCA Evaluation of Additional CBD Data

The responsibility of the Agency is to assess data and published literature presented by the applicant as part of an application. The Agency will also take into account any other information that it becomes aware of and the Agency has become aware of additional information on the toxicity of CBD. The Agency may not share this "in-house" information with the applicant unless it is in the public domain. In view of the nature of the additional data the Agency is presenting all of the evidence it has to the CSM and seeking their advice on whether the data justify an extension to trials with CBD. That is planned to occur during February. In addition, in view of the exceptional circumstances surrounding these products the Agency is also thoroughly reviewing the literature.

10. Review of the Literature on the Toxic Effects of Crude Cannabis

In response to the Committee's request the Agency has prepared an overview of the toxicological information from summaries of the literature submitted as part of applications for trials of cannabis-based medicines. This examines the toxic effects of crude cannabis extract. In addition the Agency have reviewed the references suggested by Professor Iversen. The use of cannabis extracts in toxicology is fraught with difficulties as the cannabinoid content may vary according to the source of the plant, time of year harvested, part of the plant used to produce the extract and the genus of the plant. Furthermore, toxic components from tobacco would also be present. Therefore, it is difficult to know which component(s) of extracts or inhaled cannabis is the toxic active ingredient in cannabis substances reported to have harmful effects. Most importantly the reported studies do not provide evidence of the extent of systemic availability of the components and therefore could not validate their toxicity or demonstrate their relevance to the proposed studies.

More than 60 cannabinoids and more than 400 chemical compounds have been identified in *Canabis sativa.* The pharmacology of many of the constituents is unknown but the psychoactive properties of cannabis are attributed to Δ-9 tetrahydrocannabinol (THC) which has been studied extensively. Cannabidiol (CBD) is a precursor of THC in the plant and has a somewhat different pharmacological profile to THC. Information on CBD is far less extensive than that available for THC even though it is a significant component of marijuana.

Toxicity studies reported in the literature have been undertaken almost exclusively in the THC fraction. However, a number of studies on crude cannabis extract have been reported but mainly exposing animals to inhaled smoke. A study by Thompson (1973) used the oral route. After repeated-dose oral administration in the rat of a crude extract at up to 1,500 mg/kg/day for 119 days, slight histopathological changes were noted in bone marrow, spleen, adrenals and testes. Exposure of dogs (the only non-rodent species tested) to marijuana smoke produced changes in the airways as expected.

A variety of reproductive effects were caused by marijuana smoke in Wistar rats including delayed onset of oestrus activity, shortened oestrus period, reduced fertility index, premature parturition, reduced pup weight and litter size. These reports of reproductive toxicology studies indicated that marijuana was toxic to the embryo. The evidence for teratogenicity was considered equivocal. However, it was considered debatable that THC was a teratogen at the exposures achievable in man.

Whilst this data can provide some reassurance, the absence of information on CBD content, and on systemic exposure does not alleviate the Agency's concern.

The Committee presented the MCA with a brief statement by Professor Leslie Iversen indicating some of the available literature and the significant toxicological data on pure THC. A rapid but incomplete review of the literature cited by Professor Iversen has been undertaken. It is apparent from these publications that there is a large scientific data-base on THC and to a lesser extent on marijuana extracts. These publications do provide some additional data on the toxicology of THC, mainly in terms of study details. In addition, some of the authors have attempted to put the animal data into context with regard to human doses. The MCA does not have a concern with the use of THC in clinical trials. However, the data relating to CBD is still minimal and overall, the publications referred to by Professor Iversen do not help in this respect.

The data on marijuana extracts do provide some reassurance of the likely safety of cannabis oil but the CBD content in most of these extracts would appear to be low relative to cannabis oils being used by Dr Zajicek.

In conclusion, upon review of this data, the Agency is still concerned over the lack of CBD data.

11. The evidence of toxicity from crude cannabis extract is of limited usefulness to support an application for Cannador. The toxicology studies with crude cannabis extract do not provide data on the level of systemic exposure to its different components. Also, most exposure is by inhalation, which is not the proposed route of administration. Moreover, they do not provide data on the product to be used.

However, the Agency has become aware of additional studies reported in the literature providing further information on the toxicity of CBD as described above. The Agency will ask the CSM also to evaluate the evidence and advise on whether these data can support an extension to trials with CBD. In addition the Agency will ask their advice on what further tests are required.

12. For the Agency to evaluate whether clinical trials are an adequate test of a therapeutic effect the sponsor would have to submit a data package for evaluation. The usual procedure is for an applicant to write with an agenda requesting a meeting with a list of specific questions. Those questions are then answered by the relevant professional assessors. Dr Zajicek recently contacted the Agency to ask for advice on licensing. He has been advised to seek a meeting with the Licensing Division. The Agency will be pleased to see the details of his development plan and answer his questions about additional work to meet the requirements for a marketing authorisation and to give estimates of the time required.

Medicines Control Agency

January 2001

Memorandum by the Medical Research Council

As a follow-up to the publication of the House of Lords science and Technology Committee 1998 report on the Therapeutic uses of Cannabis, the MRC welcomes the opportunity to submit further information on trials investigating the therapeutic benefits of canabinoids.

Trials

The MRC has recently made awards to two new trials:

(1) An award of £1.3 million was made in December 1999 to Dr John Zajicek, a Consultant Neurologist at Derriford Hospital, Plymouth to undertake a three year study assessing the efficacy of cannabis extract and a specific cannabinoid (tetrahydrocannabinol) on the treatment of spasticity in people suffering from multiple sclerosis (Project title: Cannabinoids in Multiple Sclerosis). The multi-centre randomised, double-blind, three-way controlled trial study has started the recruitment of 660 patients with MS from across the UK who have significant spasticity in some of their leg muscles. Assessments of muscle stiffness and mobility will be made every few weeks, with side effects and quality of life also being monitored. All patients will be provided with optimised medical treatment before and during the trial; test compound or placebo would be given in addition to existing medication. The test compounds were obtained from Germany and the USA under licences granted by the Home Office. The Medicines Control Agency has issued a limited DDX (Doctors and Dentists Exemption) whilst awaiting the results of animal toxicity studies. We understand that Dr Zajicek has recently reported on the progress of this study to the Committee.

(2) In July 2000, Dr Anita Holdcroft (Hammersmith Hospital, Imperial College School of Medicine) was awarded £400K over two years to fund a multicentre clinical trial investigating the efficacy of cannabis extract and a specific cannabinoid (THC) as a postoperative analgesic. [Project title: A clinical trial as proof of principle of the analgesic effectiveness of cannabinoids on postoperative pain (CANPOP)]. The randomised, double-blind, placebo-controlled trial will be based at the Hammersmith Hospital's Trust, Chelsea and Westminster and Northwick Park Hospitals, London. The trial will investigate the ability of cannabinoids to relieve acute pain associated with specific types of surgery (primary knee arthroplasties, standardised gynaecological surgery). The fine operational details are currently being finalised before commencement of the trial.

In accordance with MRC's Guidelines for Good Clinical Practice, both trials have obtained ethical approval and are overseen by an independent Trial Steering Committee with the unblinded data continuously monitored by a second independent Data Monitoring and Ethics Committee. The trials will report in the normal way through publication in peer reviewed journals.

Basic Cannabinoids Research

MRC has awarded over £600K to other basic research projects investigating the effects of cannabinoids. Professor Roger Pertwee, Univesity of Aberdeen, is the leader of an MRC Co-operative Group entitled "Physiological and Pathophysiological Roles of the Endoncannabinoid System". In July 2000, the MRC agreed to fund three studies within the Co-operative Group, with a duration of between two to three years, looking at various aspects of endogenous endocannabinoids, a recently discovered set of chemical messengers occurring naturally in man and other species. The three studies look at: (1) the effects of cannabinoids on the modulation of nerve signalling in the brain and the possible identification of novel cannabinoid receptor subtypes; (2) the functioning of the cannabinoid system in memory formation, and (3) the role of the endocannabinoid system in the prevention of neuropathy, a complication of diabetes mellitus affecting all peripheral nerve fibre types caused by reduced vasculature. Professor Pertwee has a number of other research projects investigating cannabinoids that are not MRC funded.

MRC also funds work by Professor Nancy Rothwell (Manchester University) investigating cytokine release (inflammatory mediators) in response to the modification of cannabinoids in brain cell culture, with neuroprotective effects of cannabinoids to be determined in cells where genes for candidate cytokines have been deleted. This study should reveal factor(s) which regulate brain cytokines, and may identify targets for therapeutic inervention. This study is expected to end in May 2001.

The MRC continues to play an important role in researching the possible medical benefits of cannabis-derived medicines which will provide rigorous data to inform the debate.

Medical Research Council

January 2001

Printed in the United Kingdom by The Stationery Office Limited
3/2001 598048 19585

ISBN 0-10-404901-4

Published by The Stationery Office Limited
and available from:

The Stationery Office
(Mail, telephone and fax orders only)
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