SOLVAY PHARMACEUTICALS



11 January 2006

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, RM 1061
Rockville, MD 20852

**RE: Docket No. 2005N-0479**

Dear Sir/Madam:

Reference is made to the above mentioned Federal Register Notice dated 13 December 2005 entitled, "International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; Butorphanol; Delta-9-tetrahydrocannabinol (Dronabinol); Gamma-Hydroxybutyric Acid; Ketamine; Khat; Tramadol; Zopiclone; Buprenorphine; Oripavine". Reference is also made to Unimed Pharmaceutical, Inc.'s letter dated 8 May 2002 in response to the Federal Register Notice 02N-0101 dated 9 April 2002 entitled, "International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; Amfepramone (Diethylpropion); Amineptine; Buprenorphine; Delta-9-tetrahydrocannabinol (Dronabinol); Tramadol".

Unimed Pharmaceuticals, Inc., a wholly owned subsidiary of Solvay Pharmaceuticals, originally provided a response to the Federal Register Notice 02N-0101 in a letter dated 8 May 2002. The enclosed document contains our comments related to delta-9-tetrahydrocannabinol (Dronabinol) as a response to the latest Federal Register Notice 2005N-0479.

This document contains information from our own Drug Safety and Pharmacovigilance database on the currently approved and marketed product, Marinol® (Dronabinol) Capsules. This data covers the period from June 1981 to January 2005. Unfortunately, due the timing of the request, a full analysis of all public databases could not be performed. The attached document contains references to published articles and data on delta-9-tetrahydrocannabinol (dronabinol) as of 8 May 2002.

We do not understand why dronabinol is being subjected to a critical review at this time. The substance was given a critical review in 2002, and a report was issued by the ECDD, recommending scheduling. WHO Expert Committee on Drug Dependence, Thirty-Third Report 11-12 (2003), available at http://www.unicri.it/min.san.bollettino/altre/915-en.pdf. It appears that that report was not presented to the Commission on Narcotic Drugs; rather, in a letter from WHO to Dr. William Steiger of HHS, it is said that "... the report was not sent out by WHO. Instead, the Director-General sent it back to the Committee." Letter from Dr. Vladimir K. Lepakhin, Assistant Director-General, Health Technology and Pharmaceuticals, to Dr. William R. Steiger, Special Assistant to the Secretary for International Affairs, Office of Global Health Affairs (Nov. 16, 2005). But the 2002 ECDD was disbanded after it made its report, so as a practical matter it could not be "sent back" to that committee.

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Some explanation is in order. Did the Director-General disagree with the decision of the 2002 ECDD? If so, why? Was there additional information that should have been considered? These issues are not addressed by WHO, and should have been in order that their questionnaire could be better understood.

The process that the ECDD is supposed to follow was prescribed by the Executive Board of the World Health Assembly in a document, Guidelines for the WHO review of dependence-producing psychoactive substances for international control (Guidelines). The Guidelines set forth a procedure pursuant to which there should be a pre-review and then critical review. See Guidelines, paragraphs 13 and 15. Note that paragraph 15 sets forth three other ways that a critical review might occur without a pre-review, but none of those conditions exists with dronabinol.[1]

The Guidelines do not provide for multiple critical reviews by successive expert committees. This is for good reason. The time of the experts and the cost of convening the ECDD should not be spent deliberating, again and again, the scheduling recommendation of a particular substance. The pre-review step is intended to allow the experts the opportunity to determine whether a critical review is necessary. WHO should respect its own rules and maintain the procedure given to it by WHO's governing body. It would be appropriate for our government to raise this breach of the rules with the Executive Board of the World Health Assembly, and we respectfully ask that our government do so.

In summary, the data continue to support the findings of the 33rd ECDD that "the abuse liability of dronabinol does not constitute a substantial risk to the public health and society." There has been little evidence of abuse of Marinol® even after the drug was rescheduled in the United States from schedule II to schedule III.

Should you have any questions, please do not hesitate to contact me at 770-578-5620.

Sincerely,

Michael F. Hare
Manager, Regulatory Affairs

enclosure

cc: Archives
Mr. Giuseppe Randazzo, Project Manager, CBER (Desk Copy)

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1 Paragraph 15. Critical review is conducted by the Expert Committee in any of the following cases: (1) there has been notification from a Party to the 1961 or the 1971 Convention concerning the scheduling of a substance; (2) there has been an explicit request from CND to review a substance; (3) pre-review of a substance has resulted in a recommendation for critical review as indicated in paragraph 13 above; (4) information is brought to WHO's attention that a substance is clandestinely manufactured, of especially serious risk to public health and society, and of no recognized therapeutic use by any Member State. If therapeutic use of the substance is confirmed subsequently by any Member State in respect of case (4), the substance shall be subjected to a pre-review.