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May 15, 2000

Dockets Management Branch  
Food and Drug Administration  
5630 Fishers Lane  
(HFA-305)  
Room 1061  
Rockville, MD 20852

**RE: International Drug Scheduling; Convention on Psychotropic Substances; 65 Fed. Reg. 24969 (April 28, 2000)**

The Pharmaceutical Research and Manufacturers of America (PhRMA) herein provides comments on the Department of Health and Human Services' (DHHS) request for comments on the World Health Organization's (WHO's) critical review of several drugs marketed in the United States and throughout the world, 65 Fed. Reg. 24969 (April 28, 2000). PhRMA is a voluntary, non-profit association that represents America's leading research-based pharmaceutical and biotechnology companies. PhRMA member companies invest approximately \$24 billion annually here in the U.S., and around the world, to discover and develop new medicines. In an industry that is increasingly multi-national in scope, these companies are the source of nearly all new drugs that are discovered and marketed throughout the world.

The WHO proposes to review two drugs currently marketed in the United States, zolpidem and diazepam. A third drug, GHB, is currently being studied under an IND for treatment of severe forms of narcolepsy. PhRMA believes the Federal Register comment period is insufficient to solicit meaningful comments on WHO's process for critical review of these important drugs. Also, having reviewed the information requested by WHO in the organization's questionnaire sent to member states, PhRMA believes that the WHO is not conducting an evidence-based analysis of both the appropriate use and potential abuse of these drugs. This raises concerns about

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*Pharmaceutical Research and Manufacturers of America*

WHO's current and future process for review of useful and important medicines. Therefore, PhRMA requests that the DHHS communicate its concern to WHO and request that action be taken to correct the process prior to consideration of any scheduling actions at the meeting of the Expert Committee on Drug Dependency (ECDD) meeting in September 2000.

### **The WHO Questionnaires are Inadequate**

At the outset, we note that the Federal Register notice modifies the questions stated in the WHO questionnaires and provided to the member countries. In fact, the questions as stated in the notice are to a small degree an improvement over the ones issued by WHO. Nonetheless, there are serious deficiencies in the information that is being requested and, consequently, the data that will be considered by the ECDD.

The Federal Register notice and WHO's letter of communication acknowledge that the questionnaires are "one of the essential elements of the established review procedure . . . to collect relevant information from Member States to prepare a Critical Review document for submission to the Expert Committee on Drug Dependence." 65 Fed. Reg. at 24969. The subject questionnaires do not collect the information needed for a proper critical review document. Specifically, the questionnaires ask questions that will elicit anecdotal information that cannot be used to make scientific evaluations of the nature of any abuse.

Equally problematic is the WHO questionnaires' failure to request information about the importance of the therapeutic uses of the drugs. The Federal Register notice and the WHO questionnaires do ask for information on the impact of rescheduling on the "availability for medical use." Id. at 24970. However, the questionnaires do not request that member countries provide detailed information on therapeutic use. They also do not inquire about the availability of therapeutic alternatives. The latter is critical

in many Third World countries where appropriate medicine is in short supply. This omission is especially egregious in light of the fact that WHO has designated diazepam as an essential drug.

The foregoing information is critical to an evidence-based decision, one that meets the criteria of the Convention of Psychotropic Substances of 1971 (1971 Convention). The findings that WHO is supposed to communicate to the Commission on Narcotic Drugs (CND) are three: (1) "the extent or likelihood of abuse," (2) "the degree of seriousness to the public health and social problems," and (3) "the degree of usefulness of the substance in medical therapy." 1971 Convention, art. 2, para 4. The questionnaires will not provide the information needed to make these findings. Without the data, from all or at least a representative portion of the member states, any decision will fail to meet the standards of the 1971 Convention.

#### **DHHS Should Take an Active Role Prior to the ECDD Meeting**

The Federal Register notice states that DHHS "will not now make any recommendations to WHO regarding whether these drugs should be subjected to international controls. Instead, DHHS will defer such consideration until WHO has made official recommendations to the CND, which are expected to be made in late 2000." 65 Fed. Reg. at 24970. Simply providing data at this juncture, without making known the medical opinions of the expert agencies – NIDA and FDA – would be a mistake.

The international scheduling process gives WHO the primary authority to make findings on medicine and science, and leaves to the CND the social and political decisions on scheduling actions. The WHO's medical and scientific findings are binding on CND. See, 1971 Convention, art. 2, para 5. It is plain that WHO is proceeding to reach its binding decision on the medicine and science with a seriously flawed process.

The United States should be heard, now, before the potentially invalid but essentially binding medical/scientific judgments are made. The ECDD should consider all available evidence in deliberating on what recommendations to make to the WHO Secretariat about the need for further scheduling. This includes the position of each member country on such actions and whether any action is required. If DHHS remains passive at this time, then the debate at the CND may never reach the issue of the validity of the WHO recommendations.

For example, in September 1997, the FDA conducted a public hearing on the appropriate scheduling of benzodiazepines. At that hearing, national experts provided a wealth of scientific and medical information on the use of these compounds. In addition, these experts gave useful opinions about scheduling and, generally, recommended that rescheduling of benzodiazepines was unnecessary. Such information, including FDA's opinion of the data collected, should be presented to the ECDD for its consideration. The current process makes it unlikely that the ECDD would fully consider the position of U.S. experts and the DHHS on scheduling actions.

Scheduling decisions are not simply matters of academic interest. They can profoundly affect medical treatment in this country and elsewhere in the world. The DHHS has an obligation to assure the people of this country that scheduling decisions have medical and scientific integrity. Our government cannot take the role of observer when WHO is taking actions that will undermine the international scheme of regulation.

PhRMA requests that DHHS take an active role and request that the WHO take immediate steps to correct the process for conducting a critical review of the drugs identified in the Federal Register notice. At a minimum, WHO should request additional information from the member states on the therapeutic use of these drugs and alternatives. If such information cannot be collected by the September 2000 ECDD

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meeting then WHO should postpone its critical review until such time as it has sufficient information to make an evidence-based decision.

Sincerely,

A handwritten signature in black ink, appearing to read "Matthew B. Van Hook", with a long horizontal flourish extending to the right.

Matthew B. Van Hook