Expert Committee on Drug Dependence
Thirty-eighth Meeting
Geneva, 14-18 November 2016

Expert Peer Review No.2 for U-47700

1. Comments based on the review report

3,4-Dichloro-N-[(1R,2R)-2-(dimethylamino)cyclohexyl]-N-methylbenzamide (U-47700) was developed in the 1970s by The Upjohn Company (Michigan, USA) and found to be a potent analgesic agent. This substance has recently appeared on the streets and is freely available for purchase as a “research chemical”. It can also be considered an isomer of the synthetic opioid 3,4-dichloro-N-[(1-(dimethylamino)cyclohexyl)methyl]benzamide (AH-7921) that is listed in Schedule I of the 1961 Single Convention, as amended by the 1972 Protocol since 2015.

a. Evidence on dependence and abuse potential

Information reported from non-clinical data suggests that U-47700 binds to opioid receptors with highest affinity toward the μ-opioid receptor (MOR) > κ-opioid receptor (KOR) > δ-opioid receptor (DOR), respectively. This trend was essentially shared with morphine. In vitro receptor activation of MOR, KOR and DOR was evaluated using the [35S]GTPγS assay which revealed that U-47700’s functional activities followed a similar trend compared to morphine (EC50 MOR > KOR > DOR) although with lower potency. Antinociceptive (tail flick, tail pinch, and HCl writhing) and sedative (inclined screen) properties were tested in mice (compared to morphine) and U-47700 was found to be more potent than morphine. Both morphine and U-47700 induced increased locomotor activity. Controlled studies in humans are not available but information obtained from a case report suggests that administration of naloxone reverses opioid-like acute toxic effects induced by U-47700.

b. Risks to individual and society because of misuse

Risks to individual drug users appear to originate from the fact that U-47700 is capable of inducing opioid-type toxicity. The risk of suffering from a fatal intoxication seems exacerbated by the fact that users might not intentionally consume this substance as demonstrated by information available in the case report literature, thus, leading to potentially fatal overdose. U-47700 has also been encountered in
counterfeit tablets mimicking branded benzodiazepine products, which indicates that users who are not necessarily intending to consume this synthetic opioid may also be at risk. Furthermore, U-47700 was found in oxycodone counterfeit tablets.

c. **Magnitude of the problem in countries (misuse, illicit production, smuggling etc)**
Epidemiological data on U-47700 use are not available but the Critical Review highlighted that U-47700 is available for purchase as a “research chemical” and that it was found in illicitly produced counterfeit tablets both in the USA and in Europe.

d. **Need of the substance for medical (including veterinary) practice**
U-47700 is not used in medical practice.

e. **Need of the substance for other purposes (e.g. industrial)**
U-47700 is not used in any industrial application apart from being employed in scientific research.

f. **Measures taken by countries to curb misuse**
At this time, U-47700 appears to be controlled in the USA, UK and Sweden by implementing national control mechanisms.

g. **Impact if this substance is scheduled**
In the absence of medical or industrial use no discernable impact is expected apart from manageable bureaucratic burden to researchers and laboratories that carry out research.

2. **Are there absent data that would be determinative for scheduling?**
Not identified.

3. **Other comments or opinions**
A key challenge associated with newly emerging drugs is the potential for initial underreporting based on a delay in the ability to identify them in forensic casework due to lack of reference material and absence in sensitive, targeted screening methodologies. Further case report examples might therefore come to light in the future.
4. Expert reviewer’s view on scheduling with rationale

The information on this “research chemical” suggests that the synthetic opioid U-47700 has no medical use and that it is liable to similar abuse and productive of similar ill-effects as the substances in Schedule I of the 1961 Convention. Specific examples include fentanyl, AH-791 and 1-cyclohexyl-4-(1,2-diphenylethyl)piperazine (MT-45), respectively. The recommendation would be to list U-47700 in Schedule I of the 1961 Single Convention, as amended by the 1972 Protocol.