Expert Peer Review for 4-Fluoroisobutyrfentanyl (4-FIBF)

1. Comments based on the review report

a. Evidence on dependence and abuse potential

   Dependence potential: No data exist on the physical dependence potential of 4-fluoroisobutyrfentanyl in laboratory animals or in humans.

   Abuse potential: No data exist on the abuse potential of 4-fluoroisobutyrfentanyl in laboratory animals or in humans.

b. Risks to individual and society because of misuse

   Risks of misuse to individuals and society may be high, although this is difficult to determine conclusively because sophisticated detection methods must be used to identify the compound in body fluids (e.g., HPLC-TOF, LC-HRMS, GC-MS, FTIR-ATR, or NMR). Deaths attributed to 4-fluoroisobutyrfentanyl have been reported in Sweden (n=16) and the U.S. (n=64).

c. Magnitude of the problem in countries (misuse, illicit production, smuggling etc)

   It is likely that illicit use, production, and trafficking of 4-fluoroisobutyrfentanyl is underreported because of difficulties in detecting the compound. Reportedly, it is sold online as a substitute for illicit and/or prescription opioids. Seizures of the compound were reported by Sweden, Belgium, Germany, the United Kingdom, and the United States.

d. Need of the substance for medical (including veterinary) practice

   No countries have approved 4-fluoroisobutyrfentanyl for either medical or veterinary use.

e. Need of the substance for other purposes (e.g. industrial)

   The only reported industrial use for 4-fluoroisobutyrfentanyl is as an analytical reference standard for scientific research and forensic applications.
f. Measured taken by countries to curb misuse
   Two possible precursors of 4-fluoroisobutyrylfentanyl, 4-aminophenyl-1-phenethylpiperidine (4-ANPP) and N-phenethyl-4-piperidone (NPP, a pre-precursor), have been scheduled under the United Nations Convention against Traffic in Narcotic Drugs and Psychotropic Substances, 1988. The U.S. DEA placed 4-fluoroisobutyrylfentanyl into Schedule I on May 3, 2017, and the EMCDDA and Europol added it to the list of new psychoactive substances to be monitored through the EU Early Warning System. Numerous countries throughout Europe have placed 4-fluoroisobutyrylfentanyl under drug control legislation.

g. Impact if this substance is scheduled
   Because no therapeutic use exists for 4-fluoroisobutyrylfentanyl, the impact of scheduling the compound is likely to be minimal from a medical perspective. However, illicit use and sale of 4-fluoroisobutyrylfentanyl may be reduced by scheduling actions.

2. Are there absent data that would be determinative for scheduling?
   Formal data are lacking with regard to the physical dependence potential and abuse liability of 4-fluoroisobutyrylfentanyl, which is somewhat of a concern.

3. Other comments or opinions
   Despite the lack of data on the dependence and abuse potential of 4-fluoroisobutyrylfentanyl, its chemical structure and selective binding to mu opioid receptors suggests that it likely produces effects that are similar to other mu opioid agonists.

4. Expert reviewer’s view on scheduling with rationale
   The chemical and pharmacological similarity of 4-fluoroisobutyrylfentanyl to fentanyl, the confirmed toxicology reports of 4-fluoroisobutyrylfentanyl in human deaths, and the lack of therapeutic use of 4-fluoroisobutyrylfentanyl suggests that it should be placed into Schedule I under the 1961 Convention.