1. **Comments based on the review report**

a. **Evidence on dependence and abuse potential**

Mephedrone is a synthetic cathinone, originally synthesized in 1929, which has been increasingly used as a recreational drug since 2007. It is a chemical analogue of methamphetamine and is used as an alternative or addition to that drug or to methylenedioxy-methamphetamine (MDMA, commonly known as Ecstasy) by substance users.

In experimental animal models of dependence liability in which it has been compared with methamphetamine, results show that mephedrone is readily self-administered intravenously and at a high level, at least matching the dependence liability reported with other restricted psychostimulants. In these animal studies the evidence is consistent using different self-administration paradigms. Studies of its abuse potential in experimental animals show that mephedrone modifies intra-cranial stimulation and enhances intra-cranial self-stimulation in a way similar to the effects of other psychostimulants. The reviewer concludes that “mephedrone has ... abuse liability”, though on certain tests lower than that of some of its analogues.

In human studies respondents who report frequent use of mephedrone describe symptoms and experiences that are typical of drug dependence. These include craving and tolerance, which can be considerable. The one caveat is that a withdrawal syndrome has not yet been characterized. Craving is the most prominent symptom of dependence on mephedrone and causes the most distress to users. It is reported to be at least comparable with (and possibly greater than) that experienced with other psychostimulants. Although epidemiological data are limited, in one study of mephedrone users attending school or college 17.6% reported dependence symptoms.

b. **Risks to individual and society because of misuse**

Intoxication with mephedrone can be fatal. The number of fatalities associated with mephedrone identified in the critical review exceeds 100; in the majority of cases mephedrone was identified toxicologically and in eight instances was the only drug present. The causes of death in mephedrone-related fatalities are acute drug toxicity and presumed suicide, including by hanging. No population-wide studies of intoxication and death from mephedrone seem to have been reported but it is clear that given the frequency of its use in some populations of young people and the accumulating number
of fatalities reported that mephedrone constitutes a substantial threat to the health of many societies.

As well as fatalities and addiction, mephedrone has been reported to lead to numerous physical and psychological symptoms and problems. These include palpitations, cardiac arrhythmias, hypertension, headaches, dizziness, tremors, impaired concentration, nausea and vomiting, abdominal pain, anorexia, bruxism (teeth grinding), anxiety, agitation, and rebound depression. In addition, more serious adverse reactions such as convulsions, paranoid ideation and hallucination are described. Chest pain has been reported but it is not known whether this is related to coronary ischaemia. More severe intoxication with mephedrone can cause seizures, hyperthermia and increases in pulse rate and blood pressure. These adverse events are reported from National Poisons Information Services and are similar to the effects of other psychostimulants.

Similar to other psychostimulants it has been reported to lead to psychosis after repeated use, though in the review only one case report is cited.

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

The main information on the magnitude of misuse of mephedrone derives from Europe, including a report published in 2011 by the European Monitoring Centre for Drugs and Drug Addiction. There are no published population-level studies on the prevalence of mephedrone. In some studies in the United Kingdom of young people frequenting nightclubs, lifetime use of mephedrone was estimated to be 40%, and among students in school and college 20% reported use, with 4.4% reported use on a daily basis. Mephedrone users have a high frequency of using other psychostimulants including MDMA and cocaine.

In terms of illicit manufacture and trafficking, in data from 72 WHO member states, 34 had information on mephedrone in their own jurisdictions. Overwhelmingly these were European countries. Mephedrone is trafficked; and seizures were reported by 16 countries and its availability via the Internet was noted in 13.

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

Mephedrone is not currently authorized as a medical product in any country surveyed. It is not indicated or used for animal/veterinary care. It has no known therapeutic applications and has never been marketed as a medicinal product. Mephedrone users report their reasons for taking it as for pleasure and also for maintaining their dependence on it when this has developed. The only reported “medicinal” effect of mephedrone is therefore to self-medicate withdrawal symptoms, which results in the dependence on it being perpetuated.

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

Mephedrone has no industrial use.
f. Measures taken by countries to curb misuse

There are no current international controls on mephedrone. In the survey of 72 WHO member countries, 32 reported that mephedrone was controlled under legislation to regulate its availability.

g. Impact if this substance if scheduled

Scheduling would be one method of limiting the use of mephedrone in that it would provide a basis for countries which are signatories to the international conventions taking steps to interrupt manufacture, importation and trafficking on the basis of its illegal status. The review notes that the use of mephedrone declined in one jurisdiction when it was made illegal.

2. Additional information to the critical review report

The rapid spread of mephedrone throughout Europe and its extensive use among young people occurred when its availability was not constrained by any legislation, given that it was not controlled by international legislation or initially by the legislation of any WHO member state. It was sold as a seemingly innocuous substance, with its true purpose being concealed by its description as “bath salts”. In some cases it was sold as a supposed plant fertilizer and “research chemical”. It therefore escaped attention (and intervention) because its true purpose, namely to induce pleasurable psychological effects for the individual was not declared. This could be highlighted further in the review.

3. Other comments or opinions

Some individuals use mephedrone only but most tend to add it to their repertoire of stimulant and other drugs. Qualitative studies have shown that the use of mephedrone is elastic among substance users, with shifts to and from mephedrone use being influenced by its legal status (van Hout & Brennan, 2012).

Overall, its use in many populations is widespread. Most individuals who use it appear not to experience significant harm; cumulatively it is causing substantial morbidity and mortality.

References

4. Expert reviewer’s view on scheduling with rationale

Mephedrone has dependence and abuse potential and causes harm to individuals. It has no therapeutic applications. Hence it is recommended that mephedrone be classed in Schedule II of the 1971 Convention on Psychotropic Substances.