1. Comments based on the review report

a. Evidence on dependence and abuse potential

*Dependence and abuse potential: Animal studies*
Several reports demonstrated that alpha-PVP produces a significant enhancement of spontaneous locomotor activity. Kaizaki et al. reported that the extracellular concentration of dopamine in the striatum, determined by *in vivo* microdialysis increased immediately after alpha-PVP administration. The most important information for evaluation of reinforcing effect of alpha-PVP is self-administration including conditioned place preference and intracranial self-stimulation experiments. In the self-administration and conditioned place preference experiments, alpha-PVP produced reinforcing effect and conditioned place preference. Furthermore, alpha-PVP activated the brain reward circuitry in intracranial self-stimulation experiment. On the other hand, subjective effect of alpha-PVP was evaluated by drug discrimination procedure. Alpha-PVP fully substituted for the discriminative stimulus effect of both cocaine and methamphetamine. These results suggest that alpha-PVP may possess a similar degree of dependence and abuse potential as methamphetamine, cocaine and MDPV.

*Dependence and abuse potential: Human studies*
Data on systematic clinical studies in humans are currently not available.

b. Risks to individual and society because of misuse
Fatal case reports (32 cases) associated with alpha-PVP have been published in the scientific literatures (12 reports). Furthermore, case-level data for death cases (101 deaths) concerning with alpha-PVP reported to the EMCDDA. Then, non-fatal case reports (35 cases) associated with alpha-PVP have been published in the scientific literatures (7 reports). Furthermore, non-fatal, case-level data concerning with alpha-PVP reported to the EMCDDA. Analytical confirmation was obtained from 21 of the 34 cases. Therefore, risks to individual and society because of misuse of alpha-PVP are high.

c. Magnitude of the problem in countries (misuse, illicit production, smuggling etc.)
The report indicates that alpha-PVP appears to be associated with the purchase of ‘research chemicals’ or comparable products that may be obtained from Internet
retailers. It has also been observed that alpha-PVP was encountered in tablets and related formulations sold as ‘ecstasy’ both in Europe and the Americas. It also appears that alpha-PVP is used by recreational and high-risk drug users, including those who inject drugs. However, surveys that systematically assess the prevalence of use are currently not available. Data from the Polish ‘I-Trend’ online questionnaire provided to the EMCDDA showed that out of 1074 respondents, alpha-PVP was the last new psychoactive substance to be used by 3.4% (n = 36) of the respondents (36 users, n = 1,074). Of these, 39% had taken it at least 20 times in the previous year.

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

Alpha-PVP was never marketed as a medical product.

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

Alpha-PVP has no recorded industrial use.

f. **Measures taken by countries to curb misuse**

Fifteen member states of the EMCDDA (Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Poland, Romania, Slovenia, Sweden, and the United Kingdom) as well as Turkey and Norway reported that alpha-PVP is controlled under drug control legislation. Four member states (Austria, Cyprus, Portugal and Slovakia) reported alpha-PVP is controlled under drug control legislation prohibiting the unauthorized supply of defined or qualifying new psychoactive substances. Other two member states (Belgium and Czech Republic) started the process of controlling the substance using drug control legislation. In the United State of America, alpha-PVP has been temporarily scheduled into schedule I pursuant to the temporary scheduling provisions of the Controlled Substance Act (CSA). In Japan, alpha-PVP has been controlled under the Narcotics and Psychotropics Control Act. Other countries with legislative control include other United Nation Member States.

g. **Impact if this substance is scheduled**

If alpha-PVP was placed under international control, they would have the laboratory capacity to identify the substance.

2. **Are there absent data that would be determinative for scheduling?**

The report includes enough data that would be determinative for scheduling.

3. **Other comments or opinions**

No other comments.
4. **Expert reviewer’s view on scheduling with rationale**

Non-fatal and fatal case reports associated with alpha-PVP have been published in the many scientific literatures. Several reports including the self-administration and conditioned place preference experiments demonstrated that alpha-PVP produces reinforcing effect and conditioned place preference. Furthermore, therapeutic and industrial usefulness has not been recorded. Higher regard was accorded to the substantial public risk than to the lack therapeutic usefulness. Therefore, I recommend that alpha-PVP be placed under international control in Schedule II of the 1971 convention.