Erratum to FDA Briefing Document

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) and the Drug Safety and Risk Management (DSaRM) Advisory Committee

October 8, 2020

This erratum contains corrections to FDA's briefing information for the October 8, 2020, joint PDAC and DSaRM Advisory Committee Meeting.

1) **Page 27, first full paragraph, third sentence:**

"The method that the Applicant identified in the in vitro studies that effectively reduced the pellets to a fine consistency (<500 μm) suitable for insufflation was chosen to manipulate the sample in the human abuse potential study."

Revised text (additions in bolded and underlined font):

"The method that the Applicant identified in the in vitro studies that effectively reduced **most of** the pellets to a fine consistency (<500 μm) suitable for insufflation was chosen to manipulate the sample in the human abuse potential study."

2) **Page 28, first paragraph:**

"Regarding the first group of analyses, the study was not designed simply to detect a difference in means between treatment groups. Instead, the Applicant designed the study so that the difference in means on the prespecified endpoints would have to meet a threshold of ***at least a 10%*** reduction with manipulated AR19 as compared to amphetamine 40 mg in order for this finding to be considered statistically significant."

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

~~Regarding the first group of analyses, the~~ **The** study was not designed simply to detect a difference in ~~means~~ **mean Drug Liking Emax** between treatment groups. Instead, the Applicant designed the study so that the difference in ~~means on the prespecified endpoints~~ **mean Drug Liking Emax** would have to meet a threshold of ***at least a 10%*** reduction with manipulated AR19 as compared to amphetamine 40 mg in order for this finding to be considered statistically significant.

3) **Page 28, second paragraph, first sentence:**

"The responder analysis was designed to determine if greater than 50% of subjects were responders, where responders were defined as those subjects having at least a 10% reduction on the prespecified endpoints."

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"The responder analysis was designed to determine if greater than 50% of subjects were responders, where responders were defined as those subjects having at least a 10% reduction on ~~the prespecified endpoints~~ **Drug Liking Emax for manipulated AR19 as compared to amphetamine 40 mg**."

4) **Page 28, fourth paragraph, first sentence:**

"A cross-study comparison (between this HAP study and AR19.005, an oral PK study) of IN administration of amphetamine sulfate API powder (40 mg) and oral administration of AR19 capsules (40 mg) showed that systemic exposures to l-amphetamine and d-amphetamine after IN administration are lower (40% lower Cmax and 30 to 40% lower AUC0-∞) than those of oral administration."

Revised text (additions in bolded and underlined font):

"A cross-study comparison (between this HAP study and AR19.005, an oral PK study) of IN administration of amphetamine sulfate API powder (40 mg) and oral administration of AR19 capsules (40 mg) **was performed using dose-normalized Cmax and AUC0-∞ values provided in the AR19.005 study report and multiplied by 40. This** showed that systemic exposures to l-amphetamine and d-amphetamine after IN administration are lower (40% lower Cmax and 30 to 40% lower AUC0-∞) than those of oral administration."

5) **Page 28, sixth paragraph, second sentence:**

"Validation of each measure (Drug Liking VAS, Take Drug Again, Overall Drug Liking, and High) was established by comparing the scores obtained for the API 40 mg treatment arm to those of placebo."

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"~~Validation of each measure (Drug Liking VAS, Take Drug Again, Overall Drug Liking, and High) was established~~ **For the purposes of study validation, the primary endpoint, Drug Liking Emax, was evaluated** by comparing the scores obtained for the API 40 mg treatment arm to those of placebo."

6) **Page 36, second paragraph, sixth sentence:**

"Third, studies examining the potential toxicity of PEO solutions following IV administration should take into consideration the potential for instability of the PEO in the solutions and confirm what molecular weight was actually administered to the animals."

Revised text (deletions in strikethrough font):

"~~Third, studies examining the potential toxicity of PEO solutions following IV administration should take into consideration the potential for instability of the PEO in the solutions and confirm what molecular weight was actually administered to the animals.~~"

7) **Page 37, first bullet:**

"The chemical composition of the syringeable material is not fully known."

Revised text (additions in bolded and underlined font):

"The chemical composition of the syringeable material is not fully known. **In addition to the PEO, talc and starch that have been characterized, the extract contains approximately 15% unidentified impurities present in the syringeable material.**"