Erratum to the FDA Briefing Document
Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee
April 19, 2023

This erratum contains corrections to FDA's briefing information for the April 19, 2023 Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee. At this meeting, the committee will discuss postmarketing requirement (PMR) 3033-11, issued to application holders of new drug applications (NDAs) for extended-release and long-acting (ER/LA) opioid analgesics to evaluate long-term efficacy of opioid analgesics and the risk of opioid-induced hyperalgesia. The discussion will focus on a clinical trial designed to address these objectives.

For corrections, deleted text was ~~struckthrough~~ and new text is <u>underlined</u>.

Page 6, Section 1.1, Paragraph 2, Sentence 2: Should read, "The objectives of the PMR ~~were~~ <u>are</u> to evaluate long-term efficacy of opioid analgesics and the risk of opioid-induced hyperalgesia."

Page 7, Section 1.2, Item 1, Paragraph 3: Repeated efforts to withdraw opioids are not specified in the protocol. Thus, should read "~~including repeated efforts to withdraw opioids~~ <u>including the opportunity to adjust dose or taper</u>."

Page 8, Section 1.4, second Question #1 at the bottom of the page: There is an error in the minimum duration on therapy. All patients will be on opioids for a minimum of 42 weeks, not 38 weeks. Thus, in Section 1.4, Specific Questions related to this protocol, draft question 1 should read, "Is ~~38~~ 42 to 52 weeks an adequate duration to assess the long-term effectiveness of opioids?

Page 10, Section 2.1 should read,

> Irrespective of the administrative change to the PMR number, the PMR description remained unchanged: 'Conduct a clinical trial to estimate the serious risk for the development of hyperalgesia following the long-term use of high-dose ER/LA opioid analgesics for at least one year to treat chronic pain. Thus, the PMR objectives included both an assessment of OIH risk and an assessment of effectiveness ~~greater than~~ <u>at least for one year</u>."

Page 21: The Section titled "Other Secondary Efficacy Endpoints (OIH Substudy patients)" does not reflect the OIH endpoints but reflects language around opioid tolerance. Correction is to remove OIH Substudy patients and the first two sentences. The bulleted endpoints pertain to opioid tolerance development.

Page 24: Should read, "~~OIH is often considered a diagnosis of exclusion, often made retrospectively; thus~~ <u>Therefore</u>, the proposed protocol for 3033-11 may produce a crude rate of

incidence of OIH based on the definition proposed in the protocol which may or may not reflect the definition of OIH once there is consensus."