Erroneously Published Fospropofol Pharmacokinetic–Pharmacodynamic Data and Retraction of the Affected Publications

To the Editor:

As described in a letter to the editor, published in ANESTHESIOLOGY, Anesthesia and Analgesia, and the European Journal of Anaesthesiology,1–3 an analytical propofol assay inaccuracy was discovered after all six initial studies on the pharmacokinetic–pharmacodynamic and tolerability of fospropofol had been published.4–9 This assay inaccuracy makes the measured propofol plasma concentrations in these previously published studies unreliable.

All six affected studies were phase I and II studies sponsored by a pharmaceutical company (Guilford Pharma, Baltimore, MD, and later MGI Pharma, Baltimore, MD) and were performed in two independent academic-based phase I centers in Gent, Belgium, and Erlangen, Germany. Because of the stage of the drug testing, the study drugs were made available by the initial sponsor. As described previously,1–3 the sponsor developed and validated a specific propofol assay. Both academic centers had no influence on the choice of methodology for sample handling and chemical analysis. For all six studies,4–9 assays were performed at an external laboratory (MDS Pharma Services, Montreal, Canada) as per the sponsor’s decision. Finally, the original publications were coauthored by both academic and sponsor-based investigators.

In a letter to the editor,1–3 the initial owner of the drug (MGI Pharma, not affiliated with the academic centers from the original studies) declared that additional studies were planned using an appropriate assay to describe the pharmacokinetics and pharmacodynamics of fospropofol in healthy volunteers and patients. They stated their intent to publish these results shortly along with an estimate of the degree of error from the previously published studies reporting results using the old assay. In the response article, the editors-in-chief of ANESTHESIOLOGY, Anesthesia and Analgesia, and the European Journal of Anaesthesiology requested a publication within the next 12 months validating the new assay, analyzing the likely error and bias in each of the six articles in question, and determining how the error and its correction would influence the conclusions.

The planning of studies was delayed primarily because of the transfer of ownership of the drug to another pharmaceutical company in mid 2009 (Eisai, Woodcliff Lake, NJ). As a result and although requested by the academic investigators immediately after the publication of the letter to the editor,1–3 the investigators from the original studies were not able to reanalyze the pharmacokinetics—pharmacodynamics of fospropofol in human volunteers within the deadline of 12 months given by the editors-in-chief. As such, we, the undersigned corresponding and senior authors from the six original articles, in the name of all coauthors, request that the articles in question that provide flawed pharmacokinetic—pharmacodynamic data be retracted. We regret that we are unable to successfully resolve the problem within the given timeframe. (See a list of retracted articles from ANESTHESIOLOGY on page 1058 of this issue.)

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References


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