The attached documents represent the response of the International Society of Pharmacometrics (ISoP) relating to the U.S. Food and Drug Administration's public docket entitled "Exposure-Response Analysis in Drug Development and Regulatory Decision Making; Request for Comments" (Docket No. FDA-2018-N-0791). We thank the Agency for giving us the opportunity to provide feedback on behalf of our membership.

Our response is comprised of two complementary, but different, parts:

1. "An ISoP Position Statement on the use of Dose-Exposure-Response in Drug Development" (Attachment 1) provides a consolidated consensus viewpoint on how we believe dose-exposure-response analysis should be applied during drug development and approval, prepared by an ISoP working group led by Alan Maloney.
2. We provide also a line-by-line review of the 2003 FDA guidance document "Guidance for Industry: Exposure-Response Relationships — Study Design, Data Analysis, and Regulatory Applications" (Attachment 2), providing specific feedback on content, structure and suggestions for terminology. This effort was led by Nick Holford.

Together, these documents represent our Society's views on this topic and make suggestions for the content and focus of a revised Guidance. We hope this feedback will be useful to you.

Yours sincerely

Jin Y. Jin, President, ISoP

Justin Wilkins, President-Elect, ISoP

On behalf of the ISoP Exposure-Response Working Group

Al Maloney, Nick Holford, Mariam Ahmed, Thierry Buclin, Joachim Grevel, David Norris, Amit Taneja, and Jonathan French