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ICH M9 Biopharmaceutics Classification System-based Biowaivers: Challenges and opportunities

The International Conference on Harmonization (ICH) M9: Biopharmaceutics Classification System-Based Biowaivers was recently adopted. A biowaiver allows for *in vitro* testing to be used in lieu of *in vivo* bioavailability and/or bioequivalence studies to facilitate product approval, where solubility and permeability are not expected to impede bioavailability. ICH M9 should minimize unnecessary *in vivo* studies in man and allow greater public access to medicines. However, this approach is not always universally aligned or recognized. The biggest area of concern is whether solubility should be based on the highest therapeutic dose or on the highest strength of the medicinal product. Different approaches to assessing permeability, i.e. *in vitro* or *in vivo* assessments, will also require harmonization. Thus, far biowaivers have been restricted to pharmaceutical equivalents and primarily to BCS class I compounds. There has been widespread concern regarding the effect of different excipients on the permeability of the drug substance and thereby the bioavailability of different formulations. For example, FDA guidance states, "Unlike for BCS class 1 products, for a biowaiver to be scientifically justified, BCS class 3 test drug product must contain the same excipients as the reference product. This is due to the concern that excipients can have a greater impact on absorption of low permeability drugs." Whilst, it is certainly true that "certain excipients, such as surfactants (e.g., polysorbate 80) and sweeteners (e.g., mannitol or sorbitol) may be problematic", it is by no means true that all excipients can adversely influence absorption. Consequently, ICH M9 faces significant challenges and a target date of 2Q 2019 for step 4 implementation may be difficult to achieve.

Speaker Biography

David P Elder has nearly 40 years of service within the pharmaceutical industry (Sterling, Syntex and for the last two decades with GSK). He is now an independent CMC Consultant and has broad based experience in excipients, biopharmaceutics, drug product and analytical method development. He obtained his PhD in crystallography from the University of Edinburgh. He is a visiting Professor at King's College, London. He is a member of the British Pharmacopoeia. He is the immediate past Chairman of JPAG (Joint Pharmaceutical Analysis Group). He is a member of the Editorial Advisory Board for the *Journal of Pharmaceutical Sciences*. He has published 114 and presented 17 webinars and 133 presentations. He has Co-edited one book on the analytical characterization and separation of oligonucleotides and their impurities (with George Okafo and Mike Webb) and is editing a second book on the ICH quality guidelines (with Andy Teasdale, AZ).

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