

Understanding Analytical Methods

Using the Assay Toolbox to Understand Your Process

As biosimilars move into the forefront of consciousness in the biopharmaceutical industry, analytical methods, especially comparability studies, have an increasingly important role to play. Additionally, as more products progress from phase 1 to 2–3 studies and require production-scale manufacturing, analytical methods are an important component of technology transfer or in-house scale-up efforts. The Analytical Methods for Biologics track will elucidate these challenges, and will include discussions about the latest changes in immunogenicity guidance, posttranslational modifications, analytical strategies, comparability testing, and bioassay development.

Robin Thorpe, head of the biotherapeutics group at the National Institute for Biological Standards and Control, and a member of the EMEA drafting group, will start off the presentations with a review of the EMEA draft guidance, *Immunogenicity Assessment of Biotechnology-Derived Therapeutic Proteins*.

Nadine Ritter, senior consultant with the Biologics Consulting Group, will speak about forced degradation studies in the Formulation and Drug Delivery track. The convenience of this meeting is that attendees are not confined to attending only one track, so if you want to hear Ritter's talk (or any from the other tracks) you can easily change rooms. Ritter, a self-described "method-head" shared her thoughts and experiences on the current state of affairs in the analytical methods community with *BioProcess International*.

"The one thing that is really challenging with regulatory guidance in Europe is the difference between EMEA guidance documents and then regional expectations," explained Ritter. "Even though it's supposed to be harmonized, and we're all supposed to be using ICH (International Conference on Harmonisation), we still have the situation in biotech where we may have some regional differences in what is expected for certain types of CMC (chemistry, manufacturing, and controls) under the EMEA." This contrasts with the US Food and Drug Administration (FDA) regulation, in which there are no different interpretations whether your product is being looked at in Kansas or Oklahoma. Ritter explained that the

difficulty for new entrants into European markets is knowing what to expect from each country.

"There are still subtle differences that can really drive some substantial CMC studies earlier in the process," said Ritter. Beyond the confusion about which countries may require which studies, other uncertainties are common in the industry where analytical methods are concerned. One of Ritter's soap-boxes is the terminology difference between *bioanalytical methods* and *bioassays* (her disclaimer is that she is very passionate about helping to "fix the industry").

"When I started in the industry, I thought what I did was a bioanalytical method," explained Ritter. "I have biological materials, and I'm doing analytical methods on them. So, isn't that bioanalytical?" Yes and no, explains Ritter. The FDA has published a guidance document on *Validation of Bioanalytical Assays* to help clear up some confusion on the topic. That document defines a bioanalytical method as one that measures the presence of target analytes in biological samples.

"So that means that we're testing a biological sample for the presence of these analytes," explained Ritter. "It doesn't mean that we're testing the characteristics of that analyte as a biological entity." All of these distinctions are important, she explained, because there are different ways to validate bioanalytical methods, biomolecular methods, and bioassay methods in terms of experimental design. Thus, the terminology is important in understanding the assays' intended use and then the design of an experiment to validate each method for its intended use.

With analytical methods in mind, Torben P. Frandsen, director of antibody chemistry at Symphogen A/S, will discuss different studies he used to release and characterize a polyclonal antibody with specific examples of techniques that address the polyclonal nature of the products. On the bioassay side, Matthias Hoffman, principal scientist at Novartis Pharma AG will be discussing the development of an assay for measuring antibody-dependent cellular cytotoxicity (ADCC). 🌐

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