

Biomolecule method development and validation with Jeff Staecker

Interviewer: Hello, I'm here with Dr. Jeff Staecker, a cGMP laboratory manager with PPD. Jeff specializes in biologics analysis and is here to talk about the underlying principles and factors affecting biomolecule method development and validation. To start with, Jeff, can you define analytical method validation?

Jeff: Sure. Analytical method validation is a process that demonstrates a method's intended performance. Besides being a regulatory requirement, validation serves as an important check on any assumptions made during development. It is through the validation process that you gain confidence a method can provide expected performance over a long period of time. While the endpoint is the same, the validation process can vary substantially between different projects.

Interviewer: What is the process for analytical method development and validation?

Jeff: Analytical methods chosen for development and validation are part of an iterative process that spans the lifetime of the product, beginning with toxicity studies and continuing through release and stability testing. Because of the complexity and uniqueness of biomolecules, the process of developing and validating suitable analytical methods poses a greater challenge than those faced during the development of a small-molecule drug.

Many factors impact method development and validation. They include technical practicality (or feasibility), direction from regulatory agencies and industry practices. Regulatory guidance documents for industry typically contain few specifics and require an approach tailored to the unique characteristics of each biomolecule under development. This frequently results in changes in the analytical method menu as more is learned about a particular drug.

Interviewer: What are the guiding principles governing the selection of analytical methodologies?

Jeff: One principle is that the benefits of applying new technology must be balanced against challenges frequently associated with the technology's application. For example, cIEF is a commonly used methodology for analyzing charge variants, but the properties of certain biomolecules require different methods to evaluate charge variants and cIEF will not be the best approach in this case. Business approaches may also vary, with some companies deferring certain key technical studies until clinical efficacy can be demonstrated, whereas others accelerate analytical method development to ensure a product reaches the market quickly.

In addition, the balanced risk management approach for biomolecule method development and validation has become increasingly important. For example, recent experiences with product manufacture, in-process development and storage illustrate some of the unique challenges in supporting biomolecule development (read the article,

[Extractables and Leachables Study Approach for Disposable Materials Used in Bioprocessing.](#)). This regulatory paradigm shift is evidenced by the introduction of a variety of regulatory guidelines into the global biotech industry by the combined effort of regulatory agencies, such as the FDA and EMEA, and the industry. [For example, the numerous ICH documents applied to the biotech industry are shown in the accompanying written material. ICH Q7 is a Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients; ICH Q8 discusses Pharmaceutical Development Process Focusing on Quality by Design (QbD); ICH Q9 is a Quality Risk Management menu; and ICH Q10 defines the total Pharmaceutical Quality System.]

Interviewer: What are your thoughts on how to navigate through this complex analytical process?

Jeff: There is rarely a single solution to the challenges and pressures pharmaceutical and biotech firms are facing. In this environment, we must deliver better, safer and more affordable medicines faster. As a partner with a drug developer, we need to understand the risks involved in a particular drug development program from an analytical point of view. What's the big picture? How does that translate into analytical development that can be supported in the QC environment? What is the best way to effectively support the biopharmaceutical product development process with minimal risks to regulatory filings? PPD provides the perspective and understanding of a company with extensive experience in these areas.

Interviewer: Thank you very much, Jeff, for taking the time to provide this introduction to the underlying principles and factors affecting biomolecule method development and validation.

Jeff: You're welcome.

Interviewer: For further information about this topic, please visit our cGMP Web pages or fill out the [contact form](#).