

A Rose By Any Other Name?

Distinctions Between *Bioanalytical* and *Analytical* Test Methods

Analytical methods used for the characterization, release, and stability testing of biotechnological/biological products are often automatically referred to as “bioanalytical” methods. Many times this term is used when trying to distinguish between analyzing small-molecule chemical products and macromolecular biologically-based products. It seems sensible enough: We use *analytical* methods to test chemical pharmaceutical products, so for products that are biomolecular entities, aren’t the tests used for their analysis *bioanalytical* methods? Anyway, who cares if the term is misapplied in this manner? What difference does it make so long as we understand what we mean by it?

That is precisely the problem: Does everyone really understand what is meant by the term *bioanalytical* methods? Based on publications and presentations in the biotechnology field over the past decade, the answer is, apparently not. Although ramifications of misapplying the term can be minor, for some people (and I include myself) this mistake is akin to people pronouncing the word “nuclear” as “nucular.” It is like the sound of fingernails on a chalkboard.

According to the FDA *Guidance for Industry: Bioanalytical Method Validation* (www.fda.gov/cder/guidance/4252fnl.pdf, May 2001), a *bioanalytical* method is used for the “quantitative determination of drugs and/or metabolites in biological matrices such as blood, serum, plasma, or urine . . . tissue and skin samples.” The applications of bioanalytical methods are for “pharmacology, bioavailability, bioequivalence, pharmacokinetic, and toxicology studies” conducted in humans and animals. Bioanalytical methods are not intended for elucidating the quality parameters of the product (e.g., identity, purity, impurities); their intended use is to determine the quantity of a pharmaceutical product in biological samples.

For this reason, the technologies used to perform bioanalytical methods vary whether the drug is a chemical or

biological entity. With chemical products, the biological components of test samples can be removed by precipitation or extraction, allowing the small molecule(s) to be analyzed with technologies such as LC-MS or GC-MS. With biomolecular products, processing away the biological components of a sample can equally remove the target analyte, making accurate quantitation of the drug technically impossible. For biotech products, bioanalytical methods require technologies that can specifically measure a biological moiety that is the drug in the presence of a biological milieu that is the sample matrix. Immunological methods that use specific antigen:antibody recognition (e.g., ELISA-like methods) are usually the technology of choice for a bioanalytical assay applied to biopharmaceutical products.

It may be that the confusion between “bioanalytical methods” and “analytical methods used for the testing of biomolecular products” is more prevalent in the biopharmaceutical community because of the nature of our products. The most accurate term for the analytical methods used to assess the physicochemical parameters of these products is thought by many to be *biomolecular methods*.

One major professional scientific organization, the Association for Biomolecular Resource Facilities (www.abrf.org), recognized the distinction in terms over a decade ago when selecting its name. “Biomolecular Resource Facilities” are core laboratories that conduct physicochemical characterizations of biologically based molecular entities. Several years ago, one contract testing facility launched its new analytical services group, which was set up to perform characterization, release, and stability testing of biopharmaceutical products, under the name “Bioanalytical Services.” Numerous inquiries for the solid-phase extraction and GC-MS of BA, BE, and PK samples (which the laboratory was not designed to perform) demonstrated clearly that this name was not appropriate, so it was changed to

“Analytical Services” to reflect this distinction. On the other hand, another contract facility that conducts biomolecular chemistry, Bay Bioanalytical Laboratories, has been very successful even with “bioanalytical” in the formal name, although they emphasize it is *instrumental analysis of biomolecules*.

If you don’t believe the choice of terms is a problem when searching for specific kinds of biotech product testing services, try this experiment. Conduct a web search using the term “bioanalytical” for contract labs and see how many hits come up for facilities that predominantly test chemical products. Most will be equipped to perform SPE and GC-MS or LC-MS, which usually only apply to small-molecules, rather than immunologically based assays for the quantitative determination of biopharmaceutical products in biological samples. Using the term “biomolecular” is even less productive in calling up facilities that perform the physicochemical analysis of biopharmaceutical products.

So a conundrum exists: Do we accede to the will of the masses and live with the erroneous use of the term “bioanalytical” both for methods used in analyzing biological samples containing biopharmaceutical products *and* methods used to assess the physicochemical characteristics of the product? Or do we use the same nomenclature as for chemical pharmaceuticals, where “bioanalytical” methods are used only on preclinical and clinical samples, and “analytical” methods are used for identity, purity, potency, concentration, and stability testing of the product?

Not to complicate matters, but perhaps next we should review the term *bioassay*. 🌐



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