The future of drug dissolution testing

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Before providing a suggestion for the future, one has to consider its present status. At present, it is clear that the drug dissolution testing (as we knew it) has died, as explained below.

If one would survey the literature of the past 15 to 20 years, one would quickly realize how active drug dissolution testing "science" was. It was presented as the frontier of modern science for the development and manufacturing of pharmaceutical products.

The word science is used within quotes to emphasize that it has never been science but made-up or pseudo-science. If it had been audited by any standards-setting organization external to the pharmaceutical area or its associated regulatory authorities, including FDA and USP, it would have immediately been rejected being a pseudo or fraudulent scientific technique.

Unfortunately, it never happened because it ("science") kept within, promoting that the authorities maintain the highest and unmatched scientific expertise and capabilities. Hence, drug dissolution testing is considered modern science.

It would be helpful to briefly describe what drug dissolution testing is so that it should be clear that the technique itself is one of the most simple testing techniques.

Drug dissolution testing is a technique in which drug release from a product such as a tablet or a capsule is determined in about 1 L of water maintained at 37C with modest stirring. The idea behind the testing is to establish that the products would release the drugs as expected, which is essential for the drug to be absorbed into the bloodstream to exert its therapeutic effect.

However, so many procedures and requirements were developed to assess the products' dissolution characteristics. Numerous new and catchy terminologies and concepts were introduced. For example, Biopharmaceutic Classification System (BCS), in vitro-in Vivo correlation (IVIVC), predictive modeling, similarity factor (f2), Quality by Design (QbD), apparatus verification and validation, sink condition, newer (arbitrary) low solubility or high solubility drug criteria, so on so forth. Almost an infinite number of standards and regulatory guidelines from national and international authorities were developed and enforced.

It was all in the name of determining relevant drug dissolution characteristics of a product, which, for all practical purposes, monitors drug release into the water. Perhaps, the most interesting part is that, after such massive "scientific" research and regulatory activities, if one is asked to determine dissolution characteristics of a given blinded sample, no one can determine its valid and relevant dissolution characteristics. For example, see my unanswered FDA Citizen Petition submitted more than two years ago (link).

Many organizations, in particular, AAPS, USP, and FDA, along with other celebrity-status scientists and experts, were at the forefront in providing all kinds of instructional and motivational courses, seminars, and "helping hands." Societies and organizations were formed for this technique. In

reality, it was one fraud after another one. Everything was sold wrapped in flashy and catchy "science" packaging and under public "health" and "safety" slogans.

However, most if not all requirements and standards have been ritual-based, often developed with external "experts' help" who then sold their services to others, primarily to industry, with exuberant compensation packages. Arguably, considerable conflict of interest practices could be noted.

Any alternate opinion is considered conspirational and non-scientific, which were promptly dismissed. Only "peer-reviewed" (effectively buddy-reviewed) mechanisms were implemented even for publishing or presenting the data or opinions. Such practices effectively lead to one-sided false and fraudulent practices in the name of "drug dissolution science."

Using non-qualified and non-validated testers became norm and "scientific" practice - a serious violation of scientific principles and practices. However, claims made by regularity authorities, experts, or manufacturers were accepted as "science" or evidence-based.

Sooner or later, the current technique and the associated "science" had to die, which it now has, at least in my opinion. Any data or their interpretation using currently recommended dissolution testers and/or methods would be challenged and discredited as unscientific and irrelevant.

On the other hand, considering that drug dissolution testing is a critical testing tool available for assessing products, it is impossible to avoid or ignore its use. The question is how, in the future, one should address the current unfortunate and fraudulent situation of using flawed and in-valid testers.

A small research project may be conducted to modify the testing approach, which can address the issues. Literature provides some clear and simple ideas and suggestions (link). However, authorities and industry need to be open to new and valid scientific ideas.

Literature shows that with slight modification to the dissolution testers, the current issues can quickly be addressed. The use of valid science and its principles will bring efficiency to product development and manufacturing and availability to the public at a much cheaper and faster speed (link).