Standardization and qualification/validation of the crescent shape spindle

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Considering the flaws of poor hydrodynamics of the most commonly used apparatuses, paddle and basket, it is very well established that these apparatuses are not qualified and validated to provide relevant and reproducible dissolution results. Therefore, it is natural that people are seeking alternatives. The vessel based apparatuses using the crescent shape spindle provides such an alternative. The next obvious question would be, are such apparatuses qualified to be used as dissolution testers? Also, have these been standardized? The answer to both questions is yes, as explained below.

Standardization: That is, will the analysts be able to obtain consistent apparatuses batch after batch. The answer is yes. Firstly, except for the crescent shape spindle itself, the rest of the apparatus is exactly the same as described in the pharmacopeias, therefore, those specifications are the same. The use of the crescent shape spindle would not require any more strict specifications than were required prior to the recent guidelines based on PVT or MQ approach. The use of the crescent shape spindle by design provides a more rugged environment than those of the paddle and basket, therefore, extended specifications are not necessary. However, there is no harm in using the recent versions if desired.

In addition, the use of the crescent shape spindle does not require a vibration free environment and/or de-aeration of the medium. Not only is the use of the crescent shape spindle insensitive to such sensitivities, controlling these specifications make the testing (bio) irrelevant as well. Therefore, the use of the crescent shape spindle provides much more analyst friendly, relevant and rugged operations.

Now let us consider the standardization of the crescent shape spindle itself. It is to be noted that at present in general dissolution analysts and the community at large are obsessed with the specifications. They may require that everything be accurate and controlled to the micro and nano levels! This is completely unnecessary in case of crescent shape spindles. Let us examine what specifications would be needed and why. In principle, a dissolution tester is a stirrer and in this respect the brush component of the spindle is no different than a magnetic stirring bar. The manufacturer provides information/ certification about the nature of the material used and dimensions of the bars. These are used on an as-is-basis from the box. This is exactly how the crescent shape spindle should be used. Manufacturer/supplier will provide the information about the nature of the material and dimensions of the spindle and analysts would just use these. That is it. If it is more complicated than this, then there is something not right with the spindles or the approach. It is to be emphasized that the analyst should not be thinking twice before using the spindles. Replacement of the spindle or the brush part should be as simple as changing a light bulb. If it is not that simple or does not change as easily as suggested, then the spindle should be returned.

Qualification: The qualification here means design qualification, i.e., are the design and operation of the testers with the crescent shape spindles suitable for its intended use. The answer is yes. To explain further, one has to first define, what is the intended use of a dissolution tester? The intended use of a dissolution tester is to provide potential in vivo dissolution characteristics of products (tablets/capsules) using simulated in vivo GI tract environment. Generally drugs are absorbed from the intestinal environment thus for dissolution testing this would be most appropriate environment to simulate. This intestinal environment is represented by an aqueous based medium such as water itself or phosphate buffer having pH of 6.8 maintained at 37 °C. If the drug under consideration has low water solubility then one may require adding some small amount of solubiliser (e.g. SLS). In addition, a gentle mixing mechanism would be required, which the crescent shaped spindle, set at 25 rpm, provides. The main and critical aspect is that these experimental conditions are linked to the physiology, therefore cannot, or should not, be changed from product to product. A simple criterion to establish "fit for intended use" is to test two different types of products such as IR and ER, using a single set of experimental conditions. These two types of products should provide corresponding fast and slow drug release characteristics as they would in humans. The use of the crescent shaped spindle provides such characteristics. Therefore, it can be concluded that the vessel based apparatuses are qualified or "fit for intended use" i.e. able to provide dissolution results reflecting in vivo characteristics. For a thorough discussion on this aspect please see the following links [link].

Performance: It is the most important and essential part of the tester and the testing. This step should be considered as an operational qualification step for the tester. The performance of a tester can only be established using a well established product of known dissolution characteristics. As there is no recognized reference product available at this time, one may use a product for which dissolution results using the crescent shape spindle have already been published. If one can reproduce those results in the laboratory with an acceptable reproducibility, then the apparatus has been qualified and validated. A suggestion in this regard at this time may be the use of 60 mg diltiazem IR tablets. They require simple experimental conditions for testing i.e. water and UV detection and have been tested extensively [link]. Therefore, this should be a good choice.

With a qualified and validated dissolution tester (vessel based apparatus using the crescent shape spindle with a medium to dissolve the expected amount of drug from the test product), an analyst/formulator is ready to test or develop a product. No further method development steps or exercises are needed. It should be emphasized again that one should not be changing experimental conditions for the test products. If a product does not provide results (dissolution) as expected, then the product should be critically evaluated as adjustments and/or changes to the product may be required.