Stability Studies: The Architecture Behind Establishing a Beyond-Use-Date Webinar Q&A

840 Research Parkway, Ste. 546 • Oklahoma City, Oklahoma • 73104
Phone: 405-271-1144 • Fax: 405-271-1174 • www.arlok.com

Stability Design

1. **What would be considered a conservative approach to assigning a BUD when using literature? 50% of the amount reported?**

   When used appropriately, BUD's from literature can be used as written. Careful considerations must be taken when selecting data to use from literature.

2. **When you look at stability data, does it really matter which chemical wholesaler you use? If you change manufacturers of an API or active pharmaceutical product but nothing else with your formulation, do you need to repeat your stability study? (Even if the API or pharmaceutical product is equivalent as far as preservatives, antioxidants, etc.)**

   Drug product stability is formulation specific. As long as the formulation is exactly the same, the wholesaler of the drug substance should not change the stability profile.

3. **As long as everything about a formulation remains the same, will the stability study results apply regardless of whether humans compound the product, or a robot?**

   The stability should be the same as long as the process is the same regardless of whether a human or a robot is performing the compounding.

4. **What is the best way to use current stability studies when determining potency time points where the BUD tests have been performed previously as in the case of Tri-Mix injections and how does the concentration affect the potential for using this previously conducted data? Can highest and lowest concentrations be used to reduce the need for certain testing?**

   Previous stability studies can be valuable in designing a stability study. You may be able to learn how long a product is stable so you can design your study so that a sufficient number of time points fall within the anticipated stability window. Stability can be concentration specific so applying a BUD from a different concentration may result in an inappropriate BUD. Bracketing (testing the highest and lowest concentrations of a product) can be an acceptable practice to reduce the stability study testing requirements. For products with multiple drugs such as Tri-mix, the ratio of drug to drug is also important in designing a bracket approach.

5. **Can stability data be extrapolated from higher concentration to lower concentration with respect to regulations?**

   The best approach is bracketing. Bracketing means to test the highest and lowest concentrations. Keep in mind the formulations must be identical except for the drug concentrations for bracketing to be scientifically sound.

6. **What cases do we need to perform stability studies? Just when we need to determine the BUD? What about if we made changes in formulation or if we change the manufacture process?**

   Stability studies are performed to establish BUD. If you have established a BUD and change your formulation or process, you may need to repeat the stability study.

7. **If during the Stability indicating method your API came in higher or lower in concentration, can you still accept this study to perform your stability study?**

   Stability can depend on the concentration of the drug so applying stability from one concentration to another may result in assigning an inappropriate BUD. The product may still be able to be used for method development/ validation of the stability indicating method.

Stability Studies: The Architecture Behind Establishing a Beyond-Use-Date Webinar Q&A

840 Research Parkway, Ste. 546 • Oklahoma City, Oklahoma • 73104
Phone: 405-271-1144 • Fax: 405-271-1174 • www.arlok.com

Stability Design (continued)

8. **What would you recommend in assigning BUD if concentration studies are only available at 1 concentration?**

   Stability can be drug concentration specific. Be careful about applying stability data to a different concentration.

9. **Do you recommend 503A compounders to start performing stability testing for BUD now or shall they wait until proposed USP<797> gets finalized i.e. Dec. 2019?**

   Anyone conducting stability studies should use stability indicating methods.

10. **With the up and coming changes to the 795 gearing towards stability indicating assay; would you still recommend doing potency over time with the indicating assay, or no?**

    Stability indicating methods are always recommended when determining a BUD.

11. **What test would allow for longer than a 28 day use for MDV vials?**

    Stability studies for MDV include these tests: appearance, pH, particulate matter, potency, sterility, endotoxin, and antimicrobial effectiveness.

12. **What are the factors that can cause increasing of endotoxins in a sterile sealed container?**

    There could be microorganisms present in the sample not caught by the sterility test at time 0. By the time the second sterility test was conducted, those microorganisms could have died. In this case both sterility tests would pass but endotoxin would indicate the situation.

13. **With regards to pH in sterile preparations, is there a general range that is allowable under USP?**

    pH for parenterals should stay between about 4.0 and 7.5.

Container Closure Testing

1. **When is container closure testing necessary?**

   Container closure testing can be used in lieu of sterility and endotoxin testing. At a minimum container closure integrity should be demonstrated at the beginning and end of the stability study.

2. **How many time points you suggest for container closure?**

   Beginning and end at a minimum. Container closure testing does not necessarily need to be performed at each time point.

3. **Is container closure testing only required when you are trying to extend the BUD?**

   Container closure integrity data is required by some state boards when assigning a BUD, but you should always know that your container closure system can maintain sterility.

4. **What about container closure testing on the Sterile Injectable PF?**

   Data to demonstrate your container closure can maintain a sterile environment is valuable for all sterile preparations.

Stability Studies: The Architecture Behind Establishing a Beyond-Use-Date Webinar Q&A

840 Research Parkway, Ste. 546 • Oklahoma City, Oklahoma • 73104
Phone: 405-271-1144 • Fax: 405-271-1174 • www.arlok.com

Preservatives

1. **What is meant by preservative potency data?**

   Demonstrating the stability of the preservative with an appropriate analytical method

2. **Is a stability indicating method required for analyzing the potency of preservatives over time in lieu of AET at each time point?**

   Ideally, the test method for the preservative(s) would also be stability indicating.

3. **To clarify - if you are using the potency in conjunction with AET (i.e. preservative content throughout the study at each time point but AET at T = 0 and T = last time point)**

   You could consider testing the preservatives potency at T=0 only and then AET throughout.

4. **Does the potency of the antimicrobial agent need to be stability indicating? Or is it just a supplemental study?**

   Ideally, the test method for the preservative(s) would also be stability indicating. The data is valuable because it shows that the correct amount of preservative is present. Testing the preservative concentration throughout the stability study may be a lower cost alternative to performing AET throughout the study. This is only acceptable if AET has passed for that specific product.