Stability Indicating Methods Webinar Q&A

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1. **Can you request to run a stability indicating method at your intended expiration date and get a true expiration without going through the extra expense of force degradation?**

   For a method to be considered stability indicating, forced degradation must occur during method development. Also, there should be sufficient data to demonstrate the concentration of the Active Pharmaceutical Ingredient (API) throughout the stability study and not just at the end. If end point data is the only data to demonstrate stability, someone could question whether the compound was purposely made super-potent so that the API degraded into specification at the end point.

2. **Does a 503B pharmacy have to identify all degradants found during a stability study? Or just the degradants named in the USP monograph?**

   It is important to demonstrate the stability indicating potency method is capable of separating all degradants from the API. See 21 CFR 211.166 for details.

3. **How do you determine what type of HPLC column will be utilized for a given compound?**

   The appropriate analytical method and column is highly dependent on the API's structure.

4. **If a validated method was created for stability studies, do you recommend using this method for batch release testing?**

   Analytical methods fully validated for your specific product is always the preference. As opposed to using stability indicating methods, it may be worthwhile to invest in shorter, lower priced validated release methods.

5. **What does it cost?**

   The cost to develop and validate formulation specific stability indicating methods is highly dependent on the formulation.

6. **What does resolution of 2 mean for HPLC?**

   Resolution indicates the amount of separation between 2 peaks on the chromatographic system. The software running the system assigns a number to the resolution to indicate how far the peaks are separated. The higher the resolution number; the further the separation.

7. **For IV solutions with API, is the placebo the diluent?**

   The placebo includes the diluent and any other ingredients in the starting material (vial).

8. **How is oxidative stress performed?**

   The oxidation stress is performed by exposing the material to hydrogen peroxide.

9. **While doing forced degradation, the assay of the API dropped to 80% label claim, but there was no degradant peak. The mass balance is not 100%. What is the rationale?**

   Not all degradants will appear under the same chromatographic conditions used to test the product. Some portion of the material may degrade to the point where it comes off the column in the void, may degrade to something that does not respond the same at the UV wavelength being monitored, or may degrade to an insoluble species. Some lack of mass balance may be acceptable, but a major loss of mass balance needs to be further investigated.

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10. Why do you have to run 8-9 injections for potency release?

To meet system suitability requirements, a typical sequence for analyzing a compounded preparation for API potency consists of multiple (6) injections of the reference standard, an injection of a blank (extraction buffer), potentially a 2nd reference standard (Quality Control Standard), and the sample being tested.

11. How do we decide whether we need an internal standard? Does this apply more in complex sample prep methods?

Typically internal standards are used for complex sample preparations and/or methods with precision issues.

12. Can we verify published analytical methods just like USP and still validate?

Yes. USP methods, once verified for your specific product, can be used and considered fully validated. Care should be taken when using methods published by other sources.

13. BUD (Stability studies) are required for 503B facilities. Are these also required for 503A (state regulated compounding pharmacies)?

To be sure an appropriate BUD is assigned to a compounded preparation, stability indicating methods and stability studies should be used regardless of the compounder's classification. Also, some states have started implementing their own regulations requiring the use of stability indicating methods.

14. When I send in an oral suspension for potency testing at certain time points (e.g potency at 0, 14, 30, 90), is the sample subject to any stress during the time point testing?

No. The stress conditions covered in the webinar are performed while developing the stability indicating analytical method to show the method is capable of separating degraded drug from non-degraded drug. Stressing the drug product during the course of the stability study is a different topic to be covered at another time.

To view webinar recording, visit: https://attendee.gotowebinar.com/register/7099938387122115841.