Fundamentals of Dissolution

MODULE 1

1. True or False
   When a *USP* monograph lists, for example, dissolution test 1, it means that it refers to the reference listed drug.

   False.
   Feedback:
   The dissolution test numbers merely represent the order in which the dissolution tests were submitted to USP. They have no relationship to the reference listed drug.

MODULE 2

2. Select all that apply
   Select the options that are goals of a dissolution test:

   A. To aid in confirming potential benefits or identifying issues due to changes in formulation or processing during drug product development.
   B. To evaluate the drug product performance in a patient's GI tract.
   C. To detect variations in the manufacturing process that have critical influence on the dosage form performance.
   D. To link performance of a drug product on the market with the batch used for bioavailability studies.

   A, C and D are correct.
   Feedback:
   B is incorrect. To evaluate the drug product performance during manufacturing.

3. Select all that apply
   Select the options that are implications of Nernst-Brunner variables:

   A. If the surface area is increased, the dissolution rate will also be increased.
   B. The higher the diffusion coefficient, the higher the dissolution.
   C. The thicker the boundary layer, the faster the dissolution rate.
   D. The dissolution rate reduces to zero as the concentration approaches saturation.

   A, B and D are correct.
   Feedback:
   C is incorrect.
   The thicker the boundary layer, the slower the dissolution rate.

4. True or False
   USP <1092> defines sink conditions as having a volume of medium at least three times the volume required to form a saturated solution of drug substance.

   True.
   Feedback:
   According to *USP* <1092>, sink conditions require a volume of medium at least three times the volume required to form a saturated solution of drug substance.

MODULE 3

5. Regarding orally disintegrating tablets, it is correct to say:

   A. They require disintegration and dissolution tests.
   B. They may require multiple disintegration tests because of differences in formulation.
   C. The FDA guidance is for disintegration in up to 30 seconds for generics**.**
   D. All of the above.
   E. None of the above

   D is correct.
   Feedback:
   All items are correct.

6. Select all that apply

   Regarding USP Apparatus 1, Basket, it is correct to say:

   A. The dosage form must be placed inside the basket.
   B. It can only be used for single units.
   C. Disintegrating dosage forms may pass through the mesh.
   D. It generates cumulative dissolution results.
   E. The formulation may clog the screen.

   A, C, D and E are correct.
   B is incorrect. It may be used for both single units and multiple units.

7. Regarding USP Apparatus 2, Paddle, it is correct to say:

   A. Dosage form should remain at the bottom center of the vessel.
   B. Sinkers should be employed for floating or sticking dosage forms.
   C. Compendial sinkers must be used.
   D. It can be used for solid dosage forms and particulates.
   E. It generates cumulative dissolution results.

   A, B, D and E are correct.
   Feedback:
   C is incorrect. Non-compendial, commercially available sinkers may be used but should be well specified and validated as part of the dissolution method.

8. Regarding USP Apparatus 3, Reciprocating Cylinder, it is correct to say:

   A. Dosage form is placed in the cylinder.
   B. It is used for extended-release products.
   C. It generates cumulative dissolution results.
   D. It is programmable to run dissolution in different media and at different speeds at various times.
   E. Attempt to simulate pH changes in the GI tract

   A, B, D and E, are correct.
   Feedback:
   C is incorrect.
   USP Apparatus 3, Reciprocating Cylinder, generates fractionated dissolution results since the dosage form is moved from one row to the next.

9. Regarding USP Apparatus 4, Flow Through Cell, it is correct to say:

   A. The dosage form is placed in a cell, where the medium flows through.
   B. The sample solution is filtered before leaving the cell and is directly analyzed or fractions are collected.
   C. Compendial cell designs and flow rates must be used.
   D. It can be used for solids, semisolids and liquids.

   A, B and D are correct.
   C is incorrect. It is acceptable to use non-compendial cell designs and flow rates as long as the validation for your method warrants.

MODULE 4

10. True or False
    It is recommended to uniquely identify each position in the dissolution tester and number each element for each unique position and keep the same position throughout the qualification process.

    True.
    Feedback:
    This practice is helpful in identifying trends in the results and consequently causes in variability.

11. Multiple choice
    The following may be a source of variability in dissolution test results, except:
    A. Loose basket clips
    B. Bent baskets
    C. Old or distorted baskets
    D. Baskets not properly cleaned and stored
    E. A clear vent hole in the basket head

    E is the correct answer.
    Feedback:

The vent hole in basket the head should be clear. All other options are potential sources of variability.

12. True or false
    When a tablet that is introduced into the medium floats in the basket, it disintegrates more evenly, allowing for more exposed surface area, which is desirable.

    False
    Feedback:
    Tablets that float and disintegrate should be discarded because that is not the proper starting procedure for the test.

13. Select all that apply.
    The USP dissolution toolkit can be used to:

    A. Help enhance procedures and control limits for mechanical qualification
    B. Provide guidelines to generate accurate PVT results
    C. Provide an information basis to develop internal SOPs for the GMP environment
    D. Serve as legal guidance on how to perform procedures

    Feedback:
    D is incorrect. The USP Dissolution Toolkit is not legally enforceable. It provides a best practices guide for dissolution qualification.

14. Select all that apply
    The following are good practices to perform a successful PVT and to obtain consistent dissolution results:

    A. Follow the procedure described in the Certificate of the Reference Standard.
    B. Use the designated vessel and shaft for each position in the dissolution instrument.
    C. Perform rigorous mechanical qualification
    D. Deaeration of the dissolution medium is required for PVT and other dissolution methods.
    E. Test should be started as soon as possible after media deaeration.
    F. Filter samples immediately after withdrawing samples from vessel.

    Feedback:
    Deaeration is required for PVT; however, for other dissolution methods deaeration may or may not be necessary.

The other sentences are good practices to perform a successful PVT.

MODULE 5

15. Regarding the interpretation of the dissolution results, it is correct to say that:

    A. S1, S2 and S3 must be performed in order to meet the acceptance criteria.
    B. The quantity, Q, is the amount of dissolved active ingredient specified in the individual monograph, expressed as absolute value of the label claim.
    C. The values in the Acceptance Table are percentages of the labeled content (label claim) and so is Q.
    D. All of the above

    C is correct.
    Feedback:
    Regarding the results of a dissolution test, if they conform at S1, there is no need to proceed to S2; if the results conform at S2, there is no need to proceed to S3.
    Also, Q is expressed as a percentage of the labeled content.

16. Select all that apply
    Select the correct sentences regarding dissolution:

    A. In vitro dissolution specifications are established to ensure batch-to-batch consistency.
    B. Specifications and dissolution methods are linked to each other but do not have a relationship to the drug product.
    C. Once a dissolution specification is set, the drug product should comply with that specification throughout its shelf life.
    D. Interpretation of dissolution results should be based on the compendial acceptance tables.

    A, C and D correct.
    Specifications and dissolution methods are linked to each other and to the drug product.
    All other statements are correct