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Meeting Report: APQ/IPA Workshop on Challenges for Dissolution Testing in the 21st Century

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A workshop on the Challenges for Dissolution Testing in the 21st Century was held in Bangalore, India on May 15 and 16, 2009. This workshop was jointly sponsored by the In Vitro Release and Dissolution Testing Focus Group of the APQ section of AAPS and the RA Division of Karnataka State Branch of the Indian Pharmaceutical Association. The workshop contents are available at http://www.aapspharmaceutica.com/inside/Focus_Groups/InVitro/index.asp.

DAY 1–MAY 15, 2009

Session One

After an elaborate inaugural ceremony that included a presentation of sandalwood garlands to each of the speakers, Dr. B. R. Jagashetty, Drug Controller for the state of Karnataka, gave a keynote address on the importance of dissolution testing in drug development.

Session Two

Introduction to Workshop

Premnath Shenoy

QBD in Analytical Methods and Biowaiver Consideration for Branded Drug Product

Jianmei Kochling, Genzyme Corporation

Jianmei talked on quality by design in analytical methods and biowaiver consideration for branded products**.** She presented case studies where intrinsic dissolution results were used to assist in polymorph selection; moreover, a biorelevant dissolution medium was used. Other cases studies where the effect of particle size and surface area/morphology had an effect on the dissolution rate were presented.

Dissolution Method Development

Saji Thomas, Par Pharmaceuticals

Saji talked on general method development considerations during product development. He discussed the considerations during different phases, and while emphasizing dissolution method development, he outlined the variables to be considered. After discussing BCS classification, he outlined the different parameters to be validated. He then showed Design of Experiments (DOE) in detail as applied to dissolution method validation.

Session Three

Citations and Case Studies

Sridhar Rao

Rao's talk was on the compliance to regulations as related to dissolution testing. Several examples and case studies of 483s issued due to noncompliance or failures during dissolution testing were cited. Possible solutions to address product failure at dissolution stage were offered.

Dissolution Method Transfer, Including Sources of Problems

Vivian Gray, V. A. Gray Consulting, Inc.

Vivian's talk emphasized the source of problems during transfer of a dissolution method. She pointed out the importance of robustness checking and the role of different parameters that affect dosage form dissolution including the basket, vessels, dissolution medium aeration, vibration, and bubbles.

Session Four

Challenges in Dissolution Testing and Setting Specification for Generic Drugs

Saji Thomas, Par Pharmaceuticals

Saji talked on challenges in dissolution method development for generic products. Examples were given for an orally disintegrating tablet and an extended-release product; dissolution profiles and specifications for generic and RLD products were compared. Recommendations were given for FDA to use QBD approach for dissolution testing and setting acceptance criteria.

DAY 2–MAY 16, 2009

Session Five

Dissolution Aberrant Data Investigation

Bryan Crist, Varian, Inc.

Bryan Crist talked about the causes of aberrant data during dissolution testing. He went through the process of investigation of OOS results, especially as it relates to dissolution testing, and provided a road map for investigation that includes checking the apparatus, the

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method, the analyst, and the materials. For each of these, he detailed specific parameters to be checked. Finally, quite a few observations by FDA investigators citing failures in dissolution testing were shown.

Impact of Dissolution in Product Development and Launch Strategy

Indranil Nandi, Sandoz

Indranil talked on the recent aggressiveness of the generic drug market in launching products within Paragraph 4 certification. He emphasized the strategy behind developing a dissolution test that allows no hurdles in product launch. Several examples were given where failure during dissolution testing, for either stability or validation batches, resulted in a delay in product launch.

Session Six

Development of Performance Tests for Semisolid Dosage Forms within QBD Design Space

Kailas Thakker, Analytical Solutions, Inc.

Kailas talked on developing a performance test for topical dosage forms in QBD design space. Examples of a performance test developed for a vaginal gel were given. The performance test was validated using attributes of precision, intermediate precision, ruggedness, robustness, and dose strength proportionality. Examples of the instances where SUPAC-SS guidance criteria were used to determine the "sameness" between batches were given.

Dissolution Regulatory GMP Issues, Including Preparing for a PAI

Vivian Gray, V. A. Gray Consulting, Inc.

Vivian's presentation was focused on GMP compliance issues surrounding dissolution testing. Examples of issued citations and 483s that were directly related to dissolution testing were given. FDA guidances for IR, MR, and SS dosage forms were cited, and suggestions were given on avoiding noncompliance to the regulations.

Session Seven

Controls in Dissolution Testing–Type 1 and 2

Sanjay Shetgar, Dr. Reddy's Laboratories

Sanjay talked about the dissolution test, its significance, and factors affecting the test. Controls such as instrumental and environmental vibrations, vessel dimensions, asymmetry, surface irregularity, wobble, shaft verticality, levelness, and temperature control were listed, and suggestions for addressing them were made. A checklist was provided to aid an analyst in checking various parameters before starting a dissolution test.

Performance Testing in Pharmacation Dosage Forms

Erika Stippler, USP

Erika talked on performance testing for dosage forms. Dosage forms are classified according to the route of administration, and the preferred apparatus for each type of dosage forms was listed (USP <1092>). Critical parameters affecting dissolution testing were listed, and the results of studies conducted to measure the effect of perturbations on the dissolution apparatus and method were cited. Performance tests for topical, transdermal, aerosol, parenteral injectables, medicated chewing gums, and mucosal delivery dosage forms were described.

IPA Organizer- Premnath Shenoy

In Vitro Release and Dissolution Testing Focus Group organizers and speakers: Left to right-V. Gray, E. Stippler, J. Kochling, B. Crist, S. Thomas, and K. Thakker.