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Development, Validation, and Transfer of Dissolution Methods

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In order to develop and validate a rugged dissolution method that can be easily transferred, it is important to have a good understanding of the theory of dissolution and the role of the key parameters. Therefore, this presentation began with a brief overview of the theory of dissolution followed by an in-depth discussion of the key parameters involved in the development, validation and transfer of a dissolution method. When developing a dissolution method, the role of the physical and chemical properties of the drug substance as well as its dosage form characteristics must be considered. The selection of the appropriate dissolution apparatus and the identification of key parameters is also critical when developing a dissolution method. Validation of dissolution methods in accordance with ICH guidelines was discussed concerning method selectivity, accuracy, precision, linearity, range and ruggedness. The importance of ruggedness determinations was emphasized. Evaluation of critical parameters identified from ruggedness testing can facilitate method transfer and troubleshooting. Other practical approaches to dissolution method transfers were provided, along with examples of troubleshooting common problems.

The experiences of the majority of the audience in Puerto Rico were from the viewpoint of the receiving laboratory. Consequently, they were extremely interested in practical approaches to evaluating the quality of a dissolution method and its ruggedness. Quite a few people had experienced poor dissolution methods that had not been adequately checked with respect to sink conditions, method parameters (media composition, agitation speed, sample positioning), absorption into tubing, sample handling and degassing procedures.

One of the primary concerns for everyone in the audience was how to handle dissolution calibration failures. At this time, nearly everyone tries to find a specific cause, fix it, and run the calibration again. The questions that are not easy to answer are: How many times do you repeat the calibration? If it fails, then passes (with or without an specific cause) how would you justify accepting the passing results? It was agreed that the approach of calling the system calibrated when it finally passes without some justification was risky in light of the Barr decision. The best approach is to have it pass more than once. We discussed at length the problems associated with the last lot of calibrator tablets, USP prednisone lot J. A new lot of prednisone tablets has recently been released by USP.

During the panel session and after the presentation, I had the opportunity to hear the experiences of many different analysts. Nearly all of them had problems with dissolution that could be traced to inadequate system maintenance and/or non-rugged methods. The importance of adequately evaluating your method for ruggedness (whether developing or receiving the method) was the primary emphasis of my talk.

** The presentation material was authored by Diane L. Peterson, Ph.D. and Michael J. Baltezor, Ph.D., Marion Merrell Dow, Inc, Kansas City, MO. Dr. Peterson gave this presentation.*