Pharmaceutical Dissolution Testing

MYLAN EXHIBIT 1030

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Taylor & Francis
Taylor & Francis Group
Boca Raton London New York Singapore

Published in 2005 by
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

Printed in the United States of America on acid-free paper
10 9 8 7 6 5 4 3 2 1

International Standard Book Number-10: 0-8247-5467-0 (Hardcover)
International Standard Book Number-13: 978-0-8247-5467-9 (Hardcover)

Library of Congress Cataloging-in-Publication Data

Catalog record is available from the Library of Congress

T&F informa

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The Role of Dissolution Testing in the Regulation of Pharmaceuticals: The FDA Perspective

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INTRODUCTION

Over the last quarter century the dissolution test has emerged as a most powerful and valuable tool to guide formulation development, monitor the manufacturing process, assess product quality, and in some cases to predict in vivo performance of solid oral dosage forms. Under certain conditions, the dissolution test can be used as a surrogate measure for bioequivalence (BE) and to provide biowaivers, assuring BE of the product. Dissolution test has turned out to be a

critical test for measuring product performance. Generally, dissolution testing of solid oral dosage form is carried out by the basket (USP Apparatus 1) or paddle (USP Apparatus 2) method under mild agitation (100 rpm with the basket or 50–75 rpm with the paddle), in an aqueous buffer in the pH range 1.2–6.8. Dissolution samples are analyzed at 15 min intervals for immediate-release (IR) products or at hourly intervals for extended-release products until at least 85% dissolution is achieved. For water-insoluble drug products, small amounts of surfactants are often employed to achieve sink conditions.

Dissolution is also used to identify bioavailability (BA) problems and to assess the need for further BE studies relative to scale-up and post-approval Changes (SUPAC), where it functions as a signal of bioinequivalence. In vitro dissolution studies for all product formulations investigated (including prototype formulations) are encouraged, particularly if in vivo absorption characteristics can be defined for the different product formulations. With such efforts, it may be possible to achieve an in vitro/in vivo correlation. When an in vitro correlation or association is available, the in vitro test can serve not only as a quality control (QC) specification for the manufacturing process, but also as an indicator of in vivo product performance.

Several in vitro tests are currently employed to assure drug product quality. These include purity, potency, assay, content uniformity, and dissolution specifications. For a pharmaceutical product to be consistently effective, it must meet all of its quality test criteria. When used as a QC test, the in vitro dissolution test provides information for marketing authorization. The dissolution test forms the basis for setting specifications (test, methodology, acceptance criteria) to allow batch release into the market place. Dissolution tests also provides a useful check on a number of physical characteristics, including particle size distribution, crystal form, etc., which may be influenced by the manufacturing procedure. In vitro dissolution tests and QC specifications should be based on the in vitro performance of the test batches used in in vivo studies or on suitable compendial specifications. For conventional-release products, a single-point dissolution

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