Pharmaceutical Dissolution Testing

MYLAN EXHIBIT 1025

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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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Dissolution Method Development: An Industry Perspective

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INTRODUCTION

In today's pharmaceutical industry, dissolution testing is a valuable qualitative tool that provides key information about the biological availability and/or equivalency as well as the batch-to-batch consistency of a drug. Therefore, a properly designed dissolution test is essential for the biopharmaceutical characterization and batch-to-batch control of the drug product. During drug development, dissolution testing is used to select appropriate formulations for in vivo testing, guide formulation development activities, and assess stability of the drug product under various packaging and storage requirements. For the dissolution test to be a useful drug

characterization tool, the methodology needs to be able to discriminate between different degrees of product performance and thus, the collection of a multi-time point dissolution profile is useful. At present, almost all solid oral dosage forms require dissolution testing as a quality control check before a product is introduced into the market place. For the dissolution test to be a useful quality control tool, the methodology should be simple, reliable and reproducible, and ideally be able to discriminate between different degrees of product performance (1).

Dissolution testing is also used to identify bioavailability (BA) problems and to assess the need for further bioequivalence (BE) studies relative to scale-up and post-approval changes (SUPAC), where it can function as a signal of bioinequivalence (2,3). The issuance of the Food and Drug Administration (FDA) guidance document, *Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate-Release Solid Oral Dosage Forms Based on a Biopharmaceutics Classification System*, allows dissolution testing to be used as a surrogate for in vivo BE testing under certain circumstances (4). The Biopharmaceutics Classification System (BCS) is a scientific framework for classifying drug substances based on their aqueous solubility and intestinal permeability. When combined with the dissolution of the drug product, the BCS takes into account three major factors that influence the rate and extent of drug absorption from immediate-release solid oral dosage forms: dissolution, solubility, and intestinal permeability (5). Based on the BCS framework, drug manufacturers may request waivers from additional in vivo studies (biowaivers) if their drug product meets certain criteria. In addition, the FDA's guidance on BA and BE (6) allows biowaivers for additional strength(s) of immediate-release as well as modified-release drug products based on formulation proportionality and dissolution profile comparison.

These changes in BE requirements that move away from the in vivo study requirement in certain cases and rely more on dissolution test results, emphasize the significance of dissolution test applications. In all cases where the dissolution

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