Guidance for Industry
Orally Disintegrating Tablets

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2008
Chemistry

Dr. Falk Pharma Ex. 1005
IPR Petition - USP 11,260,061

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TABLE OF CONTENTS

I. INTRODUCTION 1
II. BACKGROUND 1
III. DISCUSSION 2
IV. DISINTEGRATION TESTING 3

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I. INTRODUCTION

This guidance provides pharmaceutical manufacturers of new and generic drug products with an Agency perspective on the definition of an *orally disintegrating tablet* (ODT)—which is a different dosage form than, for example, a chewable tablet or a tablet that should be swallowed whole with liquid—and also provides recommendations to applicants who would like to designate proposed products as ODTs.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

In an effort to develop drug products that are more convenient to use and to address potential issues of patient compliance for certain product indications and patient populations, pharmaceutical manufacturers have developed products that can be ingested simply by placing them on the tongue. The products are designed to disintegrate or dissolve rapidly on contact with saliva, thus eliminating the need to chew the tablet, swallow an intact tablet, or take the tablet with liquids. This mode of administration was initially expected to be beneficial to pediatric and geriatric patients, to people with conditions related to impaired swallowing, and for treatment of patients when compliance may be difficult (e.g., for psychiatric disorders).

[1] This guidance was prepared by the Office of Pharmaceutical Science in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

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After the Agency received and reviewed applications for the initial products, the CDER Nomenclature Standards Committee developed the following definition for an ODT as a new dosage form in 1998:

> *A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.*[2]

Characteristics that were exhibited by the initial products included low tablet weight, small tablet size, highly soluble components, and rapid disintegration. Such characteristics supported the intended uses of these products.

However, as firms started developing additional products using different technology and formulations, many of these later products exhibited wide variation in product characteristics from the initial products. Because this shift in product characteristics can affect suitability for particular uses, the Agency developed this guidance for industry.

III. DISCUSSION

As briefly discussed in section II, an ODT has previously been distinguished as a separate dosage form because of the specific, intended performance characteristics of such a product, which are rapid oral disintegration in saliva with no need for chewing or drinking liquids to ingest these products. These characteristics, which are an aid to patient use and compliance, are the primary characteristics that constitute the basis for classifying a product as an ODT.

The recommendations in this guidance are based on the intention of the original definition and on Agency experience with new drug applications (NDAs) and abbreviated new drug applications (ANDAs) submitted for this dosage form. To determine what the Agency's experience has been, we surveyed applications for products submitted to the Agency, completed a literature review, and collected information from laboratory studies that showed that although disintegration times ranged from a few seconds to longer than a minute, a large majority of these products have in-vitro disintegration times of approximately 30 seconds or less. These products represented different manufacturing technologies, a variety of tablet sizes and weights, and various disintegration strategies, thus demonstrating that relatively rapid disintegration is readily achievable across a variety of products.

Products labeled as ODTs should match the primary characteristics for this dosage form (identified above). Based on the original product rationale and Agency experience, we recommend that, in addition to the original definition, ODTs be considered solid oral preparations that disintegrate rapidly in the oral cavity, with an in-vitro disintegration time of approximately 30 seconds or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative (see section IV).

[2] CDER Data Standards Manual.

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Although the value of 30 seconds is given as a desired result, it is not intended to represent an arbitrary distinction between an ODT and some other tablet form. It is instead representative of a general time period associated with drug products that have been found to have performance characteristics appropriate for a disintegrating tablet meant to be taken without chewing or liquids.

We recommend that as a primary consideration when developing this type of product, you use the defining characteristics for this dosage form designation (rapid disintegration in saliva without the need for chewing or liquids). Products should be developed to match these characteristics, rather than labeling a tablet as an ODT because it would eventually disintegrate when placed in the mouth. For example, tablets that take longer than 30 seconds to disintegrate or are dosed with liquids may be more appropriately considered to be chewable or oral tablets.

Additional parameters for consideration during product development are tablet size, tablet weight, component solubility, and the effect these factors have on the product's intended use. While tablet size or weight is not explicitly included in the definition, you should consider the effect large tablets have on patient safety and compliance. We generally recommend that the weight of the tablet not exceed 500 mg; however, if a tablet intended for use as an ODT weighs more than 500 mg, its ability to perform effectively as an ODT should be justified based on product performance. For such products, the extent of component solubility (e.g., tablet residue, need for liquids) can influence the acceptability of the product being labeled as an ODT.

IV. DISINTEGRATION TESTING

Part of the process of determining if a product is an ODT involves testing a product to see how long it takes to disintegrate. Determination of disintegration time appears to be method dependent. Some methods are more discriminating than others. To provide both a standard for and consistency in disintegration testing, we recommend that applicants use the USP method for disintegration testing.[3] However, other methods that can be correlated with or are demonstrated to provide results equivalent to the USP method also can be used and submitted to determine disintegration time.

[3] *USP 29, <701> Disintegration*, pp. 2670-2672.