

Guidance for Industry and Reviewers

Estimating the Safe Starting Dose in Clinical Trials for Therapeutics in Adult Healthy Volunteers

DRAFT GUIDANCE

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For questions regarding this draft document contact (CDER) Robert Osterberg, 301-594-5476 or (CBER) Martin Green 301-827-5349.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
December 2002
Pharmacology and Toxicology**

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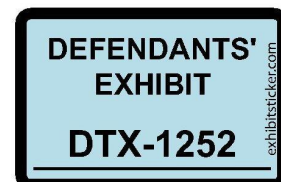
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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

I. INTRODUCTION

This guidance outlines a process (algorithm) and vocabulary for deriving the maximum recommended starting dose (MRSD) for "first in human" clinical trials of new molecular entities in adult healthy volunteers and recommends a standardized process by which the MRSD can be selected. The purpose of this process is to ensure the safety of the human volunteers.

The goals of this guidance are to (1) establish a consistent terminology for discussing the starting dose, (2) provide common conversion factors for deriving a human equivalent dose, and (3) delineate a strategy for selecting the MRSD for adult healthy volunteers, regardless of the projected clinical use. This process is diagrammed with a flow chart that presents the decisions and calculations used to generate the MRSD from animal data.

II. SCOPE

The process identified in this document pertains to determining the MRSD for adult healthy subjects when beginning a clinical investigation of any new drug or biological therapeutic that has been studied in animals. This document is not pertinent to prophylactic vaccines or endogenous proteins (i.e., recombinant clotting factors) used at physiologic concentrations. The process outlined in this document does not address dose escalation or maximum allowable doses in clinical trials.

¹ This guidance has been prepared by the Office of New Drugs in the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

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