Technical Report No. 63

Quality Requirements for the Extemporaneous Preparation of Clinical Trial Materials

2013

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PDA Quality Requirements for the Extemporaneous Preparation of Clinical Trial Materials Technical Report Team

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ISBN: 978-0-939459-60-5

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1.0 Introduction

The pharmaceutical industry is under continuous pressure to discover new medicines with fewer resources in faster time frames while maintaining the highest quality. With the exceedingly high costs of the development and launch of each new molecular entity (NME) and the low chance of success due to high attrition, the performance of clinical studies lies on the critical path ***(1)***.

Typically, the supply of clinical trial materials (CTMs) is provided through GMP manufacture of fixed-strength formulations. Regulatory guidelines for GMP manufacture and documentation of these materials are available and enforced by regulatory agencies across the world.

However, a recent benchmarking exercise conducted by the PDA technical report team (including large and small pharmaceutical companies, contract organizations and academic institutions) indicates that extemporaneous preparation (EP) techniques are widely used to prepare formulations for a variety of dosage forms for small-scale clinical studies where dosing is in-clinic (see **Section 3.2** for types of formulations and dosage form noted).

The EP approach may occur at pharmacies associated with a hospital, a clinical research unit (CRU), or academic institution (i.e., preparation site) and that specialize in dose preparation activities. These are not traditional GMP manufacturing areas for clinical trial material.

While traditional CGMP systems may not be in place in such areas, there still must be appropriate controls in place to ensure patient safety. Since the quality requirements for dose preparation activities that occur at EP sites is not always clear, this gap becomes very important as investigators are increasingly using EP approaches to support small-scale clinical studies.

1.1 Purpose

This Technical Report describes a quality system that will support the preparation of CTMs in a nonmanufacturing environment (preparation site) in a manner that will ensure product quality and patient safety.

This document will be a useful resource for drug companies, clinical sites, investigators and regulators.

1.2 Scope

This Technical Report gives suggested quality requirements for the preparation of small-scale CTMs utilizing an EP approach for in-clinic dosing. It is not appropriate to support the preparation of commercial materials for sale.

Although alternative approaches may be equally valid, pharmacists, healthcare professionals, and others engaged in the preparation of clinical supplies for small-scale studies are advised to ensure that any approach they choose to adopt is consistent with applicable regional or national laws, regulations, and guidelines.

1.3 Business Considerations

Early phase clinical studies provide critical understanding of a compound's safety and pharmacokinetics, and occasionally insight into early indications of efficacy. Practices which reduce the time to supplying quality, fit-for-purpose formulations for early phase studies are critical in leading to data that reduces later stage attrition and lowers the cost of developing new drugs. In the flexible environment of assessing early drug safety or pharmacokinetics, where the clinical investigator may want to explore a less defined dosing range, the practice of preparing the dose extemporaneously may offer distinct advantages. The benefits of EP include a significant cost savings from reducing clinical manu-