Designation: E 1298 – 89 (Reapproved 1994)

Standard Guide for Determination of Purity, Impurities, and Contaminants in Biological Drug Products[1]

This standard is issued under the fixed designation E 1298; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ϵ) indicates an editorial change since the last revision or reapproval.

INTRODUCTION

The purity of biological drug products historically has been significantly lower than that of other pharmaceutical drug products. This is a consequence of the structural complexity of biological drug products as well as the fact that, until recently, these products were obtained only with great difficulty and at high cost from natural sources such as human or animal serum or tissue. Although many of these products were of low purity, long-term use in humans proved their safety and efficacy. The development of recombinant DNA (rDNA) technology and the parallel development of sophisticated preparatory, analytical, and immunological methods, have resulted in the ability to produce high purity biological drug products. It should be recognized that the standards for purity of rDNA-derived drugs are comparable to those established for United States Pharmacopeia (USP)-quality drug substances. For example, the purity of an rDNA-derived drug substance may exceed 97 % and impurities, (see Section 4) such as host cell proteins are separately quantitated in the parts per million range (via immunoassay).

1. Scope

1.1 This guide covers the concepts of purity, impurity, and contamination in biological drug products.

1.2 This guide suggests methods for determination of impurities and contaminants in such products.

1.3 This guide is arranged as follows:

	Section
Terminology	2
Significance and Use	3
Purity	4
General Considerations	4.1
Estimation of Purity	4.2
Impurities	5
General Considerations	5.1
Major and Minor	5.2
Nature and Consequences of	5.3
Contaminants	6
General Considerations	6.1
Effects of contaminants	5.2
Methods for Determining Impurities and Contaminants	7

1.4 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Terminology

2.1 *Definitions:*

2.1.1 *contaminants*—all adventitious substances or microorganisms present in raw materials, bulk drugs, or final products.

2.1.2 *deleterious impurities*—impurities that might be a health or safety concern, particularly with respect to toxicity, carcinogenicity, or immunogenicity. Deleterious impurities must be controlled and their levels determined using suitable analytical methods.

2.1.3 *impurities, of a biological drug product*—all process-related (nonadventitious) substances present in the raw materials, bulk drug, or final drug product that are not considered to be the active material, additives, or excipients.

2.1.4 *innocuous impurities*—impurities that are not a health or safety concern in the product. The route of administration of the drug may be a significant criterion in the determination of whether an impurity is innocuous.

2.1.5 *purity, of a biological drug product*—the measure of the biologically active drug in relation to the total substances (not including additives) present in the drug product, usually expressed on a percentage basis.

3. Significance and Use

3.1 This guide suggests analytical methods generally applied within the pharmaceutical industry to identify and quantitate the level of impurities and contaminants present in the

[1] This guide is under the jurisdiction of ASTM Committee E-48 on Biotechnology and is the direct responsibility of Subcommittee E48.02 on Characterization and Identification of Biological Systems.

Current edition approved May 26, 1989. Published July 1989.