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The Standard of Quality℠

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Dr. Rosemary Versteegen
Chief Executive Officer
International Serum Industry Association
PO Box 926
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via e-mail Rockville, July 6th, 2011

Dear Dr. Versteegen,

USP is pleased to provide the International Serum Industry Association (ISIA) with answers to address issues raised by your members regarding the use of the Fetal Bovine Serum Reference Standard, currently under development with support from your association. Other related questions are addressed in this document. Additionally, please see attached fact sheet regarding the USP Reference Standards.

What is the USP?

The United States Pharmacopeia (USP) publishes a book of public pharmacopeial standards, known as the *United States Pharmacopeia-National Formulary (USP-NF).* It contains quality standards for medicines, dosage forms, drug substances, excipients, medical devices, and dietary supplements. These standards and requirements are described in General Notices (which provides the basic assumptions and default conditions for the interpretation and application of all the standards), General Chapters and Monographs. General chapters, numbered above 1000, are considered interpretive and are intended to provide information on, give definition to, or describe a particular subject. They contain no mandatory requirements applicable to any official article unless specifically referenced in these *General Notices,* a monograph, or a general chapter numbered below 1000.

A monograph includes the name of the ingredient or preparation; the definition; packaging, storage, and labeling requirements; and the specification. The specification consists of a series of tests, procedures for the tests, and acceptance criteria, intended to help ensure the identity, strength, quality, and purity of articles (both official substances/ingredients, and products) recognized in *USP-NF* and subject to compendial standards. Among the array of monograph components are USP Reference Standards, authentic specimens that have been approved as suitable for use as comparison standards in *USP* or *NF* tests and assays. These tests and procedures require the use of USP reference materials (USP Reference Standards), to ensure that testing methods are being performed properly. Medicinal ingredients and products will have the stipulated strength, quality, and purity if they conform to the requirements of the monograph and relevant general chapters.

What are Reference Standards?

USP's Reference Standards are highly characterized specimens of drug substances, excipients, impurities, degradation products, dietary supplements, compendial reagents, and performance calibrators. They are specified for use in conducting official USP tests and assays on medicines legally marketed. USP

also provides Reference Standards as authentic substances—high-quality chemical samples—as a service to analytical, clinical, pharmaceutical, and research laboratories for articles that are not themselves drugs or drug ingredients. USP's Reference Standards are used in more than 130 countries around the world.

The fetal bovine serum Reference Standard currently under development by USP is designed for use in performance verification for cell growth assays as well as for the identity assay. ISIA is providing technical advice, subject matter expertise and also helping with the acquisition of the reference material candidate.

Official recognition

USP Reference Standards are generally used to demonstrate compliance with an official USP chapter or monograph. USP develops and publishes standards for drug substances, drug products, excipients, and dietary supplements in the United States Pharmacopeia–National Formulary (USP–NF). These standards have been an integral part of the Federal Food, Drug & Cosmetic (FD&C) Act since it was first enacted in 1938. The FD&C Act defines the term "official compendium" as the official USP, the official NF, the official Homeopathic Pharmacopeia of the United States, or any supplement to them. USP–NF standards play a key role in the adulteration and misbranding provisions of the FD&C Act (which apply as well to biologics, a subset of drugs, under the Public Health Service Act). A drug (or biologic) with a name reconginzed in *USP-NF* must comply with compendial identity standards or be deemed adulterated, misbranded, or both. To avoid being deemed adulterated, such drugs must also comply with USP standards for strength, quality, and purity, unless labeled to show all respects in which the drug differs. See FDCA sections 501(b), 502(e)(3)(b), and 508, as well as FDA regulations at 21 CFR 299.5. It should be noted that while USP standards are clear about when they apply and how compliance is determined, enforcement of USP standards is the responsibility of FDA and other government authorities in the United States and elsewhere. USP has no role in enforcement. In other countries, users are not legally bound to US standards unless the USP is adopted in that country's laws (or unless drugs or ingredients are exported to the U.S. and therby subject to FDA requirements).

Current status

ISIA has worked closely with USP on the development of General Chapter *Bovine Serum* <1024>, a general chapter focused on Bovine serum, with the intent of ensuring harmonization of quality expectations.

This chapter contains no mandatory requirements applicable to any official article unless specifically referenced in a monograph. ISIA membership had a chance to comment on the chapter when it was published twice in the *Pharmacopeial Forum,* USP's vehicle for announcing proposed standards and receiving public comments. While the chapter is currently official, members are encouraged to propose future revisions of this chapter, provided that the proposals are supported with scientific data.

General Chapter *Bovine Serum Quality Attributes* <90> is official but has not yet been implemented. We are very pleased and grateful that ISIA continues to

support USP in the development of a reference standard associated with this chapter. USP is still seeking collaborators to participate in the inter-laboratory study for the evaluation of the reference material and will welcome additional participation from the ISIA Members.

We hope this will help you address concerns and questions raised by your membership. Please let us know if you have any other questions.

Sincerely,

Tina S. Morris, Ph.D.
Vice President, Biologics & Biotechnology