EXHIBIT 1

Guidance for Industry

Container and Closure System Integrity Testing *in Lieu* of Sterility Testing as a Component of the Stability Protocol for Sterile Products

For questions on the content of the guidance, contact CBER's Office of Compliance and Biologics Quality at 301-827-3031; CDER's Office of Pharmaceutical Science at 301-796-1228; CDRH's Office of Device Evaluation at 240-276-3747; or CVM's Office of New Animal Drug Evaluation at 301-827-6963.

U. S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Center for Devices and Radiological Health
Center for Veterinary Medicine
February 2008

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Additional copies of this guidance are available from:

Office of Communication, Training and Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448
Internet: http://www.fda.gov/cber/guidelines.htm
Phone: 800-835-4709 or 301-827-1800
or
Office of Training and Communication
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, Rockville, MD 20857
Phone: 301-827-4573
Internet: http://www.fda.gov/cder/guidance/index.htm
or
Division of Small Manufacturers, International, and Consumer Assistance (DSMICA), HFZ-220
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, Rockville, MD 20850
Phone: 800-638-2041
Internet: http://www.fda.gov/cdrh/guidance.html
Email: dsmica@cdrh.fda.gov
Fax: 240-276-3151
or
Communications Staff, HFV-12
Center for Veterinary Medicine (CVM)
Food and Drug Administration
7519 Standish Place
Rockville, MD 20855
Internet at http://www.fda.gov/cvm/guidance/published.htm

Contains Nonbinding Recommendations

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Contains Nonbinding Recommendations

GUIDANCE FOR INDUSTRY[1]

Container and Closure System Integrity Testing *in Lieu* of Sterility Testing as a Component of the Stability Protocol for Sterile Products

This guidance represents 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. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. PURPOSE AND SCOPE

This guidance document provides recommendations to you, manufacturers, for using methods other than sterility testing to confirm container and closure system integrity as a part of the stability protocol for sterile biological products, human and animal drugs, and medical devices. This guidance document finalizes the draft guidance of the same title dated January 1998 (January 28, 1998, 63 Federal Register (FR) 4272).

Manufacturers of drugs and biologics purporting to be sterile must test each batch or lot, as the case may be, to ensure that the product in question conforms to sterility requirements. 21 CFR 211.167(a); 21 CFR 610.12. Such drugs and biologics are also subject to stability testing requirements. 21 CFR 211.166. The stability testing requirements include maintaining a written testing program designed to assess stability characteristics. Manufacturers of medical devices must validate processes, including sterilization for a device purporting to be sterile. 21 CFR 820.75. Stability testing should be part of the design validation of such devices. In vitro diagnostic products for human use are required to be labeled with stability information. 21 CFR 809.10. For products labeled as sterile, we consider sterility to be a stability characteristic.

The purpose of stability testing is to provide evidence on how the quality of a substance or product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light, which enables you to establish or modify recommended storage conditions, retest periods, and shelf life or dating period, as the case may be.[2] This guidance document applies only to the replacement of the sterility test with an appropriate container and closure system integrity test in the stability written testing program (referred to in this guidance

[1] This guidance document was prepared by an intercenter working group with representatives from the Center for Biologics Evaluation and Research, Center for Devices and Radiological Health, Center for Drug Evaluation and Research, and the Center for Veterinary Medicine.

[2] "Dating period" being the term used for biologics, as defined at 21 CFR 600.3(l), and "shelf life" being the term used for other drugs.

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