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PAREXEL

November 3, 2003

Division of Dockets Management
Food and Drug Administration
HFA-305, Room 1061
5630 Fishers Lane
Rockville, MD 20852

Re: Formal Comments on Draft Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing

Dear Sir/Madam,

Reference is made to the FDA Draft Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice (Docket number 2003D-0382) that was issued on September 5, 2003 in Federal Register Volume 68, Number 172. This guidance when finalized will replace the current guidance document issued in 1987.

PAREXEL International is submitting on behalf of its clients that use highly automated Blow-Fill-Seal technology, formal comments disagreeing with the FDA proposed requirement for classified environment surrounding BFS machinery to meet Class 10,000 standards. The proposed classification is listed in lines 1749-1755 in the guidance document.

We look forward for FDA's concurrence with our comments.

Please do not hesitate to contact me at 781-434-4738 if you have any questions.

Sincerely,

David J. Pizzi
Senior Regulatory Consultant
PAREXEL International

FDA Draft Guidance to Industry "Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice"
(Docket number 2003D-0382)

In "Appendix 2: Blow-Fill-Seal Technology", line 1749 begins a discussion of the classified environment requirements for BFS machinery. It is our contention that FDA reconsiders this point and strikes the requirement that BFS machinery be housed in a Class 10,000 (ISO 7) environment. BFS technology is an advance aseptic processing technique that should not be treated as traditional aseptic processing methods where components are left exposed to the environment for up to many hours during processing. The concern of risk to the public health is unsubstantiated. Many BFS operators in the industry have operated their BFS process with the surrounding environment at Class 100,000 (ISO 8) conditions for many decades without any sterility issues. There is a preponderance of data to include Process Validation, Media fills, and final product sterility results that prove that a BFS operation maintains a sterile product when the room environment is classified at 100,000 (ISO 8) and the sterile filling space (where the product and product container is exposed) is maintained at Class 100 (ISO 5).

BFS Technology should be considered an advanced aseptic processing system as it uses its unique design (as an isolator system would) to minimize the extent of personnel involvement and the potential of external contamination. As in other advanced technologies, the FDA is recommending the machinery to be housed in Class 100,000 (ISO 8) - in fact the specific wording (Line 1614) "A Class 100,000 (ISO 8) background can be appropriate" is used. We would recommend that FDA consider similar wording for BFS technology and allow individual manufacturers demonstrate control of their specific process and the ultimate outcome of a sterile, pure and effective product.

Additionally, it is of concern that alignment with our counterparts in Europe is again being neglected on this point. Specifically, the EMEA allows for BFS machinery used for aseptic production of a sterile product to be placed in a Class 100,000 (ISO 8, Grade C) environment.

Please carefully consider the concern of product risk in this point - there is no evidence to show that BFS machinery should be housed in a class 10,000 (ISO 7) environment, In fact, the majority of BFS operations world-wide have proven successful when housed in a class 100,000 (ISO 8) environment.