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20th October 2003

UNIVERSITY
of
GLASGOW

Dockets Management Branch (HFA-305),
Food and Drug Administration,
5630 Fishers Lane,
rm. 1061,
Rockville, MD 20852,
USA.

Ref: Docket No. 2003D-0382

Dear Sirs

I wish to comments on your document 'Sterile Drug Products produced by Aseptic Processing - Current Good Manufacturing Practice', issued on August 2003. I have sampled air for over 35 years and believe the following information to be scientifically correct:

1. On line 1264 of your document it is suggested that active air samplers should be 'calibrated and used according to appropriate procedures'. It is widely accepted and documented that the collection efficiency of samplers varies, and that some samplers are very inefficient. Pharmaceutical cleanrooms can therefore appear to have substantially less airborne micro-organisms when low efficiency samplers are used. It is therefore necessary to know their **collection efficiency**. The new ISO 14698-1 standard has a method of establishing the collection efficiency that is now being used by air sampler manufacturers. I would recommend that this ISO standard be referenced. The reference is as follows. 'ISO 14698-1:2003, Cleanrooms and associated controlled environments- Biocontamination control- Part 1: General principles and methods; Annexe B - Guidance on validating air samplers'. I would also recommend that the words 'collection efficiency' be used instead of 'calibrated' in your document.

2. On line 1270/1271/1272 it is stated that ' Settling plates lack value as quantitative air monitors because only micro-organisms that settle onto agar surface will be detected'. I suggest that this sentence be removed. Settle plate measurements **are** quantitative and measure deposition rate. People report this as the number of micro-organism depositing onto a plate (of known area), in a given time. However, this can be more scientifically reported in the format no/cm2/hour, and by doing so the quantitative nature of the method is more apparent. Also, the fact that a settle plate detects the number of micro-organisms that will deposit onto a surface is a great advantage, as this is the mechanism of airborne deposition into, or onto, a product. Active air sampling is an indirect method, and not nearly as good. Information on this topic is given in the following reference:

Whyte W. In support of settle plates. Journal of Pharmaceutical Science and Technology 1996; **50**: 20

I trust that these comments are of use to you.

Yours faithfully

W Whyte

DEPARTMENT OF MECHANICAL ENGINEERING