March 2008
Canada's Revised Guidelines

Health Canada issued revised cleaning validation guidelines on January 1, 2008. Here is a link to those guidelines: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/validation/gui-0028_cleaning-nettoyage_ltr-doc_e.html (You can also find them under the "Resources/Specific documents" section of this web site.) This document keeps the same structure and most of the same basics as the previous version, with the following changes. The changes listed below do not include slight changes in format.

1. At the beginning was added a "disclaimer" stating that the guideline was not part of official regulations, but is only an "administrative document that is intended to facilitate compliance".

2. In Section 3.1 was added a phrase to indicate that one objective of cleaning validation is "control of potential microbial contaminants". In that same section, the phrase (referring to a purpose of cleaning validation) "so that analytical monitoring may be reduced to a minimum in the routine phase" (a phrase that comes from the PIC/S document) was deleted.

3. In Section 4.4, referring to the "test until clean" concept, the sentence "For the system or equipment with a validated cleaning procedure, this practice of resampling should not be utilized" was deleted.

4. A new Section 4.9 was added regarding campaigns. That section states "During a campaign (production of several batches of the same product), cleaning between batches may be reduced. The number of lots of the same product which could be manufactured before a complete/full cleaning is done should be determined."

5. Old Section 4.10 became new section 4.11, and a statement was added regarding grouping for equipment: "Equipment which is similar in design and function may be grouped and a worst case established for validation."

6. A new heading called "Personnel" was added before Section 5.5 (section 5.5 deals with operators and manual cleaning).

7. Section 7.2 was significantly expanded with additional parts of a Cleaning Validation Protocol. I won't go through all the additions and changes, for it includes fifteen bullet points, and only seven of the bullet points are covered in the old guidance.

8. Section 7.6 is an entirely new addition. It deals with the issues related to the Final Validation report.

9. The following statement (which was a copy of a statement in the FDA guidance on cleaning validation) was deleted from Section 8.2: "The specificity and sensitivity of the analytical methods should be determined."

10. In Section 9.4, TOC is added as an example of "indirect testing".

11. A new heading called "Detergents" was added before Section 9.7 (Sections 9.7 and 9.8 deal with detergents.)

12. The following statement (based on what is in the PIC/S guidance) was added to Section 9.7: "The manufacturer should ensure that they are notified by the detergent supplier of any changes in the formulation of the detergent."

13. A new heading called "Last Rinse" was added before Section 9.9 (Sections 9.9 and 9.10 deal with the water quality for the final rinse.)

14. Section 9.10 was modified by adding "sterile products for ophthalmic use" as an application for a final Purified Water rinse.

15. Section 10.3 was modified to change an approach for setting limits from "grouping into groups of risk" to "grouping by properties".

16. In Section 10.4 examples of setting limits, item "iv" was modified to say "For certain highly sensitizing or highly potent ingredients (such as penicillins, cephalosporins or potent sterioids and cytotoxics, the limits should be below the limit of detection by best available analytical methods."

17. The "Note" in the old guideline under Section 10.4 that started "Some limits that have been mentioned by industry representatives…" (which was essentially a copy of what is in the FDA guidance) has been deleted. Furthermore, the following paragraph regarding what "Environmental Protection Agency and toxicologists suggest…" as safe levels based on toxicity data has also been deleted.

18. Section 11.0, entitled "Conclusion", in the old guideline has been entirely deleted. It has been replaced by a new Section 11.0 entitled "Change Control/Revalidation". Section 11.1 deals with having a change control system in place. Section 11.2 gives examples of changes which "require evaluation". Section 11.3 deals with reassessment of the cleaning process at "regular intervals" and revalidation.

I have made no attempt to assess the rationale for or the impact of the changes. Certainly for any decisions on the potential impact of the new guidance, one should consult the guideline directly.