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November 28, 2000

Docket Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

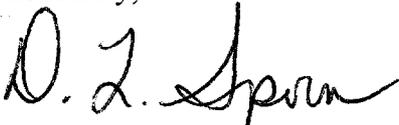
RE: Draft Guidance for Industry on Analytical Procedures and Methods Validation:
Chemistry, Manufacturing, and Controls Documentation (Docket 00D-1424)

Dear Sir:

Abbott Laboratories is pleased to have the opportunity to provide comments on the Draft Guidance on Analytical Procedures and Methods Validation as published on August 30, 2000, in the *Federal Register*. We propose the attached comments and suggestions to help strengthen the utility of the proposed guidance.

On behalf of the 57,000 Abbott employees who help produce healthcare products marketed in more than 130 countries, we thank you for your consideration of these comments.

Sincerely,


Douglas L. Sporn

cc: Dave Brown, PARD

00D-1424

C17

**COMMENTS TO FDA
DRAFT GUIDANCE ON ANALYTICAL PROCEDURES
AND METHODS VALIDATION (Docket 00D-1424)**

General Comments

It would be beneficial if the term "raw data" (e.g., peak areas, chromatograms, etc) were given definition in the guidance to ensure that there is no confusion with 21 CFR Part 11 definitions.

It is also recommended that the Agency consider adopting the ICH required elements of methods validation table as written. Modification of the table would reduce the value of harmonization and create confusion as to requirements.

SPECIFIC COMMENTS

Line

89-92

Missing a limit test discussion for residual solvent assays such as "Residual solvent levels in drug products are governed by the 'ICH Guidance on Impurities: Residual Solvents,' *Federal Register*, Vol. 62, No. 247, 12/24/97, pp. 67377-67382."

268

Alternative to Methods statements of useable shelf life for reagents may include the use of an operational procedure on reagents.

535

In Table 1 under the column labeled "Assay" on the "Specificity" line: Specificity should not be included for content uniformity and dissolution. Content uniformity can also be performed by nIR and by weight. The dissolution finish could use UV detection, which is not specific.

581

Verification of compendial procedures is discussed. It is not clear what is the basis for the Agency's proposed requirement of specificity, intermediate precision and stability of sample solutions, for compendial methods applied to compendial products. 21 CFR 211.194 (a)(2) specifies that "The suitability of all testing methods used shall be verified under actual conditions of use," but does not require that data should be on file for compendial methods. The Agency may be requiring more than is justified by the CFR.

**COMMENTS TO FDA: DRAFT GUIDANCE ON ANALYTICAL
PROCEDURES AND METHODS VALIDATION (Docket 00D-1424)**

SPECIFIC COMMENTS (continued)

Line

599-603

An editorial correction: "well-test" should read "well-tested."

600-603

There should be a clarification that an implied validation protocol is not intended for method development. Method development should be driven by sound scientific expectations such as found in the CDER reviewer guidance on *Validation of Chromatographic Methods*, 11/94.

1049

Strike "HPLC". A UV spectrophotometer could also be used as stated in line 1055.

1089

Clarification is needed as to what is considered "Automated Analytical Procedures." Would the use of HPLC or GC autosamplers be included?

799-1095

Section XI, Methodology is probably not needed since this information for the most part is already included in the USP.

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