ABBOTT

Diagnostics Division

Abbott Laboratories
100 Abbott Park Road
Abbott Park, Illinois 60064-6092

February 9, 2001

Dockets Management Branch (HFA-3 05)
Food and Drug Administration
5630 Fishers Lane, Room 106 1
Rockville, Maryland 20852

Re: Docket Number OOD-1587

Dear Madame or Sir:

Abbott Laboratories (Abbott) submits the following comments in response to the November 14, 2000 publication in the Federal Register of "Guidance for Prescription Use Drugs of Abuse Assays Premarket Notifications" (Guidance). The following general and specific comments are grouped under topical headings for ease of reference:

Specimen Collection Devices

We recommend removal of the "Specimen Collection Devices" section from the Guidance. The types of specimen collection information contemplated by this Guidance are intended to "assure specimen identity and integrity between the collection site and point of analysis." Concerns, relating to specimen identify and integrity, derive from chain-of-custody issues. Chain-of-custody issues should be reserved for the Department of Justice, while the safe transport of potential biohazards resides with the Department of Transportation, Inclusion of such information in premarket notifications for drugs of abuse is not relevant to the safety and efficacy of the assay itself

Similarly the section regarding sample acceptance criteria involves issues related to compliance with drug testing as opposed to the diagnostic assay performance. Specimens used for diagnostic evaluation need to be handled appropriately regardless of the analyte to be tested. For example, urine is a common specimen used in diagnostic testing. Premarket submissions for most analytes do not require extensive documentation on specimen handling and acceptance criteria. It seems inappropriate to require extensive documentation in premarket notifications for drugs of abuse diagnostic assays. For these reasons, we recommend deletion of this section from the Guidance.

Performance Characteristics

The Guidance recommendations in the "Overview" and "Cutoff Concentration" studies subsections of the "Performance Characteristics" are good recommendations.

In the subsection discussing "Cutoff Concentration," we recommend removing or clarifying the sentence that reads, "[f]or complete characterization of device performance, the concentrations of samples should be extended to drug levels that read with 100% agreement to a reference method such as GC/MS." In the case of assays that are designed to recognize a class of drugs and/or drug metabolites, e.g., opiates, benzodiazapines, or barbiturates, 100% correlation with GCNS may not be feasible because GCNS generally identifies and quantitates a single compound.

Similarly, in the method comparison section, the recommendation to compare assays to GC/MS as a reference standard may not be appropriate for all drugs of abuse assays. Many drug screening assays are class assays and not single analyte assays. For example, opiates and benzodiazepine assays both recognize more than one drug compound (plus metabolites) because there are many abused drugs in that class plus multiple active metabolites. GC/MS is the gold standard, but it will analyze and quantitate only one compound. Due to the specificity of GC/MS, immunoassays that recognize a class of drugs often do no correlate to GC/MS. We recommend clarification of this point in the Guidance.

Labeling Considerations

Section 809.10 of the Code of Federal Regulations (C.F.R.) describes labeling requirements for ***in vitro*** diagnostic devices. Based on these requirements, some of the labeling recommendations contained in the Guidance could be applied differently. For example, inclusion of an assay cutoff or the statement "for in vitro diagnostic use" in the product intended use is not specifically called for under § 809.10 of the C.F.R. Frequently, such information is contained in other sections of ***in vitro*** diagnostic labeling, such as "summary and explanation of the test," "expected values," or "warnings and precautions." We recommend acknowledgement of these options in the Guidance to prevent strict reviewer application of the Guidance recommendation.

Similarly, we recommend that the Guidance recognize other labeling options for the following statement:

> This assay provides only a preliminary result. Clinical considerations and professional judgment must be applied to any drug of abuse test result, particularly in evaluating a preliminary positive result. In order to obtain a confirmed analytical result, a more specified alternate chemical method is needed. Gas chromatography/Mass Spectroscopy (GCNS) is the preferred confirmation method.

Unlike over-the-counter drugs of abuse devices, the subject of this Guidance is professional use drugs of abuse devices. The placement of a similar statement in another part of the labeling may be more appropriate. Professional devices are used in diagnostic settings in addition to routine workplace screening or similar screening situations.

Therefore, we recommend that the Guidance reflect that additional labeling options are acceptable to prevent strict reviewer application of this labeling guidance.

The Guidance recommendation to include the following statement presents similar concerns:

> It should be noted that although the cutoff of this assay is identified as xxx ng/mL, ***a significant*** number of samples below and/or above this cutoff may render incorrect results. Please refer to the performance section of this package insert (emphasis added).

The inclusion of this statement may not be appropriate. Precision data will provide information about the assay performance near the cutoff, so it is unnecessary to provide an additional statement. Furthermore, such data may not necessarily support that a significant number of samples may render incorrect results. Therefore, we recommend deleting this item from the Guidance.

The Guidance suggests providing a table of drug clearance rates in the product labeling. Providing such a table in the labeling could potentially mislead and confuse the device user. Clearance rates vary widely in the population. There are many factors that impact drug clearance rates including: occasional versus chronic drug use, drug dose, number and types of drugs used, personal metabolism, amount of body fat, etc. Therefore, we recommend reconsidering this proposal.

The Guidance recommends providing the following statement under the labeling subsection "Limitations :"

> There is a possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

Section 809.1 O(b)(10) of the C.F.R. describes the content of the "limitations" section for ***in vitro*** diagnostic labeling. It states, "state known extrinsic factors or interfering substances affecting results." The above recommendation is beyond the scope of the regulation. Therefore, we recommend deleting it from the Guidance.

The Guidance recommends including the following statement on the outside box labeling and on all promotional material:

> This assay provides only a preliminary result. A more specific alternate chemical method is needed to obtain a confirmed result (see package insert).

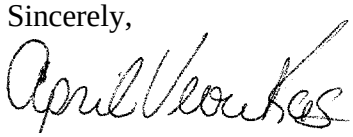
We recommend deleting this item from the Guidance. The subject of this Guidance is professional use devices. Although the statement may be appropriate for over-the-

counter devices, it is not necessary for professional use devices. Furthermore, ***in vitro*** diagnostic products are subject to many federal and international labeling requirements. Product labels contain limited space. The addition of a statement that is not necessarily appropriate for professional users of the device further restricts the availability of product labeling space.

We also recommend removing the recommendation to include this statement on all promotional material. The Federal Trade Commission governs advertising for unrestricted medical devices, such as premarket notification drugs of abuse assays. Therefore, we recommend deleting this item from the Guidance.

Thank you for the opportunity to comment.

Sincerely,



April Veoukas, J.D.
Regulatory Project Manager
Abbott Diagnostics Division
Abbott Laboratories

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359