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Division of Dockets Management (HFA-305)
Food and Drug Administration
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VARIAN

Re: Docket No. 2003D-0522
Comments to "Draft Guidance for Industry and FDA Staff; Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests"

Dear Sir or Madam,

I am writing with regard to the "Draft Guidance for Industry and FDA Staff; Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests" issued on December 2, 2003. On behalf of Varian, Inc. we appreciate the opportunity to comment on this important guidance.

General support:

We appreciate the agency's effort to clarify the 510(k) data requirements and labeling recommendations for drugs of abuse screening tests, especially with respect to their various intended use settings (i.e., use in a laboratory setting, use in the workplace or other repetitive testing sites, and screening tests that are intended to be used at home).

For screening tests intended for home use, we appreciate the clarification that bundling the cost of confirmatory testing into the costs of screening tests was not and is not required.

We also agree that premarket notification submissions for drugs of abuse screening tests used in workplace and other repetitive testing sites do not require the same types of data as submissions for screening tests that are intended for sale directly to untrained users who perform these tests on an occasional basis (e.g., home use).

General concerns:

1. We would, however, like to express concern over the number of drugs of abuse tests currently marketed that do not adhere to these recommendations and we would like to know if or how the agency intends to enforce its thinking equally or consistently for all such manufacturers. For example, will there be an effort made to require 510(k) submissions for devices sold for workplace testing that do not currently have premarket clearance? And for

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all manufacturers of devices with instructions for use that do not meet minimum recommendations, will the agency require 510(k) submissions to change the labeling within a certain period of time?

With respect to the presentation of performance characteristics in the labeling, again we wish to express our agreement on the importance of clear guidance and a consistent application of the recommendations. Product labeling (package inserts) for currently marketed products vary widely especially with respect to how accuracy and precision are expressed and how agreement with predicate device and or quantitative results are determined, oftentimes resulting in vagueness to the users or purchasers of the products and/or misleading conclusions. Will there be an effort by the agency to identify such instances and recommend 510(k) submissions to modify the labeling to follow the recommendations?

2. For tests intended for workplace or other repetitive testing sites (outside of laboratories), you recommended that labeling clearly indicate the experience or training of the users who participated in the studies to characterize the analytical performance of the test. In addition, you recommended that labeling should note that performance may be negatively impacted or that performance may be inferior to the labeled performance if the test is performed by users with less experience or training.

For visually read devices we do not agree that the performance may be inferior to labeled performance because extensive training is not required to perform the test or interpret results correctly.

3. The draft guidance recommends that the following table be incorporated into the instructions for use package inserts noting that it "accurately reflect the false positive rate of drugs of abuse screening tests, and that communication of these limitations will help ensure that operators properly interpret results from drugs of abuse screening tests."

Services Administration (SAMHSA) reports the accuracy of drug tests as^a:

<i>60 out of 100 times a "preliminary positive" result from an opiate test is a "false preliminary positive" result. A "false preliminary positive" result means that the result of the first test was "preliminary positive" even though the person did not take an illegal drug.</i>
<i>50 out of 100 times a "preliminary positive" test result from an amphetamine or methamphetamine test is a "false preliminary positive" result.</i>
<i>50 out of 100 times a "preliminary positive" result from a PCP (phencyclidine) test is a "false preliminary positive" result.</i>
<i>10 out of 100 times a "preliminary positive" result from a marijuana test is a "false preliminary positive" result.</i>
<i>2 out of 100 times a "preliminary positive" result from a cocaine test is a "false preliminary positive" result.</i>

^a Data was generated from laboratory tests that have the following cutoff concentrations: Marijuana, 50 ng/mL; Cocaine, 300 ng/mL; Phencyclidine, 25 ng/mL; Opiates, 2000 ng/mL;

Amphetamines, 1000 ng/mL. In general, the rates of false preliminary positive results will increase as the cutoff concentration of the test is lowered.

Because the performance reported in the above table is negative and would have a detrimental effect on companies' ability to market product, we very strongly feel it is important that the source of the information, how it was obtained, and the reasons for the concluding performance levels be provided. Other studies from respected toxicologists show performance equal to or better than laboratory testing, and therefore conflict with the proposed language.

Furthermore, our experience with these types of devices also conflicts with the performance noted in the draft guidelines which is in no way reflective of performance, or the receptivity of these tests in the market.

We do not think this information would be helpful to users of the tests, and would in fact be more confusing

4. The draft guidance also provided an opportunity to modify the information presented above if we believed our assay performs in a superior manner, by providing information to support the modification in the 510(k).

We would like to know the source of the information presented in the table and the opportunity to review the method used to obtain the information. We also need clear guidance on what type of information is acceptable to support a modification.

5. In Section C.9, Studies in the Workplace and Other Sites Performing Repetitive Testing, it is recommended that the intended user use the test in both the method comparison and precision studies in the environment where the product ultimately will be used. Furthermore, for visually read single-use tests that involve well characterized analytes and well established technologies, the study described in section C.1, Cutoff Characterization, is appropriate for characterizing precision when performed at three different workplace sites with representative operators. However, the description of method comparison studies recommends the use of clinical specimens.

We do not agree that testing actual clinical specimens is necessary or appropriate for this purpose. For tests where the performance has already been established in laboratory or professional use settings, a study involving the use of the same contrived specimens used in the Cutoff Characterization and Precision studies is more appropriate since the intent is only to demonstrate that the test can be performed with the same accuracy and precision as in the laboratory setting. Use of clinical specimens would only complicate and burden the study unnecessarily, and would possibly introduce error from another source of variation if the same clinical specimens could not be tested at all the sites. It is not

In a footnote, this definition was provided: "For the purpose of this document, "workplace and other repetitive testing sites" (or similarly worded phrases) include settings such as sports, schools, insurance, and rehabilitation centers where multiple individuals are tested."

For the repetitive testing sites mentioned, e.g., rehabilitation centers and schools, health care professionals such as nurses or counselors perform the testing and physicians are involved. Would this then fall under the "laboratory setting" definition?

2. Under section II, DEVICE DESCRIPTION, the device panel, review method, regulations, and product codes for the assays addressed in this guidance document were listed but do not list assays for other analytes such as Barbiturates, Benzodiazepines, and Methadone. Would assays for these analytes fall under the intended scope of the draft guidance?

Conclusion:

We appreciate the opportunity to comment on the proposed guidance, and hope that these comments are helpful in ensuring that drugs of abuse screening tests are subject to uniform premarket notification and labeling requirements.

Sincerely,



Lorna Gamboa
Regulatory Affairs Manager
Varian, Inc.