

SUMMARY MINUTES

MEETING OF THE CLINICAL CHEMISTRY AND
CLINICAL TOXICOLOGY DEVICES PANEL

OPEN SESSION

NOVEMBER 13–14, 2000

Meeting of the Clinical Chemistry and Clinical Toxicology Devices Panel

Attendees

November 13, 2000

Chairperson

Martin H. Kroll, M.D.

Executive Secretary

Veronica J. Calvin, M.A.

Members

James Everett, M.D., Ph.D.
Cassandra E. Henderson, M.D.
Barbara R. Manno, Ph.D.
Arlan L. Rosenbloom, M.D.

Consultants

Thomas L. Kurt, M.D., M.P.H.
Sherwood C. Lewis, Ph.D.
Diana G. Wilkins, Ph.D.

Consumer Representative

Stanley M. Reynolds

Industry Representative

Fred D. Lasky, Ph.D.

Guest/Federal Liaison

Donna M. Bush, Ph.D., D-ABFT

FDA Representative

Steven I. Gutman, M.D., M.B.A.

CALL TO ORDER

Chairperson Martin Kroll called the meeting to order at 10:03 a.m. He noted that the purpose of the meeting was for the committee to make recommendations on two draft guidance documents. Executive Secretary Veronica Calvin reviewed the outcome of the panel's March 24, 2000, meeting and asked the panelists to introduce themselves. She then read the conflict-of-interest statement, noting that panelists Martin Kroll and Arlan Rosenbloom had unrelated interests in firms at issue and could participate fully in the meeting.

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS (CLIA)

Clara Silva, MT (ASCP), MPA, Acting CLIA Coordinator, Division of Clinical Laboratory Devices, presented an update on the CLIA program. She described FDA's role in CLIA and the program's key features and noted that as of November 7, 2000, FDA had categorized 913 tests. Ms. Silva described the CLIA waiver process and said that FDA will publish a draft guidance on waivers before the end of the year.

FDA PRESENTATION

Jean M. Cooper, M.S., D.V.M., Branch Chief, Clinical Chemistry and Clinical Toxicology Branch, Division of Clinical Laboratory Devices, summarized the study design described in the draft guidance "Prescription Use Drugs of Abuse Assays Premarket Notifications." She noted that the guidance differs from the previous version in that it provides examples of study designs and focuses on characterizing performance around the cutoff. She provided background information on assays for drugs of abuse and on confirmation testing, then described the consumer study required in the guidance. She noted that the guidance had been revised to clarify the description of the consumer study design and that the committee's input was needed on that design. Finally, she reviewed the questions concerning the guidance that were before the panel.

OPEN PUBLIC HEARING

David G. Evans, Executive Director, National Onsite Testing Association, stated that the FDA does not have jurisdiction over workplace, criminal justice, athletic, insurance, school, or other nondiagnostic testing and that its jurisdiction is limited to products that diagnose disease or other conditions. He cited legislation and case law in support of his argument.

Salvatore Salamone, Ph.D., Vice President, Research and Development, Drug Monitoring, Roche Diagnostic Systems, expressed concern over cutoff issues. He said that because it is difficult to find clinical samples with levels close to the cutoff, the FDA should allow companies to use artificial matrices to characterize performance around cutoffs. The guidance should use the term “cutoff information” instead of “detection limit” for qualitative assays. In addition, the FDA should take into account the role of customer demand in setting its requirements for cutoff levels. Because with visually read assays, it is not possible to determine the point of perfect agreement to the reference method, the FDA should require companies to report the level at which 95 percent confidence is achieved. Testing three lots of reagent at the external sites is overly burdensome; only one lot is necessary for testing operator or site variability. Finally, Dr. Salamone asked that the guidance clearly state that it is not limited to the “NIDA 5” drugs.

OPEN COMMITTEE DISCUSSION

Question 1: Are the suggested study designs in the guidance for the following performance characteristics appropriate: precision, comparison to GC/MS, sensitivity or cutoff validation, interference, cross-reactivity, and studies for point-of-care devices?

Some panelists raised questions concerning the difference between limits of detection and cutoffs. Others stated that the guidance needs to be clear on whether point-of-care testing is for workplace testing or therapeutic use. Dr. Kroll thought that comparison to gas chromatography/

mass spectrometry (GC/MS) was a good idea and that such comparisons needed to be separated from precision and cutoff validation. He suggested that it was important to be able to detect concentrations below the cutoff. Panelists expressed concern over the impact of adulterants and the timing of GC/MS, noting that a sample may be lost or contaminated before GC/MS is performed, and asked whether other confirmatory tests were acceptable. Dr. Gutman said that the FDA could take under advisement that there should be liberalization of permitted confirmation tests. He noted that information on sample storage was not required to be included in the guidance document.

Panelists generally agreed that the criteria in the guidance are appropriate minimal characteristics. They expressed concern over the relation between cutoffs and intended use, noting that a cutoff minimum detection limit is not the same as a cutoff, which is based on intended use. Dr. Lasky suggested that one option would be to declare GC/MS the gold standard and to use a comparative study to evaluate the new device. He noted that lot-to-lot variability is best monitored by manufacturers and added that light variability is considered during design phases. Dr. Kroll said that the document should state that the intended use should determine the cutoff.

Dr. Manno said that the product insert needs to mention that the test cannot determine the time at which a substance was used. She added that the results from a clinical application could not predict performance. Dr. Lasky pointed out that the committee's concerns illustrate the point that one test may not satisfy all needs and that a qualitative test in and of itself may not be enough.

Panelists also raised issues involving quality control of specimens, including dilution of urine, future difficulty with obtaining specimens, and individual variability in metabolites. Dr.

Gutman asked the panel to address the appropriate nature of specimens. Dr. Wilkins said that fortifying drug-free urine to determine a particular performance characteristic is a different issue from looking at the robustness of an assay on real-life specimens; fortified urine is not a substitute for a real-world specimen. Dr. Lasky said that several critical issues exist regarding old samples and their use in light of patient confidentiality issues. He pleaded for the FDA to move slowly until agreement is reached within the agency.

Question 2. . . . FDA often reviews other drugs, for which there are not SAMHSA guidelines. What are appropriate methods for establishing valid cutoffs and assessing accuracy of these tests? . . .

Panelists generally agreed that the FDA proposals seemed reasonable but encouraged working with sponsors to determine the most appropriate methods, particularly as future SAMHSA guidelines become available and new drugs are considered. Some panelists said the methods should be the same regardless of the drug (i.e., current or future). It was noted that the manufacturer should establish cutoffs on the basis of intended use of the test. Panelists stressed that manufacturers take cross-reactivity into account in determining cutoffs: If a drug has a large number of metabolites, and they vary from person to person, the range needs to be specified. Panelists acknowledged that the guidance should not make it too difficult to get a product to market. In addition, manufacturers have a responsibility to monitor literature, improve the device, and adjust the labeling, if necessary.

FDA PRESENTATION

Dr. Cooper presented an overview of the guidance document “Over the Counter (OTC) Screening Tests for Drugs of Abuse: Guidance for Premarket Notifications.” She described the revisions that had been made to the guidance and said that the FDA intended to require the cost

of confirmation to be included in the price of the device. The panel was being asked to answer eight questions concerning OTC drug tests and two questions concerning OTC alcohol tests.

OPEN PUBLIC HEARING

David Evans again raised issues concerning FDA jurisdiction over drug tests. He noted that CLIA already regulates many hospitals and laboratories and that many states do not assert jurisdiction over onsite tests.

Bob Aromando, an independent industry consultant, also raised concerns over FDA's jurisdiction, saying the FDA assumes that concerns related to OTC use of drug tests are similar in all settings. He said that the intended use of drug tests differs by setting and that most settings do not have medical diagnosis as their purpose. Consequently, workplace, sports, and other drug-test settings are outside the jurisdiction of FDA.

LuAnn Ochs, M.S., Regulatory Program Manager, Roche Diagnostics Corporation, suggested that the guidance separately address home-use requirements, noting that home users have different labeling needs. She expressed concern that lay users cannot order confirmatory tests on their own in some states; the FDA had to take that into consideration.

Carl A. Mongiovi, Vice President, Phamatech, described the results of his company's consumer testing for home-use drug tests and some of the difficulties uncovered (e.g., users do not read the instructions or are under stress). He said that confirmation testing is necessary because the test is subject to user error and is not 100 percent accurate. Companies should provide consumers with referrals to substance abuse counselors.

Naresh C. Jain, Ph.D., Laboratory Director, National Toxicology Labs, Inc., said that any test on the market should be accurate, reliable, and reproducible. All tests are based on

immunoassays and will cross-react with unrelated substances. Confirmation testing is absolutely necessary and no manufacturer should be permitted to sell OTC tests without it.

Carl M. Good III, Ph.D., Vice President, Research and Development, Avitar Corporation, expressed support for confirmation testing but added that costs are an issue. He described the benefits of saliva testing and noted that for oral fluids testing, a requirement of negligible performance error with samples at concentrations of ± 50 percent of the cutoff concentration was too tight.

Ken Berger, Vice President, Regulatory Affairs, Lifepoint Corporation, described a product for the rapid detection of alcohol and other drugs in saliva. He described the benefits of saliva testing and said that the guidance should reflect—and not discourage—its growing use. He added that the guidance should take into account that regulations already exist for a variety of environments in which drug tests are used. He, too, raised the issue of FDA jurisdiction.

Tony Toranto, CEO, Guardian Angel, said that onsite tests for alcohol were significantly different in intended use from onsite drug tests and that existing Department of Transportation (DOT) standards were sufficient. Confirmation tests are not needed for onsite alcohol tests.

OPEN COMMITTEE DISCUSSION

Dr. Gutman noted that the legal issues raised in the public comments were not germane to the committee's charge for the day.

Question 1: . . . FDA has been requesting that confirmatory testing be a mandatory component in design of the screening test. Is this necessary and reasonable? Are there other approaches that might be equally effective?

Although panelists agreed that confirmation testing was essential, they raised several concerns involving what the labeling in home-use kits should recommend for positive test results and how FDA would enforce the use of confirmatory testing. Panelists suggested that the information in

the package should tell the consumer that more information is necessary before a final result can be determined and that a confirmatory test is required. They concurred that the cost of confirmatory tests could be offset by the price of the initial test. Some panelists raised the question of whether confirmation should be obtained for negative results as well, but Dr. Gutman responded that the intention is to catch false positives, not false negatives. By building the cost of confirmation testing into the price, the FDA hopes to encourage the practice.

Question 2: Are the studies and labeling guidelines as outlined in the guidance appropriate for home, workplace, insurance, sports, and other OTC settings?

Panelists again strongly agreed that labeling should state that confirmation testing is necessary. Some panelists noted that the document uses the term “uncertain” to describe presumptive results and asked whether that was appropriate. Another issue was whether the guidance needs to address different entities separately. Although some panelists thought that labeling guidelines should depend on where the test is being used, others said that the rules for using a device in different environments should not change. Several panelists thought that manufacturers should provide an 800-number helpline.

To expedite matters, the committee decided to answer the questions on alcohol tests first, then return to the drug-test questions. The panel grouped the questions by topic.

Alcohol Question 1: Are the same types of studies appropriate for alcohol tests? Should other approaches, such as the one used by DOT, be considered?

Alcohol Question 2: In what settings are confirmatory testing for OTC alcohol tests appropriate? What matrices, and what time span between collection of the original sample and collection of the sample for confirmation would be appropriate?

Many panelists said that the DOT/National Highway Traffic Safety Administration standards work well and provide a reference point; it would be helpful for FDA to have input on labeling, but not to take the lead. Dr. Kroll said that confirmatory testing was necessary only if punishment (e.g., job loss) was attached to a positive result. The panelists also agreed that

including alcohol in a drug kit with other drugs of abuse does not preclude single-drug alcohol tests.

Question 3: FDA is suggesting that OTC devices render negligible performance error with spiked samples at concentrations of $\pm 50\%$ of the cutoff concentration. Is this reasonable? If not, what alternative performance criteria would be appropriate?

Question 8: Visually read devices frequently render positive results well below the claimed cutoff of the assay. Should there be certain performance requirements to support a claimed cutoff concentration?

Some panelists indicated that the range was broad and could be tightened; some felt this performance criterion was too tight; whereas others indicated that no change was needed. Dr. Henderson noted that tightening the range might help to reduce false positives. Dr. Manno said that if the range were going to stay as is, it should be discussed in the labeling—if a test is negative, perhaps it should be repeated on another day. Several panelists said that without linear regression data, the questions could not be definitively answered. Dr. Wilkins said that the term “negligible performance error” should be defined in the guidance document.

Concerning question 8, the panelists agreed that there should be certain performance requirements to support any claimed cutoff. Several panelists noted that the results of qualitative tests are not linear. Dr. Rosenbloom said that any positive test requires confirmation testing. Dr. Lasky referred to the European Commission on Clinical Laboratory Standards document and said that it was an excellent reference for determining characteristics of qualitative tests in general.

Question 5: Is the study design described in the guidance appropriate for demonstrating performance of the device in the hands of the lay user?

Question 6: FDA is suggesting that sponsors conduct only the consumer studies described in the OTC document, when the device has already obtained prescription clearance. Are any other studies warranted?

The panelists agreed that the study designs are appropriate; they expressed some concern about the requirements for the distribution of samples because it may not suit the needs of the

particular device. Also, it is virtually impossible to get large numbers of samples at particular concentrations. Dr. Kurt stated that spiked samples should be carefully defined and that it would be helpful to run a trial in a small sample of consumers. Panelists also expressed concern about the use of spiked samples—because the metabolites are so important, it might be better to dilute urine with other samples. Companies should budget for postmarketing consumer surveys.

Question 4: FDA does not encourage inclusion of performance data in OTC labeling. Do you feel such information should be included? If so, what types of studies should be done to characterize performance well enough that it would be meaningful to the consumer? How should performance be relayed to consumers in the labeling?

Dr. Gutman said that FDA does not currently require performance data to be included because it is difficult to provide the information in terms that make sense and because FDA does not want data to be misrepresented. Panelists agreed that, given the variety of environments in which the tests will be used, performance data should be included because people need to know what a given result means. Including certain types of performance information is essential (e.g., when the device could malfunction). Several panelists suggested simple ways for providing performance information, including referral to a Web site.

Question 7: Should only those devices with SAMHSA cutoffs be eligible to be cleared for OTC use?

The panelists agreed that the guidance should not be restricted—OTC tests could be helpful for other classes of drugs. Dr. Kurt said that manufacturers should explain how they arrived at the cutoffs for drugs other than the SAMHSA 5. The other panelists concurred.

Dr. Kroll asked members of the audience if they wished to add anything. Bob Aromando stated that confirmation of negative test results would be burdensome because more than 90 percent of tests are negative. He pointed out that nearly every state requires positive test results to be confirmed before any consequences or action can be taken as a result of those tests.

Jemo Kang, Ph.D., President, Princeton BioMeditech Corporation, noted that adding the confirmation test to the price of the kit would increase costs. He suggested that the FDA allow kits to be sold both with and without the price of the confirmation test included. He added that it was a good idea to have a highly accurate test; however, he felt that tightening the ± 50 percent standard was not an added benefit to the consumer. Dr. Lewis clarified that the issue was not whether all negative results should be tested but whether to confirm the results if a person wanted them confirmed.

Bob Aromando said that studies show onsite tests to be comparable to lab tests. David Evans asked the FDA to slow the process and ask whether it has the evidence it really needs. He suggested consulting with DOT and the U.S. Postal Service. Lorraine Hogan, Clinical Toxicologist, said that from her experience in writing the user training manual for Phamatech, immunoassays are beyond the scope of most people's knowledge. She said that packaging is important and that a toll-free number should be provided; although a mechanism for confirmation testing is needed, it should not be built into the price of the device. Dr. Kang added that additional performance data on the package would not necessarily be helpful and that an 800 number might work well.

Dr. Kroll thanked the participants and adjourned the meeting at 4:35 p.m.

Attendees

November 14, 2000

Chairperson

Martin H. Kroll, M.D.

Executive Secretary

Veronica J. Calvin, M.A.

Members

Stephen Clement, M.D.
James Everett, M.D., Ph.D.
Cassandra E. Henderson, M.D.
Barbara R. Manno, Ph.D.
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Stanley M. Reynolds

Industry Representative

Fred D. Lasky, Ph.D.

FDA Representative

Steven I. Gutman, M.D., M.B.A.

CALL TO ORDER

Chairperson Martin Kroll called the meeting to order at 9:08 a.m. Executive Secretary Veronica Calvin noted that the purpose of the meeting was for the committee to discuss and make recommendations on a premarket notification (510[k]) for a first-of-a-kind prescription use screening device for heroin in human hair. She read the conflict-of-interest statement, noting that panelists Martin Kroll and Arlan Rosenbloom had unrelated interests in firms at issue and could participate fully in the meeting. Diana Wilkins had imputed interest in a firm at issue, but because that interest was indirect, she could participate fully in the discussion.

OPEN PUBLIC HEARING

David Brill, M.D., M.A., M.P.H., described some of the benefits of hair testing and noted that the method tests only for chronic use, not immediate impairment. Hair testing is noninvasive, witnessed, and impossible for the user to substitute. It is an excellent approach to both scheduled and unscheduled drug tests.

Robert L. DuPont, M.D., Vice President, Bensinger, DuPont and Associates, described his extensive experience in the addiction field and said that hair testing had much to offer practitioners of addiction medicine. He outlined the weaknesses of urine for identifying heroin: difficulties with identifying 6-mono-acetyl morphine (6-MAM) and the confounding effects of poppy seeds. He also countered criticisms of hair testing by addressing concerns about external contamination and hair color effects. He concluded by stating that hair testing should be approved for heroin detection in the workplace and other settings.

SPONSOR PRESENTATION

Representatives of Psychomedics Corporation presented information on the device at issue. William Thistle, Esq., Vice President and General Counsel, presented background on the

company, the use and advantages of hair testing, and the many unsuccessful legal challenges to hair testing. Thomas Cairns, Ph.D., D.Sc., presented an overview of hair testing for drugs of abuse, including Psychomedics' analytical procedures. He also provided information that addressed panel questions 1 through 5.

Richard Newel, M.A., Professor of Statistics, Research, Methodology, and Forensics, University of South Florida, presented statistical information on hair color as a biasing factor in hair analysis, concluding that the research does not demonstrate a statistically significant effect between hair color or curvature and drug concentration. He presented data from five small-*N* studies and five large-*N* studies. One study that did find differences related to hair color was a small-*N* study that focused on codeine, not heroin.

Dr. Cairns then presented material addressing panel questions 6 and 7. Finally, Carl Selavka, Ph.D., Director, Massachusetts State Crime Lab, described the efforts of the Hair Testing Working Group (HTWG), an advisory group to the Drug Testing Advisory Board (DTAB) of the Department of Health and Human Services. The HTWG formed a consensus on many issues, including sampling requirements, screening analytes and cutoffs, screen precision around cutoffs, interpretive guidelines, and dose-response relationships. He also elaborated on why poppy seeds create problems for detecting heroin in urine. He noted that the DTAB incorporated the HTWG guidance into a draft Notice of Proposed Rulemaking for Federal workplace drug-testing programs.

FDA PRESENTATION

Albert Peacock, Ph.D., Scientific Reviewer, Division of Clinical Laboratory Devices, presented information on Psychomedics' radioimmunoassay (RIA) for opiates in hair, describing its intended use, the flowchart of the testing operation, and field studies. Of the 11 field studies

described in the submission, most were government-funded studies designed by independent scientists who contracted the analytical services to Psychemedics on a blind basis. Field studies found an average clinical sensitivity of 81 percent and clinical specificity of 100 percent. FDA's concerns with the field studies are that the sponsor collected the data from research reports and other sources; the sponsor saw the self-report and urinalysis data after publication or just before publication; the sponsor did not control, monitor, or validate the studies; the sponsor did not control the sample collection process or approve the study protocols; the sponsor provided no demographic data; and no "gold standard" test was used in the studies to determine true drug-use status.

FDA's concerns with the clinical study design include problems with self-reporting (e.g., inaccurate recall, unknown drug purity, and unknown efficiency of drug administration). Dr. Peacock also presented data on Psychemedics' environmental studies, which focus on how treatments affect drug content in the inaccessible region of the hair. Although FDA is generally satisfied with the methodology, it has concerns over whether the studies adequately evaluated the effects of washing and hair treatment procedures and whether the studies should have addressed the potential for bias by race, age, and other demographic factors. Likewise, the methodology of the company's studies on contamination and hair color bias appears to be satisfactory, but the studies did not fully address the possibility of bias arising from individual characteristics. Dr. Peacock discussed literature studies on potential hair color bias and Psychemedics' responses, then presented the FDA questions for panel deliberation.

OPEN COMMITTEE DISCUSSION

Panelists raised questions concerning differences in results for African American and Caucasian hair samples. Arleen Pinkos, of the Division of Clinical Laboratory Devices, said that part of the

dilemma with Psychomedics' data is that the studies provided did not include demographic information. Dr. Clement noted that the lack of a prospective control study is a problem but added that such a study would raise many ethical issues. Dr. Peacock suggested that it might be possible in hospital settings and that because Psychomedics did not design the protocols, some questions that could have been answered were not asked.

Dr. Manno asked whether data were available that compared melanin extraction methods, and Dr. Peacock answered no. Dr. Henderson raised the issue of whether the Glasgow and London studies had been performed on homogeneous populations. The panel asked for and received clarification on which portion of the assay was part of the submission. Dr. Kurt asked whether any attempts had been made to test the assay in a detox unit or methadone clinic. Panelists asked questions concerning the rate of false negatives, the methodology of the studies that support approval, and whether the sponsor had proposed a monitoring program.

Dr. Kroll asked Psychomedics to respond to the panel's concerns. Regarding the methodology concerns, Dr. Cairns said that the studies submitted are more appropriate than studies on the chronically ill and that the large- N studies all used the same RIA method and cutoffs. He added that demographic data are included in the original studies and referred the panel to the references provided in the submission and stated that the studies do not show conflicting results regarding bias. Mr. Newel stated that the small- N studies did not use Psychomedics' methodology and did not have statistical power. He added that a study of hair testing in a racially diverse police department found no bias. Dr. Selavka said that determining false negatives requires the true-use history, which is subject to self-report issues; nevertheless, hair testing does provide a higher rate of positive results than urine testing and is a better approach. Dr. Lewis asked whether, in the 13-year history of the test's use, court cases or other

problems had arisen. Mr. Thistle responded that one claim had occurred; it involved a drug user and raised union issues. Panelists asked additional questions to clarify issues concerning intended use, bias, methodology, and contamination, which company representatives answered. Dr. Peacock noted that FDA needed guidance from the panel specifically because of the conflicts in the literature.

Question 1: The clinical data in this application was from research reports and data collected from diverse sources and not from a prospective, controlled clinical trial that evaluated heroin use. . . . Can assay performance be established with these types of data? Why or why not? Do the data presented provide adequate characterization of assay performance?

The majority of the panelists felt that the current data do not adequately characterize performance; more data are needed. Panelists raised issues concerning the ethical and other difficulties of prospective studies. Panelists also suggested that additional data be gathered with diverse populations. Dr. Lasky said that the small-*N* studies should be disregarded because they are not statistically valid. Mr. Reynolds said that even though one could not set up a controlled clinical study for heroin, it did not preclude the possibility of gathering demographic information from methadone clinics and so forth.

Question 2: With respect to making claims for clinical sensitivity and specificity: (a) is a single negative urinalysis plus a negative self-report of drug use a sufficient unbiased standard for establishing true drug-free status, and (b) is a positive urinalysis that is not always confirmed plus a positive self-report of drug use a sufficient unbiased standard for establishing true drug-use status?

The panelists had mixed responses to this question. Several panelists acknowledged the problems with self-reports, but because few other options exist, they were inclined to accept the criteria; others answered no to both questions. Dr. Kroll said that the problem of false negatives means that something more is needed. Some panelists pointed out that a single negative urine test is the

DOT standard, even though it is easy to cheat. Dr. Everett said that it is not reasonable to rely on self-reports; if a screen is positive, a secondary test must be performed regardless of self-report.

Question 3: Should the minimum dose required to produce a positive result be determined?

The panelists also were mixed in their responses to this question. Some indicated that the minimum dose depends on what one intends to do or say with the result. Other said that the minimum dose should be determined for any system because detection limits and cross-reactivity are important issues. Dr. Manno noted that hair tests determine chronic, not acute, use and that it is important to know the point at which 6-MAM shows up in hair. Several panelists noted that establishing a minimum dose would be interesting but not necessary because there is no level of acceptable use for heroin.

Question 4: Should the relationship of the pharmacokinetics of drug use and the incorporation of drug into the hair (i.e., single dose, multiple doses, and chronic use) be determined?

The panel generally agreed that this was not necessary. Panelists raised questions concerning the relation of time of drug use to its ability to be detected in the sample and reproducibility, and company representatives noted that the information was in the submission. Dr. Rosenbloom mentioned that pharmacokinetic data would be useful if hair tests could detect a single-dose exposure, but he doubted that was important for workplace testing.

Question 5: Should the potential for bias by race, age, sex, hair color, or other individual differences in the incorporation and retention of drug in the hair be evaluated? If yes, what additional studies should be requested?

The panel was in agreement that additional studies should be done in this area and that they could be done on a postmarketing basis.

Question 6: Is the information provided by the sponsor adequate to address the issue of retention of drug in the hair from environmental exposure? If not, what additional information should be requested?

The panel agreed that the information was adequate. Dr. Wilkins suggested that the company's data would have been enhanced had the studies looked at hair contaminated with cigarette smoke. Dr. Lasky noted that he was intrigued by the extrapolation process the company used and suggested that it should perhaps be extended.

Question 7: Has the sponsor adequately demonstrated the effect of various washing or hair treatment procedures on the internally incorporated/bound drug? If not, what additional studies should be requested?

The panel agreed that the sponsor had adequately demonstrated the effects of the procedures and suggested that postmarketing studies on, for example, badly damaged hair could be helpful. The panel had some questions on the methodology, and Dr. Cairns referred them to the appropriate place in the submission.

OPEN PUBLIC HEARING

Rosemary Mumm, Director, Diversionary Program, Orleans Parish District Attorney's Office, New Orleans, Louisiana, said that hair testing has become a vital tool for her program. She described hair testing's advantages over urine testing and summarized the positive effects of hair-testing programs in 10 local New Orleans high schools. Panelists asked clarifying questions about the programs, which she answered to their satisfaction.

ADJOURNMENT

Ms. Calvin and Dr. Kroll thanked the participants and FDA staff. Ms. Calvin noted that the next panel meeting would be January 17, 2001, and Dr. Kroll adjourned the meeting at 3:14 p.m.

I certify that I attended the Open Session of the Clinical Chemistry and Clinical Toxicology Devices Panel meeting on November 13-14, 2000 and that this summary accurately reflects what transpired.

_____/s/_____
Veronica J. Calvin
Executive Secretary

I approve the minutes of this meeting as recorded.

_____/s/_____
Martin H. Kroll, M.D.
Chairman