

UNITED STATES OF AMERICA  
DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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CLINICAL CHEMISTRY AND CLINICAL  
TOXICOLOGY DEVICES PANEL

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MEETING

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MONDAY,

NOVEMBER 13, 2000

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*This transcript has not  
been edited and FDA  
makes no representation  
regarding its accuracy.*

The Panel met at 10:00 a.m. in Salons C and D of the Gaithersburg Hilton, 620 Perry Parkway, Gaithersburg, Maryland, Dr. Martin H. Kroll, Chairperson, presiding.

PANEL MEMBERS PRESENT:

- MARTIN M. KROLL, M.D., Chairperson
- DONNA M. BUSH, Ph.D., D-ABFT, Guest/Federal Liaison
- JAMES EVERETT, M.D., Ph.D., Member
- CASSANDRA E. HENDERSON, M.D., Member
- THOMAS L. KURT, M.D., M.P.H., Consultant
- FRED D. LASKY, Ph.D., Industry Representative
- SHERWOOD C. LEWIS, Ph.D., Consultant
- BARBARA R. MANNO, Ph.D., Member
- STANLEY M. REYNOLDS, Consumer Representative
- ARLAN L. ROSENBLOOM, M.D., Member
- DIANA G. WILKINS, Ph.D., Consultant
- VERONICA J. CALVIN, M.A., Executive Secretary

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## FDA REPRESENTATIVES:

STEVEN I. GUTMAN, M.D., M.B.A., Division  
Director

JEAN M. COOPER, M.S., D.V.M., Branch Chief

CLARA SLIVA, M.P.A., Acting CLIA Coordinator

LINDA R. MANLEY, Secretary

## PUBLIC SPEAKERS:

BOB AROMANDO, Independent Industry Consultant

KEN BERGER, Lifepoint Corporation

DAVID G. EVANS, National On-Site Testing  
Association

DR. CARL M. GOOD, III, Avitar Corporation

LORRAINE HOGAN

DR. HARESH C. JAIN, National Toxicology Labs

DR. JEMO KANG, Princeton Biomeditech

CAROL A. MONGIOVI, Pharmatech

DR. LUANN OCHS, Roche Diagnostics

DR. SALVATORE SALAMONE, Roche Diagnostics

TONY TORANTO, Guardian Angel

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## P-R-O-C-E-E-D-I-N-G-S

(10:07 a.m.)

1  
2  
3 DR. KROLL: Good morning. I would like  
4 all the members of the panel to please take their  
5 seats. My name is Martin Kroll, and I am the Panel  
6 Chair, and we would like to start this meeting. This  
7 is a panel meeting that will discuss and make  
8 recommendations on two draft guidelines.

9 One is the "Guidance for Prescription-Use  
10 Drugs-of-Abuse Assays, Premarket Notifications." And  
11 the other is "Over-the-Counter (OTC) Screening Tests  
12 for Drugs of Abuse: Guidance for Premarket  
13 notifications."

14 I would now like to turn things over to  
15 our executive secretary, Veronica Calvin.

16 MS. CALVIN: Good morning, and welcome to  
17 this meeting. I want to recap briefly what occurred  
18 at the last panel meeting. On March 24th, 2000 the  
19 panel reviewed a PME for Biosite Diagnostics Triage,  
20 B-Type Natriuretic Peptide Test, indicated as an aid  
21 in the diagnosis of congestive heart failure.

22 The majority of the panel had major

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1 concerns with clinical data and voted 6 to 3 for non-  
2 approval. At this time, I would like to welcome our  
3 new industry representative, Dr. Fred Lasky.

4 I would also like to acknowledge Mr.  
5 Stanley Reynolds, who is filling in for our consumer  
6 rep, Ms. Davida Kruger, who is the consumer  
7 representative on the Microbiology Devices Panel. And  
8 I would also like to acknowledge Dr. Donna Bush, who  
9 is here from SAMHSA.

10 Now, if the panel could introduce  
11 themselves, starting with Dr. Rosenblum.

12 DR. ROSENBLOOM: I am Arlan Rosenblum, O  
13 I am an Emeritus Professor of Pediatrics at the  
14 University of Florida, and a member of the panel, a  
15 regular member of the panel

16 DR. LEWIS: I am Sherwood Lewis, Director  
17 of Toxicology at the Office of the Chief Medical  
18 Examiner, State of Connecticut, and I am serving as a  
19 consultant to the panel, having formerly been a voting  
20 member of that panel.

21 DR. MANNO: I am Dr. Barbara Manno, and I  
22 am a professor in the Department of Psychiatry at the

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1 Louisiana State University Health Sciences Center in  
2 Shreveport, Louisiana, and I am a member of the panel.

3 DR. KROLL: I am Martin Kroll, and I am a  
4 pathologist at the Dallas Veterans Administration, in  
5 Dallas, Texas; and an associate professor of pathology  
6 at the University of Texas, Southwestern Medical  
7 School.

8 DR. KURT: I am Tom Kurt, and I am a  
9 founder and medical toxicologist for the Certified  
10 Regional Poison Center in Dallas, called the North  
11 Texas Poison Center, where I am also a clinical  
12 professor in the Department of Internal Medicine.

13 I am a certified medical toxicologist, a  
14 medical review officer, and a former FDA medical  
15 officer and member of this committee from '94 to '98,  
16 and now I am a consultant to CCCTDP MDAC.

17 DR. WILKINS: I am Diana Wilkins, and I am  
18 the assistant director of the Center for Human  
19 Toxicology at the University of Utah, in Salt Lake  
20 City. I am also an associate professor of  
21 Pharmacology and Toxicology at the University, and  
22 today I am servicing as a consultant to the committee.

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1 DR. EVERETT: I am James Everett, Medical  
2 Director for Madison Memorial Health Healthcare, in  
3 Madison, Florida.

4 DR. BUSH: My name is Dr. Donna Bush, and  
5 I am the Chief of Drug Testing, Division of Workplace  
6 Programs, in SAMHSA.

7 DR. REYNOLDS: I'm Stanley Reynolds, and  
8 I am a supervisor of immunology and virology at the  
9 Pennsylvania Department of Health, Bureau of  
10 Laboratories, and I am the consumer representative.

11 DR. LASKY: I am Fred Lasky, the Director  
12 of Regulatory Affairs, Ortho-Clinical Diagnostics, and  
13 I am the new industry rep, and this is my first  
14 meeting.

15 MS. CALVIN: Thank you. And seated at t  
16 he end of the table is Dr. Gutman, and he is the  
17 Director of the Division of Clinical Laboratory  
18 Devices. I will now read the conflict of interest  
19 statement.

20 The following announcement addresses  
21 conflict of interest issues associated with this  
22 meeting, and being part of the record to preclude even

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1 the appearance of an impropriety. To determine if any  
2 conflicts existed, the agency reviewed the submitted  
3 agenda and all financial interests reported by the  
4 committee participants.

5 The conflict of interest statutes prohibit  
6 special government employees from participating in  
7 matters that could affect their or their employer's  
8 financial interests.

9 However, the agency may determine that  
10 participation of certain members and consultants, the  
11 need for whose services outweighs the potential  
12 conflict of interest involved, is in the best  
13 interests of the government.

14 We would like to note for the record that  
15 the agency took into consideration certain matters  
16 regarding Drs. Martin Kroll and Arlan Rosenbloom.  
17 These panelists reported unrelated interest with firms  
18 at issue.

19 Since the interests are unrelated to the  
20 issues before the panel, the agency has determined  
21 that they may participate fully in today's  
22 deliberations. In the event that the discussions

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1 involve any other products or firms not already on the  
2 agenda for which an FDA participant has a financial  
3 interest, the participant should exclude him or  
4 herself from such involvement, and the exclusion will  
5 be noted for the record.

6 With respect to all other participants, we  
7 ask that in the interests of fairness that all persons  
8 making statements or presentations disclose any  
9 current or previous financial involvement with any  
10 firms whose products they may wish to comment upon.  
11 Thank you and I will turn the meeting back over to Dr.  
12 Kroll.

13 DR. KROLL: Thank you. Now, we would like  
14 to hear about CLIA from Ms. Clara Sliva.

15 MS. SLIVA: Hi. I'm Clara Sliva, and I am  
16 the Acting CLIA Coordinator. I have also -- I have  
17 handouts, and they are up front. If I have not passed  
18 them out to you, there are some more up front. I want  
19 to give you a nine month report.

20 What I am doing is that for each of our  
21 devices panel meetings, I am just going to make a  
22 presentation probably for the first year of CLIA to

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1 update people on what we are doing.

2 I will talk a little bit about FDA's  
3 history and the transfer from CDC, CLIA regulations,  
4 FDA's accomplishments, CLIA waiver, the CLIA waiver  
5 workshop, and really what are the next steps that we  
6 are going to be taking.

7 The CLIA regs were issued in 1992, and FDA  
8 was assigned the responsibility for complexity  
9 categorization. Between 1993 and 1994, we actually  
10 completed 900 categorizations. But then there were no  
11 resources and funding issues, and the responsibility  
12 was delegated back to CDC in 1994.

13 The CLIA transfer. There was an impetus  
14 to change from manufacturers, and the manufacturers I  
15 believe went to Congress and said that there was  
16 confusion and duplication of its efforts.

17 Congress asked the CDC, HFCA, and FDA for  
18 some form of consensus, and then we signed an inter-  
19 agency agreement in February of 1999, because HFCA  
20 actually pays for us to do the categorization. But  
21 again, HFCA, CDC, and FDA, we are all CLIA partners.

22 We began hiring scientific reviewers and

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1 medical officers in the fall of 1999, and we have  
2 actually completed all of our hiring in the fall of  
3 2000.

4 And FDA has a dual challenge. We do an  
5 FDA review and a CLIA categorization review, and  
6 always the training is in a continuum. Again, the key  
7 features of CLIA is that it is based on the complexity  
8 of the testing, and not the laboratory site and it  
9 applies to virtually all laboratories.

10 And if I looked on HCFA's home page, it  
11 really is about 170,000, versus 12,000 that were  
12 previously regulated before CLIA '88. And the key to  
13 understanding categorization is the analyst and the  
14 complexity of the testing.

15 Again, CLIA '88, the law specified that  
16 laboratory requirements be based on complexity, and  
17 the regulations were published to implement CLIA on  
18 February 28th, 1992.

19 Three complexity categories that the FDA  
20 regulates, which are commercially marketed products,  
21 -- high, moderate, and waived, and waive tests were  
22 defined as cleared by the FDA for home use, are simple

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1 and accurate as to whether the likelihood of erroneous  
2 results legible.

3 The CDC and HCFA actually published a  
4 criteria for waiver as a notice of proposed rule  
5 making, because the purpose was to clarify the  
6 statutory criteria for waiver, and then on November  
7 9th, 1997 the CLIA waiver provisions were revised by  
8 Congress, and it said the tests approved by the FDA  
9 for home use are automatically waived.

10 And then they also changed the one phrase  
11 in there, "simple and accurate" to render the chance  
12 of an erroneous results by the user negligible. So it  
13 looked at that instance that it was taking it away  
14 maybe from the test and saying can a user perform this  
15 accurately. And then also no reasonable risk of harm  
16 if performed incorrectly.

17 And this was actually put in the Food and  
18 Drug Modernization Act, in Section 123, under  
19 biologics, under the biologic exception and not  
20 devices. If you need any more information, that is  
21 basically me right here. I won't be there and you can  
22 just leave me a message if you want to call me.

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1                   And this is also our fax number, but the  
2 web page is really a very effective way to give out  
3 information. Again, we have done really a lot of  
4 accomplishments since we started. On 913 categorized,  
5 797 moderate and high, again about 75 percent are  
6 moderate, and probably about 24 percent are high.

7                   And really only about one percent are  
8 waived. We have the waiver notifications on the CLIA  
9 home page, and we also have an administratives  
10 procedures guidance, which was published in August.

11                   The purpose of that is to just give you an  
12 idea that if you have an exempt device, what do you do  
13 if it is exempt from 510(k), but it still needs a CLIA  
14 categorization. That is some of the information that  
15 is on there.

16                   Again, you can see that waived is  
17 certainly a very small part of it. The majority of it  
18 really is moderate, by far a moderate complexity.

19                   FDA's waiver responsibilities. As I said  
20 before, that the proposed rule was published by HCFA  
21 and CDC in September of 1995, and they were to clarify  
22 the statutory criteria for waiver. The CLIA committee

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1 provided input into the guidelines for a waiver, and  
2 I believe our new panel chair, Fred Lasky, was part of  
3 that. Weren't you, Fred?

4 DR. LASKY: Yes.

5 MS. SLIVA: So he is not really that new.  
6 And so what we did was that CLIA provided input into  
7 the guidelines for waiver, and now the FDA needed  
8 information from the stakeholders to implement new  
9 responsibilities for waiver decisions.

10 Waive test systems. They are certainly  
11 controversial, and waiver labs do not need to meet  
12 national personnel standards, waiver inspections,  
13 proficiency testing. But another thing is that  
14 manufacturers really have shown the technology to be  
15 very reliable.

16 Again, the three paths to waiver. This is  
17 the nine by regulation. The waiver criteria in the  
18 notice of proposed rule making, where you would  
19 actually have to meet the criteria published by HCFA  
20 and CDC. And then those cleared or approved by the  
21 FDA for over-the-counter or prescription home use.

22 Again, the regulation is the dipstick, the

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1 spun hemacrits, hemoglobins, urine pregnancy tests,  
2 ovulation tests, and this is where the majority of  
3 tests are the waived category, the nine by regulation.

4 Again, you can see pregnancy tests are  
5 probably the number one. But a growing number of new  
6 tests have been included by the FDA for over-the-  
7 counter use, and this does include drugs-of-abuse and  
8 triglycerides, and estrone-3-glucuronide, HOL  
9 cholesterol and microalbumin.

10 A drug test cleared by the FDA as over-  
11 the-counter are automatically waived, but this, the  
12 CLIA regulations are not currently applied to  
13 workplace testing. The delay in implementation  
14 applies to employee workplace testing. But employee  
15 testing for health or treatment purposes is subject to  
16 CLIA.

17 Again, what is prescription home use, and  
18 this was given to us by a lawyer, and so FDA devices  
19 are either over-the-counter prescription, and  
20 prescription home use is a prescription device that  
21 the physician instructs you to use at home, or it is  
22 any device that is not used in the home that is not

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1 over-the-counter.

2 And examples are prothrombin, and that was  
3 our first over-the-counter, a bladder tumor antigen,  
4 and hemoglobin A1C, which we just cleared in the last  
5 couple of months.

6 Again, we had a public workshop, and we  
7 needed to obtain additional comments, and there really  
8 were -- it really represented all of our stakeholders;  
9 the public, the government, inspectors, lawyers,  
10 clinicians, industry, professional lab groups, and  
11 medical societies.

12 There were probably over 300 people  
13 present for both days. I thought it was a wonderful  
14 workshop. There was really a lot accomplished. There  
15 were 28 presenters, and we did accept written comments  
16 through October 16th.

17 Why did we have this? It really was that  
18 the time was ripe to revisit the criteria for waiver.  
19 The proposed rule is really over five years old, and  
20 FDA needs to re-propose the rule to implement its  
21 responsibility for CLIA, and it is beneficial to all  
22 groups to actually know what criteria you need, and

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1 the interest in waive test is very high.

2           Where are we? We continue to meet with  
3 manufacturers requesting waiver, and we have a  
4 priority on the transition waiver. These are waivers  
5 that are in transition from CDC. There are really  
6 about 21 of them that we are reviewing.

7           We are putting out or drafting a level one  
8 guidance on criteria for waiver, and this will just  
9 give FDA -- it is a proposed guidance that gives  
10 manufacturers another route to obtain waiver. But  
11 manufacturers may still request waiver based on the  
12 criteria in the '95 proposed rule.

13           The guidance on waiver criteria. These  
14 are just some of the questions that we are asking. Is  
15 the test simple, meaning does it have simple  
16 characteristics; say something like it only takes five  
17 steps.

18           Can users in waive labs achieve results  
19 that are as accurate as results achieved by moderate  
20 and high complexity labs. And are there no  
21 significant differences between lay user and  
22 laboratorian; and there are no significant differences

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1 between the lay user and the expected result.

2 So again the emphasis is not on is the  
3 test a perfect test, but the guidance on criteria is  
4 asking the question can the untrained user repeat and  
5 get the same results as a trained professional. But  
6 remember that these are all proposed, and we are going  
7 to re-propose the rule.

8 Well, one thing that I think is really a  
9 good part of our guidance is going to be a data based  
10 QC recommendation, because we all know that one side's  
11 QC does not fit all, and we do want studies to  
12 demonstrate that there is alternative QC for the  
13 advanced technology.

14 What are we doing? Well, we are still  
15 accepting requests for waiver based on the proposed  
16 rule, and we continue to listen and interact with our  
17 stakeholders.

18 DR. KROLL: Thank you very much. Now, we  
19 are going to have the FDA presentation from Dr. Jean  
20 Cooper.

21 DR. COOPER: Good morning, Mr. Chairman,  
22 and panel. My name is Dr. Jean Cooper, and I am the

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1 Chief of the Toxicology and Chemistry Branch in the  
2 Division of Clinical Laboratory Devices.

3 It is my pleasure to have the opportunity  
4 to discuss our revised drugs-of-abuse guidance  
5 documents. The policies set by these guidances will  
6 have significant public health impact. We will  
7 discuss the prescription guidances this morning, and  
8 the OTC guidance this afternoon.

9 We would like to focus this morning's  
10 discussion on the proposed study designs for  
11 characterizing device performance. I will summarize  
12 the study design described in the guidance. This  
13 guidance differs from earlier versions in, one,  
14 providing examples of study design formats; and, two,  
15 focusing more on characterizing performance around the  
16 cutoff.

17 We would like your comments on the study  
18 design as proposed in the guidance, and we would like  
19 you to discuss evaluating tests without SAMHSA  
20 guidelines, including tests to detect drugs with  
21 multiple metabolites, and tests intended to detect  
22 members of a large family of drugs, such as

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1 barbiturates and diazepam.

2 Let's begin with some background  
3 information. Drugs-of-abuse tests are intended to  
4 detect the presence of drugs-of-abuse or their  
5 metabolite examples. These tests do not indicate  
6 whether a person is impaired.

7 The guidance focuses on testing urine  
8 samples for amphetamines, methamphetamines, cocaine,  
9 opiates, cannabinoids, and PCP. The revision expands  
10 the application of the guidance.

11 The guidance recognizes that most of the  
12 studies would also be appropriate for characterizing  
13 other drugs and drugs found in alternate matrices.  
14 The prescription guidance describes study designs used  
15 to characterize the performance of tests that are  
16 performed by medical professionals.

17 The studies are typically done within the  
18 sponsor's own facility. The study results are then  
19 put into the products package insert to better assist  
20 the professional in understanding the device  
21 performance and limitations.

22 The prescription guidance addresses

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1 analytical performance by trained technicians  
2 performing the tests in either a central laboratory or  
3 by near-patient personnel performing the tests under  
4 the supervision of professionals.

5 Performance testing needs to reflect the  
6 site in which the device is intended for use. The  
7 guidance outlines the information needed in a 510K  
8 application to support substantial equivalence to  
9 other marketed drugs of abuse-testing devices.

10 The information used to support clearance  
11 includes, but is not limited to, studies demonstrating  
12 the devices' minimum detection limit, cutoff  
13 concentration method comparison studies, cross-  
14 reactivity, interference, and precision.

15 The specimen collection process needs to  
16 be prescribed, and the guidance asks that each data  
17 set include the following information.

18 And they are the number of samples in the  
19 study, the concentration of the specimen, the methods  
20 used to determine drug concentration, the number of  
21 replicates, the number of operators involved in the  
22 study, the description of the testing facilities, and

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1 the qualifications of the individuals performing the  
2 tests. And I would refer you to the guidance for  
3 specifically additional information.

4 The minimum detection limits are  
5 determined by analyzing 20 repeat determinations of  
6 the zero calibrator and calculating the mean and  
7 adding two standard deviation.

8 The detection limit for a qualitative  
9 visually read assay may be estimated by serially  
10 diluting a sample with a known amount of the drug  
11 until the sample no longer renders a positive result.

12 To reduce the impact of assay imprecision,  
13 we suggest that multiple aliquots at each level be  
14 evaluated. Sample concentrations should be confirmed  
15 by analytical techniques, such as a GC/mass spec.

16 The guidance was revised to help clarify  
17 the information provided characterizing performance  
18 around the cutoff. Cutoff concentrations and  
19 applications are generally consistent with a level  
20 established by SAMHSA for the five drugs-of-abuse in  
21 urine.

22 Product applications contain studies to

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1 support each cutoff by testing a statistically valid  
2 number of spiked samples with known drug  
3 concentrations equally distributed around the cutoff.

4 Concentrations at 25 percent above and  
5 below the cutoff allow the reviewer to evaluate the  
6 product's performance around the SAMHSA established  
7 cutoff.

8 In the absence of SAMHSA recommendations,  
9 the rationale for a cutoff may be based on analytical  
10 studies or scientific literature. Tests intended to  
11 detect drugs with multiple metabolites, and tests  
12 intended to detect a large family of drugs, raise  
13 questions related to complex cutoffs.

14 For example, barbiturates have many  
15 related compounds and many metabolites. A potential  
16 review criteria might be to evaluate the performance  
17 around the cutoff using the compound most commonly  
18 observed in urine.

19 We would like your suggestions on review  
20 criteria when addressing complex cutoffs. The  
21 guidance strongly recommends that all or part of  
22 method comparison studies be performed against

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1 referenced testing methodologies.

2           Comparisons between varying immunoassays  
3 often provide limited information on device  
4 performance because of a variable reactivity of these  
5 assays around the cutoff. Most screening tests would  
6 agree a hundred percent of extreme upper and lower  
7 drug concentration.

8           A method comparison using a quantitative  
9 record method allows the reviewer to assess  
10 qualitative performance at defined drug  
11 concentrations.

12           The guidance suggests at least 80 clinical  
13 samples be tested per drug. All positive samples, and  
14 any portion of the negatives, should be characterized  
15 by GC/mass spec.

16           Causery activity is determined by adding  
17 drugs with similar molecular structures likely to  
18 cause a test to be positive to drug free urine.  
19 Compound concentrations should reflect those normally  
20 seen in subjects.

21           The guidance suggests if a compound causes  
22 a positive reaction, dilute it until negative results

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1 are observed, and report the impact concentration in  
2 the label.

3 Interference is determined by adding  
4 commonly prescribed prescription drugs, and common OTC  
5 remedies, such as acetaminophen and caffeine, at a  
6 minimum concentration of a hundred milligrams per  
7 milliliter to see if the drug alters performance.

8 Effects on performance due to Ph and  
9 specific gravity, or other properties, needs to be  
10 identified. Precision, provisionally read,  
11 qualitative tests, is determined by asserting multiple  
12 lots by at least three operators.

13 The guidance suggests that each operator  
14 evaluate 10 samples for each level over a minimum of  
15 2 to 3 days. For semi-quantitative assays, replicate  
16 measurements or calibrators is acceptable.

17 If the device is to be marketed to a point  
18 of care settings, studies should be performed in the  
19 hands of personnel without training as medical  
20 technicians or technologists at least three  
21 representative point-of-care sites.

22 Data should be presented according to site

1 and operator, and information on education background  
2 of operators needs to be included. During point-of-  
3 care studies, the written and verbal information  
4 available to operators should parallel that expected  
5 under usual conditions of use.

6 The prescription drugs-of-abuse guidance  
7 document describes the testing and labeling  
8 information needed for clearance, and we have revised  
9 the guidance based on what we have learned from  
10 reviewing applications, and we look forward to hearing  
11 your thoughts when you have a question.

12 Are the suggested study designs in the  
13 guidance for the following performance characteristics  
14 appropriate. We would like you to give us your  
15 comments on precision, comparison to GC/mass spec,  
16 sensitivity to cutoff validation, interference, cross-  
17 reactivity, and studies for point-of-care devices.

18 And our second question is the guidance  
19 addresses the five classes of drugs for which SAMHSA  
20 publishes guidelines. The FDA often reviews other  
21 drugs for which there are not SAMHSA guidelines.

22 What are the appropriate methods for

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1 establishing valid cutoffs and assessing accuracy of  
2 these tests? Consider especially tests intended to  
3 detect drugs with multiple metabolites and tests  
4 intended to detect members of a large family of drugs,  
5 such as diazepam or barbiturates. Thank you.

6 DR. KROLL: Thank you. Do any members of  
7 the panel have any questions for Dr. Cooper?

8 (No audible response.)

9 DR. KROLL: No? Then we will proceed, and  
10 now we open the floor up for a public hearing, and  
11 these are lawyers who have previously contacted the  
12 executive secretary, and they will address the panel  
13 and present information relevant to this agenda.

14 Again, we ask the speakers to identify  
15 themselves, and please state whether or not they have  
16 any financial involvement with the manufacturer of the  
17 product being discussed or with their competitors.

18 And we are giving each speaker 10 minutes.  
19 So the first speaker we have on the list is David G.  
20 Evans.

21 MR. EVANS: Hi. Good morning. I am David  
22 Evans, and I am the Executive Director of the National

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1 On-Site Testing Association. NOTA is a consensus  
2 group of the manufacturers, users, and distributors of  
3 on-site drug and alcohol tests.

4 I also have a private law practice where  
5 I provide legal assistance to the manufacturers of  
6 drug and alcohol tests, and I have litigated in these  
7 areas, including the U.S. Supreme Court.

8 When clients come to me, I usually give  
9 then one of three answers. I give them either a yes,  
10 that they can do what they want to do; I give them a  
11 maybe pending further research; and sometimes I say  
12 no.

13 If I was representing the FDA, and the  
14 issue was presented to me as to whether or not the FDA  
15 had authority to regulate on-site testing other than  
16 the very narrow category of diagnosing it or using it  
17 for disease diagnosis, my response would be, no, you  
18 do not have the authority to do this.

19 But why do I say that? Well, in looking  
20 at the FDA regulations and the statutory authority of  
21 the FDA, looking at the definition of devices, it is  
22 clear that the only authority the FDA has is to

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1 regulate devices that are used for a mediastinal  
2 purpose.

3 Now, let's look at the definition. It  
4 includes re-agents instruments and systems intended  
5 for use in the diagnosis of disease or other  
6 conditions, including a state of health. But then  
7 what is the purpose of that?

8 Then it goes on to say that in order --  
9 which gives you the purpose -- to cure, mitigate,  
10 treat, or prevent disease or sequelae. The FDA has no  
11 lawful jurisdiction over drug testing unless it is  
12 used only to diagnose a disease.

13 There is case law on this. There is the  
14 case of the U.S. versus An Article of Drug...Ova II,  
15 out of the District of New Jersey. It was affirmed in  
16 the 3rd Circuit Court of Appeals, saying that the  
17 product must be used for mediastinal use. That is the  
18 intent of it.

19 Intended use under the FDA Regulation 21  
20 CFR 801.4 determines whether these products are  
21 medical devices. Now, this afternoon, I am going to  
22 go into detail about the intended uses of these types

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1 of products and show how the intended use does not  
2 meet the FDA definition.

3 The FDA recently tried to regulate  
4 cigarettes as a medical device, and it went up through  
5 the court system and up to the United States Supreme  
6 Court, and the FDA was turned down.

7 The Supreme Court said that an  
8 administrative agency's power to regulate in the  
9 public interest, no matter how intense that public  
10 interest is, must be grounded in a valid grant of  
11 authority from Congress.

12 Well, what has Congress and the courts had  
13 to say on this issue? Well, there have been several  
14 court cases now under the Americans With Disabilities  
15 Act where people who were given a drug test and then  
16 fired complained that the drug test was -- because it  
17 was positive, determined that they had a disease.

18 And the disease was that they were drug  
19 users, and therefore they could not be fired, because  
20 that was discrimination. Well, the courts clearly  
21 have said -- and I am not aware of a single court that  
22 has ever held to the contrary, that a drug test only

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1 detects the use of drugs.

2 It does not detect whether somebody is an  
3 addict, or an alcoholic, or anything else. It just  
4 merely means that within a 2 or 3 day period before  
5 the test that somebody ingested drugs. That is not a  
6 diagnosis of a disease.

7 Congress went on to say again in the  
8 Americans With Disabilities Act -- and this is a  
9 direct quote, a test to determine the illegal use of  
10 drugs shall not be considered a medical examination.  
11 That is a statutory holding by Congress.

12 And I will be going into this in a little  
13 more detail later. There are adequate laws to provide  
14 protection to consumers. The FDA not only has to  
15 consider the intent of Congress according to the case  
16 law, but the FDA also has to consider if there are  
17 alternatives to FDA regulations.

18 And we have a lot of laws regulating  
19 workplace drug testing programs and other types of  
20 drug testing programs. We have been working with  
21 SAMHSA for several years on this issue, and they are  
22 about to come out with some draft regulations that

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1 will provide regulation of on-site testing.

2 Several States now have laws on on-site  
3 testing. There are also other laws; the Federal Trade  
4 Commission laws, Consumer Product Safety Commission,  
5 the U.S. Postal Service, all have laws protecting  
6 consumers.

7 Several State's Attorney Generals now have  
8 looked at the issue as to whether or not a drug test,  
9 and specifically an on-site drug test, is a laboratory  
10 test or a medical test. They have all come down on  
11 our side of the issue.

12 They have all said that it is not a  
13 laboratory test, and it is not a medical test. And  
14 they didn't even get into the issue of intent. They  
15 just looked at some of the other issues involved in  
16 this.

17 I am also concerned that the FDA is  
18 seeking to impose confirmatory testing after an on-  
19 site test is used. Where is this going to stop? If  
20 you decide that you have the right to mandate that  
21 employees engage in confirmatory testing, are you then  
22 going to decide that they have to use an MRO.

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1           Are you then going to decide that they  
2           have to used a licensed specimen collector, and on,  
3           and on, and on, and on. It is not going to stop. If  
4           you decide that we have to fine tune this to ensure  
5           test accuracy, you can add on other requirements that  
6           are going to be very burdensome to employers.

7           I am going to have further comments on  
8           this afternoon, but I would like to hear from the FDA  
9           where is the problem that needs fixing. I would like  
10          to know what evidence are you basing this on.

11          We have now been using on-site tests for  
12          10 years. I am not aware -- and I have written two  
13          books on the subject, on the legal aspects of drug  
14          testing, and I am not aware of a single court case in  
15          this 10 years, in employment or any other matter,  
16          where an on-site test has not been found to be valid.

17          And in fact we have several court cases,  
18          many of them in the criminal justice system, where on-  
19          site tests and the method of using those on-site  
20          tests, have been found to be valid, where the  
21          manufacturer instructs people on how to use the tests.

22          And those court cases have specifically

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1 mentioned this as an issue, and these are cases where  
2 people have to prove -- and these are cases that are  
3 already before courts, and they had to use the  
4 standards of proof to prove that these tests were  
5 valid.

6 And I have written testimony that cites  
7 all these cases, and I am not aware of a single case  
8 to the contrary. So if there was a big problem out  
9 there, we would have heard from it by now in the  
10 courts.

11 The U.S. Postal Service -- and I am going  
12 to end on this -- has been doing about 250,000 on-site  
13 tests a year since I believe 1998. They testified  
14 before SAMHSA when they were looking into this issue,  
15 and I suggest that you talk to the U.S. Postal  
16 Service.

17 These are a -- you now, a large  
18 organization, and a quasi-government organization, and  
19 it has been using on-site testing, and they have not  
20 had the issues that the FDA is concerned about.

21 Mr. Chairman, I have some written  
22 testimony, and if I may, I would like to add it to the

1 record, and I brought 20 copies. So I will give it to  
2 you. Thank you very much, and I will have further  
3 comments this afternoon.

4 DR. KROLL: Thank you. Before we go on to  
5 the next speaker, one of our panel members just came  
6 in, and I would like her to introduce herself.

7 DR. HENDERSON: Hi. My name is Cassandra  
8 Henderson, and I am the Medical Director of the MIC  
9 Women's Health Services in New York City. I am also  
10 Chief of the Maternal-Internal Medicine at Our Lady of  
11 Mercy Medical Center in The Bronx.

12 DR. KROLL: Thank you. Now we are going  
13 to go to our next speaker, which is Mr. Bob Aromando.

14 MR. AROMANDO: Good morning. I had  
15 indicated to the Chairperson earlier today that I  
16 wished to decline my opportunity to speak in the  
17 morning session, and save my comments for the  
18 afternoon session.

19 DR. KROLL: All right. Thank you. Then  
20 we will go to our next speaker, which is Dr. Salvatore  
21 Salamone.

22 DR. SALAMONE: Hi. I'm the vice president

1 of research and development at Roche Diagnostic  
2 Systems, and I have been at Roche for about 18 years  
3 now, and I have been intimately involved with the  
4 development of many different product lines for drugs-  
5 of-abuse testing.

6 In fact, I was also involved with the  
7 first full complete line of on-site drugs-and-abuse  
8 tests, and that was the abuscreen On Trak System, and  
9 we launched that in, what, 1989 or so.

10 And as I was reading through the draft  
11 document, I thought that I might make some comments on  
12 some of the aspects, or some of the points that were  
13 brought up there.

14 The first point is this whole aspect of  
15 clinical samples around the cutoff. I have talked  
16 with people about this in the past, and for a number  
17 of different assays, it is very difficult to procure  
18 samples that have values around the cutoff.

19 This would be especially true for samples  
20 like morphine or cocaine; and for cannabinoids, yes,  
21 you would find more around the cutoff; and with  
22 amphetamines, you would find more around the cutoff.

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1 But it has been our experience that when  
2 we submit documents to the FDA -- and we don't force  
3 those analytes that we don't have materials around the  
4 cutoff samples, around the cutoff, they ask us to  
5 dilute the samples.

6 And dilution of samples, clinical samples,  
7 drugs-of-abuse samples, is not like when you dilute a  
8 therapeutic drug, or a clinical chemistry sample.  
9 There you get linearity upon dilution.

10 But with drugs-of-abuse screening tests,  
11 the antibodies are designed to pick up a wide range of  
12 metabolites, and when you dilute a sample like that,  
13 you really don't get linearity upon dilution, and it  
14 makes it extremely difficult for us to try to hit with  
15 values around the cutoff.

16 So what would be better for us to do, and  
17 be more informative, would be to take samples and  
18 spike -- take clinical negative samples, and spike  
19 them with a specific drug that we are interested in,  
20 and look at the performance around the cutoff of those  
21 drug standards in those sample matrices.

22 It just -- it does not work out in many

1 cases, and it just makes it very difficult, and it  
2 also makes it very confusing. The other point is  
3 about the detection limits in cutoffs.

4 The document describes a quantitative test  
5 quite well in terms of detection limits, and it also  
6 in the first paragraph talks about -- I think it  
7 alludes to detection limits in qualitative tests, and  
8 it says this, "Alternatively, this may be defined as  
9 a minimum concentration of a drug or drug metabolite  
10 that is capable of generating a positive result."

11 Then we go down to study design, and this  
12 is on page 8. The way that I look at qualitative  
13 tests is that the cutoff value is the detection limit,  
14 okay? Because in a qualitative test the presence of  
15 a drug above a certain level will give rise to a  
16 positive test result.

17 And if the drug level is below -- if the  
18 drug concentration is below that level to the visual  
19 or to the user, it is a negative result. And it says  
20 here -- and that's why I am confused. It says here  
21 under study design on page 8, "The detection limit for  
22 a qualitative visually read assay may be estimated by

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1 serially diluting a sample with a known amount of drug  
2 until the sample no longer renders a positive result."

3 So does this mean that the detection limit  
4 is the cutoff value, or -- well, it is just confusing,  
5 okay? But I think detection limits with a qualitative  
6 test are meaningless if we just use a cutoff value in  
7 whether seeing the presence or absence of the drug.

8 Okay. The establishment of cutoff. Well,  
9 that is another aspect. A lot of times these cutoff  
10 values are marketing driven, and when we develop  
11 different types of tests, especially instrument-based  
12 tests, certain unions require a certain cutoff, and  
13 other laboratories require a different cutoff. And in  
14 hospital emergency rooms, they want the most sensitive  
15 tests generally.

16 And so the only thing that manufacturers  
17 can do in terms of establishing cutoffs is to look at  
18 a particular cutoff and make the comparisons with  
19 GC/MS to see if it is a valid cutoff, and how accurate  
20 a screening cutoff is, or how clinically effective a  
21 screening cutoff is relative to GC/MS.

22 Now, I heard some description about

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1 perfect agreement and now I have a better  
2 understanding of that. I guess what we are looking  
3 for here is at what levels in the testing do we get  
4 perfect agreement.

5 And I guess with every amino assay, you  
6 can dilute to a certain level or concentrate to a  
7 certain level until you get close to a hundred percent  
8 agreement. In general, the way that we have gone  
9 about looking at precision of these assays, or  
10 agreements, was at the 95 percent confidence level.

11 We would use a standard and either dilute  
12 it or concentrate it to a point where we would see 95  
13 percent confidence. This is the way that we have been  
14 developing drug tests for the past 18 years.

15 And this is the SAMHSA requirements, which  
16 give that same confidence interval of 95 percent. I  
17 think that would probably be a better way of going  
18 than looking at something at a hundred percent,  
19 because the window would be very large at that point.

20 As far as additional drugs, I think that  
21 has been talked about a bit. Yes, there are a number  
22 of other drugs that aren't under the SAMHSA guidelines

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1 that the market needs, and we currently have tests  
2 available for them.

3 And one other point about multiple lots of  
4 re-agents when you are doing the clinical testing out  
5 in the field. I think it is a good idea to do  
6 clinical testing in the milieu of where the test is  
7 going to be performed. It will give a nice assessment  
8 of things.

9 But the point made in the guidance  
10 document is that we should use three different lots of  
11 re-agents. That will really put a very large burden  
12 on the manufacturer, because these lots generally are  
13 production lots, and the cycles to make these  
14 production lots are quite long.

15 And to make three different lots, and then  
16 to send them out into the field for testing really  
17 puts a lot of strain on the system. And I don't  
18 really know if it is necessary. We are under good  
19 manufacturing practices that are very highly  
20 regulated.

21 And when we make pre-production lots or  
22 production lots, the performance of them has to be

1 within specifications of the performance of all of the  
2 subsequent lots.

3 And so what we would like to ideally see  
4 with this type of testing is that, yes, we allow one  
5 lot to go out to be tested, and then our other lots --  
6 just like the way we make any of our re-agents, our  
7 other lots are compared to the original lot.

8 This is the way we have been doing things  
9 for years, and the accuracy that we see, and the  
10 variation that we see, is kept to a minimum. I  
11 understand that there may be a concern with a lot of  
12 new entrance to this whole business that it may be  
13 necessary to ensure that you get lot-to-lot  
14 reproducibility.

15 But it really does put a burden,  
16 especially on the large manufacturers that have been  
17 doing this for many years, and doing it in a very  
18 accurate way. So that is about all that I have to  
19 say. Thank you.

20 DR. KROLL: All right. Thank you. Now we  
21 are ready to go to our open committee discussion, and  
22 one way to do this is that we can go around the table

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1 and have each person, each panel consultant, go ahead  
2 and give their comments on this document and see if  
3 they can help answer the questions that the FDA has  
4 put before us.

5 So why don't we start with Dr. Rosenbloom.  
6 So why don't we put up question number one first from  
7 the FDA, and see if we can answer that question  
8 specifically. All right. Why don't we start with Dr.  
9 Rosenbloom.

10 DR. ROSENBLOOM: Well, regarding question  
11 number one, I am not an expert in laboratory. Those  
12 are all laboratory questions, and I am going to defer  
13 to those who are.

14 And so lacking immediate laboratory  
15 experience, I will be interested in those people who  
16 are working directly in this area and their comments,  
17 and I will respond to those in addressing this. So I  
18 defer to the laboratory experts in the group.

19 DR. HENDERSON: Similarly, I will have to  
20 defer to my laboratory colleagues.

21 DR. LEWIS: Not so much a question as a  
22 comment, and I think that the presentation regarding

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1 the sensitivity or the cutoff validation, I have been  
2 wrestling with that very question of what is meant by  
3 the limit of detection, as opposed to the cutoff, when  
4 you are talking about the types of tests where either  
5 it is positive or negative, and there is no numerical  
6 value associated with that result as being positive or  
7 negative.

8 So to me it is either confusing, or a non-  
9 existing entity as to the distinction between cutoff  
10 and limit of detection or sensitivity. That's my only  
11 comment at this particular moment.

12 MS. CALVIN: For the record, that was Dr.  
13 Lewis, and panel members, please remember to state  
14 your name.

15 DR. LEWIS: Sorry.

16 DR. MANNO: Barbara Manno. I am a little  
17 confused between the document and the presentations  
18 because by the wording of the document the document  
19 contains the wording for therapeutic use, and it needs  
20 to be very clear on point-of-care testing whether it  
21 is for workplace testing, or whether it is for  
22 therapeutic use.

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1                   And I agree with Dr. Lewis' confusion on  
2 the limit of -- on the wording of limited detection  
3 and cutoff. There has to be a difference or a clear  
4 definition of the terminology here.

5                   I was reading again the document last  
6 night, and I was reading at the same time, or during  
7 that time, the DOT guidelines. And they make a point  
8 in there on visual read-out tests; that they should be  
9 tested under varying lighting conditions, and I would  
10 suggest that that be considered to be put into this as  
11 well.

12                   So that having worked with some of these  
13 myself, I know that varying lighting conditions can  
14 give you varying results based on the intensity or a  
15 lack thereof of color at the point of reading. So I  
16 would think that some consideration needs to be given  
17 there. Thank you.

18                   DR. KROLL: Thank you. Martin Kroll. One  
19 thing or one comment that I would like to make is that  
20 when we look at things like comparison to GC/MS, which  
21 I think is a good idea, as that is always good to know  
22 how much is actually in a sample by some means that we

1 would consider a reference or almost as a reference  
2 method.

3 So that is an accuracy issue, and we need  
4 to clearly separate that out from precision. And the  
5 same thing in terms of sensitivity or cutoff  
6 validation. That we need to clearly separate that out  
7 from the precision issues, even though precision does  
8 play a role in evaluating the accuracy, sensitivity,  
9 or cutoff validation.

10 When I was looking at this document, I  
11 actually liked the idea that they had a separate one  
12 for the minimal detection limit, and I do think it is  
13 appropriate to use samples in which in some way we can  
14 dilute them down by using some appropriate matrix.

15 I take a different view than some people,  
16 and that is that I do believe even on a device that is  
17 meant for qualitatively that you can go down to a very  
18 potentially low concentration of drugs or drug  
19 metabolite, and yet your cutoff can still be  
20 significantly above that limit of detection.

21 Because it is one thing to say that I can  
22 detect a certain amount of drug here, or metabolite,

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1 but then you get into other issues, which is, for  
2 example, if the person did take drugs or they were  
3 exposed, how did they get in there.

4 Is it really important, and what are the  
5 probabilities that this person is potentially going to  
6 be, let's say, abusing a certain drug. So those are  
7 distinct types of entities.

8 For many years I was involved in an  
9 emergency room where we had people come in, and you  
10 knew that a lot of these people were drug users. But  
11 there was a clear separation; did they use something  
12 recently, or is it something that is sort of hanging  
13 around; or is it really not that important in terms of  
14 what we are dealing with today for that person.

15 And you would like to have your ability to  
16 detect the concentration, and to go below your cutoff.  
17 So then you can set your cutoff above that. In some  
18 cases, depending on the situation, the cutoff could be  
19 set at a minimal detectable concentration, but it does  
20 not always have to be.

21 So I think that is important that those  
22 two things are separated out. All right. Those are

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1 all the comments that I have for right now.

2 DR. KURT: I am Tom Kurt, and I would like  
3 to point out something that I don't think is on the  
4 list, and which has become important in recent years,  
5 and that is adulterants, because adulterants are  
6 frequently done as a pretest.

7 And since as a medical review officer,  
8 there is an adulterant presence, such as chromium or  
9 sodium hydroxide, and that is positive, that is  
10 considered a refusal to test, and the test itself is  
11 not performed, and the person might lose their job.

12 And so I think that there should be  
13 something about the quality, control, and precision of  
14 the adulterant testing that is included in this if the  
15 adulterant testing is indeed performed.

16 The next under GC/MS accuracy, there are  
17 times in my experience where a non-DOT testing for a  
18 specimen has either been discarded, lost, or  
19 contaminated before the GC/MS testing could be  
20 performed.

21 The question then arises is confirmation  
22 testing absolutely necessary, or is the test that is

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1 performed absolutely worthless. I think based upon  
2 the SYVA information, that in a test or a study of  
3 20,000 alert tests, there was a 98.2 percent accuracy  
4 of testing of your remit methods that as a stand alone  
5 testing is relatively accurate.

6 And something should be said -- instead of  
7 categorizing this as a screening test in these  
8 categories, as something more like an initial test,  
9 with GC/MS being necessary or preferred in the  
10 situation. Thank you.

11 DR. WILKINS: Diana Wilkins. I want to  
12 apologize ahead of time because I am going to ask  
13 probably some questions that may have come up at prior  
14 meetings or something, and so being a first-time  
15 member, I am not sure if these have already been  
16 discussed.

17 I just want to mention that I concur with  
18 the comments of Dr. Kroll and Dr. Manno regarding the  
19 definitions of terminology for detection limits and  
20 cutoffs for these assays, as well as the lot-to-lot  
21 variability with the color issues and visually read  
22 tests.

1           The one thing that I had a question of is  
2 with the issue of comparison to GC/MS testing as the  
3 reference method, I wondered if it has already been  
4 discussed at some point whether or not that could be  
5 limited theoretically to mass spectrometry as the  
6 detection method in general.

7           I am just looking further down the road.  
8 There maybe come times when, for example, a  
9 manufacturer or someone else might be looking at a  
10 polar drug or metabolite, and might be interested in  
11 using an alternative method of introducing the sample  
12 to the detector, possibly LC/MS, for example, or  
13 capillary LC/MS.

14           And if it is limited to GC/MS, my concern  
15 would be that that really may not -- if you strictly  
16 use that interpretation -- allow the manufacturer to  
17 use the best, and most reliable, and accurate method  
18 of establishing sensitivity, or reproducibility about  
19 the cutoff. That's number one.

20           And the second thing is that I was curious  
21 on whether in the proposed document that the sponsor  
22 was going to need to include the length of time

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1 between sample collection and testing, or whether they  
2 needed to evaluate the stability of samples between  
3 the time that a sample might be collected, wherever  
4 that happens to be, and the time that it is actually  
5 received at a laboratory in the documents provided for  
6 submission.

7 DR. GUTMAN: I would be happy to address  
8 and to answer both of those questions. I don't recall  
9 -- and somebody from the group can quality control me.  
10 But I don't actually recall a panel meeting where  
11 there has been previous discussion about what the  
12 appropriate gold standard or yardstick is.

13 There has been a lot of internal  
14 discussion with certain submissions about the novelty  
15 of some of the alternative gold standards, and how to  
16 be sure that what you are dealing with is gold and not  
17 an alloy of uncertain proportion.

18 We could certainly take it under  
19 advisement that there be a liberalization. I don't  
20 think there was an intent to restrict or to create any  
21 artificial barrier that was a comfort with GC/MS. But  
22 certainly as science changes, and credible

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1 alternatives are available, we wouldn't want to be in  
2 any way limiting.

3 We don't currently have any requirements,  
4 I don't believe, either as a review practice or in the  
5 guidance document, that there be information on  
6 duration of storage of the sample. If you would like  
7 to put that recommendation on the table, we would  
8 certainly consider it.

9 DR. EVERETT: James Everett. This  
10 particular question I actually agree with. That is,  
11 if any laboratory task is going to be developed, and  
12 in essence in a research laboratory, and then later  
13 put into practice, there should be some perimeters to  
14 decide if the test performed as indicated.

15 The characteristics listed here,  
16 precision, comparison to GC/MC, and sensitivity, and  
17 interference, and cross-reactivity, and studies for  
18 point-of-care, these are studies that get to the heart  
19 of whether or not the device actually works.

20 The only real thing it seems to me that  
21 seems to be left off is specificity. But in essence  
22 I generally agree that with any test that is going to

1 be used on the public interest, there should be some  
2 performance characteristics.

3 And I think that these are minimal. And  
4 the list, in essence, could go on and on. But  
5 assuming that Mr. Evans is incorrect, and the FDA does  
6 have some authority to regulate these devices, then I  
7 agree. I think as minimal characteristics that these  
8 are certainly appropriate.

9 DR. BUSH: Thank you. This is Donna Bush.  
10 I was unsure as an associate here whether I was to  
11 participate directly with comments. Thank you for  
12 that opportunity. My training is as a chemist, first  
13 and foremost, and I concur with several of the other  
14 panel members who have reflected on the list of  
15 characteristics here in question one.

16 In very basic analytical chemistry, they  
17 are the minimum essentials to define an assay, and at  
18 the heart of qualitative assays, and I have had an  
19 awful lot of experience in these testing technologies  
20 with these testing technologies, both laboratory based  
21 and instrumental read and visually read, at the heart  
22 of that is that you can't tell me if something is

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1 there or not unless you know an awful, awful lot about  
2 that assay.

3 Unless you can be quantitative and  
4 specific about every aspect of the assay, then you can  
5 go qualitative. You actually have to be very defined,  
6 very specific, in establishing the criteria about an  
7 assay before you can go general.

8 It is kind of an oxymoron when you think  
9 about it, but for something as simple as it is or that  
10 it appears to be, that's how complex it generally is  
11 underneath.

12 And so I wholeheartedly concur with these  
13 as minimum requirements, as well as with the comments  
14 that Dr. Wilkins and Dr. Everett, and other board  
15 members have made about that. Thank you.

16 MR. REYNOLDS: Stanley Reynolds, consumer  
17 rep, and again I would pretty much agree with the rest  
18 of the panel that I don't believe the study design is  
19 laid out at this point is unreasonable or  
20 unnecessarily burdensome. And it does give you the  
21 minimum amount of information that you need to make a  
22 judgment.

1 DR. LASKY: Fred Lasky. I have several  
2 comments actually. From an overall prospective, these  
3 characteristics I think are appropriate, but let me go  
4 into some of the details, because that's where the  
5 devil is from a manufacturer's perspective.

6 First of all, I was interested in Mr.  
7 Evan's comments, and I was concerned about some of the  
8 directions that it seems that the FDA was moving in,  
9 and his comments were ones that I had not considered  
10 and were beyond my level of expertise.

11 But let me bring up an issue that is, I  
12 think, within my realm of knowledge, and that is what  
13 is contained in the labeling of the device. And how  
14 the manufacturer actually conducts studies in order to  
15 support the submission, and in fact demonstrate that  
16 the device is safe and effective.

17 Part of that has to do with the intended  
18 use of the device. The FDA has authority to review  
19 submissions based only on the intended use that the  
20 manufacturer puts in labeling. Anything beyond that  
21 -- off-label use, and use, for instance, in workplace  
22 drug screening.

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1           If a manufacturer seeks not to have that  
2 as an intended use, that is beyond the realm of the  
3 FDA's authority for a review based on the FDA  
4 Modernization Act. So I think that has to be  
5 considered very carefully.

6           That being said, let me go on to some of  
7 the specifics, in terms of the technical issues.  
8 There is a comment there about the comparison to GC/MC  
9 for accuracy. But there is also an option as I  
10 understand it to compare a device to a predicate, a  
11 device that has been cleared or approved for market by  
12 the FDA.

13           And a question arises is or how are the  
14 two comparisons going to be used. I would suggest  
15 that it should be at the option of the manufacturer to  
16 submit data, and then of course there is always  
17 negotiation with the FDA.

18           And the two options I think would be to  
19 compare it to GC/MS as a standard, and have FDA  
20 declare that as an acceptable standard under their  
21 authority, also under the Modernization Act.

22           And use that comparative study to

1 demonstrate that the new device in fact compares  
2 favorably or in ways known to the GC/MS method, for  
3 instance, in this case which is generally accepted as  
4 the most definitive method for assay, and definitive  
5 with a little "d" for those of us who are hung up on  
6 standards.

7           The other is compared to a predicate, if  
8 that is appropriate, and in fact might be more  
9 appropriate depending upon what the intended use of  
10 the device is.

11           I have another comment about cutoff, and  
12 I would like to emphasize that the minimum detection  
13 limit is not equivalent to the cutoff. The cutoff is  
14 to determine, based again on the intended use of the  
15 device, whether or not for a qualitative test a sample  
16 is positive or negative.

17           And there again it really depends on what  
18 the intended use of the device is, because there are  
19 always uncertainties around the cutoff level, the  
20 simple statistical or random variability that always  
21 occurs with any measurement.

22           It is not unique to these tests, and if

1 you were going to count a jug of pennies, there would  
2 be uncertainly around the accuracy of that count. So  
3 that really has to be carefully considered.

4 If you are looking for increased  
5 sensitivity, or increased specificity for patient  
6 population, then that's how the cutoff should be  
7 determined. And again that is based on the  
8 manufacturer's intended use, and has to be decided  
9 upon by the manufacturer and by FDA.

10 Another comment on precision, and as Dr.  
11 Salamone mentioned, lot-to-lot variability is most  
12 often best determined and monitored by the  
13 manufacturer within the plant, and is at least to my  
14 knowledge always a consideration when products are  
15 released for sale as production continues, hopefully  
16 for a long time from a manufacturer's standpoint.

17 Most often it is not a function of  
18 operator' use. Most often. And that's because I hate  
19 the never and always times of scenarios. But again  
20 that is up to the manufacturer to determine and for  
21 FDA to agree to.

22 So I have some concerns about the

1 recommendations about what sort of variables have to  
2 be considered in the end use test, which by the way I  
3 do agree with. The tests should be looked at in the  
4 area of intended us.

5 And lastly I have just one small comment  
6 about specific issues, like under particular light  
7 conditions, which I think is a very valid comment.  
8 But those are the sort of variables that have to be  
9 considered during the design phase of the test.

10 And there are regulations that in fact  
11 manufacturers must adhere to in order to consider the  
12 major points of variability that must be addressed,  
13 mitigated, resolved, or addressed in labeling when a  
14 product goes out.

15 That's not to say that the FDA shouldn't  
16 ask those pertinent questions, but also to consider  
17 that those are the sort of things that I don't think  
18 in a guidance should be specifically noted, but given  
19 as examples. So those conclude my comments at this  
20 point.

21 DR. KROLL: Thank you. What I would like  
22 to do is open this back up to the panel members and

1 see if anybody else has any additional comments.

2 DR. HENDERSON: Cassandra Henderson. As  
3 a clinician, I am very concerned about any of the  
4 testing, and taking care of high risk pregnant women,  
5 I want to understand and be certain that the negative  
6 predictive value is something that I can rely on in  
7 taking care of women, and being concerned about  
8 abortion, and pre-term labor, and fetal death, and all  
9 of that.

10 Can we eliminate the possibility that some  
11 of the problems are related to the use of drugs,  
12 immediate or in the immediate past. And I think in  
13 listening to all of my laboratory colleagues that I  
14 have just been educated very much here, and I thank  
15 you.

16 What I am very interested in, I guess, is  
17 qualitative analysis. I mean, quantitative seems to  
18 me to be more of a research tool for me as a  
19 researcher when I am evaluating a test.

20 But when I am taking care of somebody at  
21 the bedside, it seems to be the most important thing  
22 is something that would be qualitatively reliable,

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1 whether it is in the dark or in the light, or how that  
2 affects it certainly is of concern.

3 And then finally the adulterants. We know  
4 that a lot of people who are using substances are  
5 using other things, and things that are used on the  
6 street. We are not clear on what else they have  
7 taken.

8 So certainly how the qualitative analysis  
9 would be affected by any adulterants that they might  
10 have been exposed to.

11 DR. KROLL: Thank you. Any other of the  
12 panel members have any additional comments to make?

13 DR. MANNO: Barbara Manno. I am concerned  
14 again about this intended use of the product. I am  
15 hearing things that disturb me as a practicing  
16 forensic toxicologist, and also a member of the  
17 Department of Psychiatry, where I teach people how to  
18 interpret drug screens in both environments.

19 And, number one, there needs to be  
20 something considered for the insert in the product  
21 that you cannot tell the time of use on a qualitative  
22 test. It is either there or it isn't there.

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1           If you talk about cutoffs, per se, or --  
2           well, again, it is getting back to there also should  
3           be something about not only time of use, but very  
4           definitely for those taking qualitative results from  
5           an emergency room setting, let's say, where the full  
6           intended use would be for a clinical application in a  
7           person with an uncertain history, that those results  
8           later cannot be used in any way to predict based on a  
9           qualitative test performance decrement.

10           And this bothers me because we have the  
11           door open for alternative matrices to be used. You  
12           cannot go from altered performance based on a  
13           qualitative urine, for example; a urine test.

14           And a lot of the performance that goes  
15           along with this issue, for decrement of performance,  
16           we don't know a lot about that yet. The only one we  
17           have out there that is tested is alcohol.

18           We are working as fast as we can that the  
19           financial resources in the research community allow us  
20           to work. But it is very difficult and it is really  
21           impossible on a qualitative test in my opinion.

22           DR. HENDERSON:        Cassandra Henderson.

1 That's why as a clinician that I am very concerned  
2 about negative values. I want to cross that off the  
3 list of my differential.

4 Positives I understand. They can be plus-  
5 minus, and I don't know what to make of it, and when  
6 does she use it, and does she really use it. But a  
7 negative, I would like to be able to be comfortable  
8 that that is for sure.

9 DR. MANNO: I am agreeing with you.

10 DR. ROSENBLOOM: Arlan Rosenbloom. I  
11 would just like to confirm that I get involved in a  
12 lot of medical legal cases, where people have things  
13 in their urine, and the question always comes up,  
14 well, does this really mean that they have taken up,  
15 does it tell you when they took it, and of course, how  
16 much they took.

17 There is all variables in what you find,  
18 but the importance of saying that if it is there, it  
19 really was taken has extremely great significance and  
20 more than just diagnosis, but in a legal context.

21 DR. LASKY: Fred Lasky. I think this  
22 discussion illustrates the point that one test may not

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1 satisfy all of the needs of the community in general;  
2 that if a qualitative drug test was used, for  
3 instance, for workplace monitoring, just in and of  
4 itself -- and I am not reporting or supporting that.

5 But in the event that it was, then in that  
6 situation, if I was an employer, I would want to be  
7 damn sure that a positive was truly a positive. And  
8 yet in the clinical setting as I am hearing, you want  
9 to be sure that a negative is truly a negative.

10 And there is always going to be a gray  
11 zone somewhere in between, and depending upon the  
12 performance characteristics of that test, that gray  
13 zone may be extremely narrow and very easy to  
14 distinguish between a positive and a negative.

15 But to my knowledge there are very few --  
16 some, but very few -- tests that in fact offer that  
17 sort of a characteristic. So I go back to the  
18 statement that I made earlier about the intended use  
19 of the test.

20 I think that has to be very clear, and the  
21 documentation and the data supporting the test has to  
22 be with regard to the specific intended use, and there

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1 are obligations that people who may use the device  
2 off-label, or where the manufacturer did not provide  
3 data or information for other than the intended use,  
4 that the obligation reside elsewhere.

5 DR. KURT: Tom Kurt. I would like to  
6 refute David Evans' comment that the FDA is an agency  
7 only involved in approving tests or drugs, and to  
8 diagnose disease.

9 Concerning the ADA and the testing that  
10 you were pointing out in disease, the ADA is involved  
11 with fitness for duty testing. So if a person has a  
12 positive drug test, that is considered a person who is  
13 not fit-for-duty.

14 The FDA is involved in approving  
15 biologics, such as immunizations, that protect against  
16 disease. It is involved in lowering cholesterol  
17 medicines that are not necessarily diseases in and of  
18 themselves, such as lipitor and other medicines that  
19 lower cholesterol levels.

20 It is involved in the Center for Devices  
21 here in reviewing the standards for rubber gloves that  
22 protect people from different substances, but not

1 necessarily as a diagnosis of disease.

2 And it is involved in the Center for  
3 Veterinary Medicine, and approving and reviewing  
4 animal foods. So those are not necessarily diseases.  
5 So the FDA's perview, I think, is a little bit wider  
6 than your perception.

7 DR. EVERETT: Can I respond?

8 DR. KROLL: I think we will hold that off  
9 for now. I think we want to get the comments from the  
10 panel. Any other comments?

11 DR. WILKINS: I actually don't have a  
12 comment, but again I have another question as a panel  
13 member, and that is -- and it does relate to something  
14 that I had not thought about until one of the  
15 presenters this morning, Dr. Salamone, brought it up  
16 about the issue of diluting native urine samples, and  
17 that whole issue using to demonstrate the reliability  
18 of the device and the minimum detection limits and  
19 such.

20 And one question I had was that it seems  
21 to me that -- my general impression is that the  
22 availability of clinical specimens is going to be come

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1 increasingly difficult, I think, in the future,  
2 because I don't know about in the commercial sector,  
3 for example.

4 But I certainly know in academic  
5 institutions that urine, blood, whatever, is no longer  
6 considered biological waste; that you can simply go  
7 ahead and give to someone to be looking at.

8 It is not even something that many  
9 laboratories in that setting could receive if you  
10 understand what I am saying, because that contains  
11 information about an individual, DNA or what have you,  
12 that belongs to that individual.

13 And so I am just bringing it up that I  
14 don't know what impact that plays on here, but I think  
15 if there needs to be some mechanism to get around  
16 that, it may involve fortification of urine that is  
17 known to be drug free, with the drug that the test is  
18 targeted at, to be able to get around that.

19 Again, this may have been an issue that  
20 has been discussed at some other point in time, but I  
21 am just mentioning it.

22 DR. KROLL: Okay. Dr. Rosenbloom.

1 DR. ROSENBLOOM: Arlan Rosenbloom again.  
2 That brings up an issue of all of the metabolites, and  
3 the variability from individual to individual, which  
4 I don't pretend to be an expert on.

5 But I don't know if this is going to come  
6 up in another of the questions. I didn't see that it  
7 would, but the device, the point-of-care device that  
8 I am familiar with that is most relevant here is the  
9 glycohemoglobin that we use in the clinic.

10 And in order to use that device  
11 effectively, we have to with each run send a specimen  
12 or two to the laboratory for confirmation. I was  
13 wondering about quality control as a question here.

14 It says comparison to GC/MS, but that  
15 sounds like it is in the approval phase rather than in  
16 an ongoing point-of-care usage. Maybe we need some  
17 discussion of that issue.

18 DR. KROLL: Dr. Gutman, can you comment on  
19 that?

20 DR. GUTMAN: Well, I hadn't actually  
21 thought of it in the context of a quality control  
22 program, where you would run samples at the site, and

1 samples at the central lab. But anything is fair  
2 game, and so any advice that you have on the quality  
3 control that we ought to consider, we would certainly  
4 be willing to hear.

5 DR. KURT: Tom Kurt. I think that would  
6 be important in specimens where you biologically decay  
7 particularly is cocaine, cocaine metabolites.

8 MR. REYNOLDS: Well, one thing I would  
9 like to mention here again, and as Mr. Evans commented  
10 on the workplace testing, and we do have two very  
11 different testing arenas.

12 And that is where we have clinical  
13 testing, where you are going to have tests being done  
14 in hospital labs and clinical laboratories who are  
15 regulated by other agencies, such as CLIA, CAP, Joint  
16 Commission, State agencies.

17 And then you have workplace testing, where  
18 the question comes up if in any or many of those cases  
19 if those labs are regulated at all by any agency. I  
20 know that in Pennsylvania our law considers it to be  
21 a clinical laboratory test, and we don't care if it is  
22 done in the workplace, or done for screening, or for

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1 job performance, or whatever. It is a regulated test  
2 in Pennsylvania.

3 And you are governed by our clinical lab  
4 regulations, but that may not be the case in every  
5 State. So you do have two very different testing  
6 arenas, and that is another thing that you need to  
7 consider.

8 DR. KROLL: Thank you.

9 DR. MANNO: Barbara Manno. Going back to  
10 the quality control, I agree with you Dr. Rosenbloom  
11 that it is a very important issue. What I hear some  
12 of my colleagues who are using point-of-care testing  
13 in a clinical setting are complaining about is the  
14 fact that the point-of-care testing is expensive to  
15 do, as compared to where you can batch process  
16 something in a main lab, which is true.

17 Given that, they are saying that they are  
18 having to run one particular test with a QC, and one  
19 with the donor specimen, the patient's specimen. I  
20 think that there has to be some quality control on  
21 that; running a parallel test once a day with that lot  
22 would give you some indication as long as it meets a

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1 positive and a negative.

2 And that would give you two extra that you  
3 would have to run, but if you are in an emergency room  
4 setting, for example, you are going to have very  
5 likely more than one patient a day that you would need  
6 something like that on.

7 That would at the very minimum would be  
8 once a day, and then jumping to once a shift,  
9 depending on your workload. But most labs will go  
10 with the same lot number. They try to earmark a lot  
11 number for their use for a year, or the people  
12 supplying this, so that you don't have so much  
13 confusion and possible difference by lot number.

14 DR. ROSENBLOOM: Dr. Rosenbloom again.  
15 Yes, I think in terms of practicality, point-of-care  
16 testing is very expensive, unless you are doing a lot  
17 of it.

18 And that that kind of system once a day,  
19 or once a lot, or once a shift, makes sense. I doubt  
20 that you would be doing point-of-care testing  
21 otherwise unless you had enough.

22 DR. MANNO: Well, I am basically agreeing

1 with you that QC is very important on this subject,  
2 and just making some suggestions for consideration, I  
3 think it needs to be given consideration on  
4 presentations.

5 DR. KROLL: Thank you. Actually, coming  
6 back to the issue of -- this is Marty Kroll, back to  
7 the issue of cutoff concentration. I have been  
8 reading this over several times, this definition and  
9 how it is established.

10 And I wonder if in the document it could  
11 specify that this is done in a clearer fashion,  
12 depending upon its type of use. I think as some other  
13 people mentioned, the use determines where you want  
14 your cutoff to be.

15 If it is a medical situation, like in an  
16 emergency room, you want to know that -- you want to  
17 detect almost any drug that is there, because that  
18 could become important in terms of how you manage the  
19 patient.

20 In terms of trying to decide if somebody  
21 has been using drugs inappropriately, and you want to  
22 do something about their job status -- and I have been

1 in that situation, you want to make certain that your  
2 positive is probably absolutely certain.

3 You are not talking about manufacturer's  
4 competence intervals here. We are talking about that  
5 you want to be certain, like 99.99 percent, because  
6 you are going to do some really nasty things to  
7 somebody based on that result.

8 And so you want -- those calls have to be  
9 different, and the probabilities that you work with  
10 are different. And I am not saying that the witness  
11 document is written that it is inadequate, but that it  
12 may need to clarify those types of issues so it is  
13 dependent on the type of use.

14 And when someone goes ahead and forward  
15 with the product, they say that if you are going to  
16 use it this way, this is what the cutoff needs to be,  
17 and this is how it is interpreted, and that we know --  
18 for example, if we say it is positive, and you are  
19 using it in an occupational setting, that the  
20 probability that it is actually a negative is so  
21 remote that it is not going to cause harm.

22 I mean, we could go back to this old adage

1 that worries clinicians that what is worse, not having  
2 the test, or having a test that is wrong. And if you  
3 work in a lab long enough, you realize having a test  
4 that is wrong, or gives the wrong answer, is sometimes  
5 a lot worse than not having any answer.

6 Any other comments from the panel on  
7 question number one? Let me ask Dr. Gutman if we have  
8 discussed this sufficiently?

9 DR. GUTMAN: Yes. I would actually like  
10 to revisit the issue that Dr. Salamone raised, and  
11 that Dr. Wilkins touched upon, which is whether -- or  
12 what is the appropriate nature or specimens, and it is  
13 one that we have been very hung up about, in terms of  
14 trying to get samples that are more naturalistic.

15 I would be curious to get a sense for  
16 whether the suggestion that was put on the table -- I  
17 think both in the public panel meeting and by Dr.  
18 Wilkins -- about using a calibrator control, as  
19 opposed to samples, seems like an reasonable  
20 alternative.

21 I actually do think you have access to  
22 samples as long as you are very careful about de-

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1 linking them, but I also recognize that this is  
2 controversial, confusing, and more intense than it  
3 might have been a couple of years ago. So I would be  
4 very curious to know how far you would encourage us to  
5 go.

6 DR. WILKINS: This is Dr. Wilkins again.  
7 I think that I had not really thought about this  
8 before the comments this morning, and it seems to me  
9 that again it depends on the intent and what it is  
10 that you are trying to use it for.

11 I think that if you are fortifying drug  
12 free urine in order to determine a particular  
13 characteristic, such as sensitivity, or  
14 reproducibility, at a certain specified cutoff for a  
15 certain specified acolyte, then I would think the use  
16 of fortified materials seems appropriate and  
17 reasonable.

18 I think that is a different issue though  
19 than looking at the robustness of the system or the  
20 assay on real life specimens that are complex mixtures  
21 of the drug and the metabolites, and everything else.

22 And I am not sure what the answer to that

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1 is, but I think they are two different issues, and at  
2 least in my mind I think that fortifying materials to  
3 specify a performance characteristic for a particular  
4 acolyte seems reasonable.

5 But that would not answer the question of  
6 how well it would do in a true urine, with a complex  
7 mixture of metabolites or other compounds.

8 DR. LASKY: Fred Lasky. I just want to  
9 emphasize something that Dr. Gutman alluded to; that  
10 there are several very critical issues that are being  
11 sort of bandied about between industry clinical  
12 laboratories and the FDA with regard to old samples,  
13 historical samples, and whether or not in fact they  
14 will be available for use.

15 So far no conclusions have been reached,  
16 but the thing that I am concerned about is -- and as  
17 I am sure we all are, is that there will be two  
18 guidances that will be written, one with issues of  
19 patient confidentiality, and historical samples, and  
20 their appropriateness for use.

21 And other guidances that might require  
22 them in order to deal with this very important issue

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1 about metabolites and different pharmacokinetics, et  
2 cetera, et cetera.

3 And I would just -- I wouldn't say  
4 caution, but I guess I would say plead for all of our  
5 sakes that things be done very slowly at this point  
6 until there is agreement between different parts of  
7 the agency so that in fact the right work can go on to  
8 address the needs as best as possible.

9 I am not sure at this point that it is  
10 possible to address all of the needs satisfactorily,  
11 but this story is not over yet.

12 DR. BUSH: Donna Bush. I would like to  
13 amplify a couple of comments that have come up here  
14 towards the end about looking at specimens, and  
15 looking at drugs and metabolites, and looking at  
16 spiked samples.

17 And one example that comes to my mind that  
18 I hear a great deal about in non-Federally regulated  
19 workplace drug testing, and the types of testing  
20 technology, whether it be laboratory based, or whether  
21 it be point-of-collection based.

22 And I will just pick a class of compounds

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1 here, and that is the benzodiazepines, and let's warp  
2 back a few years, and take a look at the old classics  
3 of the diazepam class, and then let's fast forward up  
4 30 years and took a look at the new benzos of the  
5 halcyon type.

6 And I have many puzzled colleagues  
7 repeatedly saying to me, well, you know, I did a benzo  
8 test, and I didn't detect this compound, and I'm like,  
9 well, you wouldn't. And then I lapse into  
10 pharmacokinetic talk.

11 But in the case of labeling, and again  
12 back to the basic analytical characteristics about an  
13 assay, and intended use, so much needs to be clear and  
14 understood by the parties developing the assay, as  
15 well as marketing it to individuals who need to know  
16 in hospital settings, and other settings, about such  
17 complex characteristics.

18 And one size does not fit all for many  
19 drug categories, and benzos is just one example.  
20 Thank you.

21 DR. KURT: As an afterthought -- Tom Kurt,  
22 and I would like to comment on the cross-reactivity.

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1 I did not notice anything said about cigarette smoking  
2 or cigarette smokers, which introduces not only  
3 nicotine, but aldehydes, and other chemicals into the  
4 blood. I can think of at least 400.

5 And I think that something should be  
6 determined that cigarette smokers are tested in the  
7 cross-reactivity.

8 And in addition there are a whole  
9 multitude of dietary supplements now on the market,  
10 such as St. John's Wort, in which the active  
11 ingredient is hypericum, in which perhaps some  
12 exploration should be sought as to whether it is  
13 cross-reactive to any of the drugs-of-abuse.

14 DR. KROLL: All right. Thank you. Let's  
15 put a question to -- and it is on page 5, and it deals  
16 with guidance, and it addresses five classes of drugs  
17 and what not.

18 So why don't we go around the panel, and  
19 we will start at the other end. We will start with  
20 Dr. Lasky.

21 DR. LASKY: I have no comments about this.  
22 Thanks.

1 MR. REYNOLDS: No comments at this time.

2 DR. BUSH: Donna Bush. I have more  
3 questions than I have comments on how to do this, and  
4 I am going to wait for somebody with a sage beginning  
5 point, and I promise I will come back to it. Thank  
6 you.

7 DR. EVERETT: James Everett. This is an  
8 interesting question, because from reviewing past  
9 devices, it brings to heart one of the biggest  
10 problems by the time the manufacturer gets here.

11 And the issue usually is that they have  
12 already developed a method for determining what the  
13 valid cutoffs are, and what the accuracy, as well as  
14 the many other variables are.

15 But the problem really seems to be that  
16 there was an earlier consultation with the  
17 biostatisticians for the FDA, and when they present  
18 the data, a lot of times the data has been changed in  
19 such a way that it appears as though the manufacturer  
20 still doesn't understand why the data was changed, and  
21 to determine whether it was valid, or whether the  
22 information they presented is not really valid at all.

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1           So that when you look at the information  
2           to decide whether this is something where I can say a  
3           negative is truly a negative, or is this something  
4           that is positive, and I can truly feel comfortable  
5           that it is positive.

6           The question really becomes when do you  
7           select the method for determining whether or not the  
8           valid cutoffs are truly valid, or if you are going to  
9           select other perimeters.

10          And these things are usually determined  
11          during study design. But many manufacturers appear as  
12          though they generate the data, and then they went back  
13          to find the mathematical test that will match their  
14          data, and that really creates lots of problems by the  
15          time that they get here.

16          So the question is who should select the  
17          method for determining a valid cutoff, and for  
18          determining the accuracy of the test. I still think  
19          that is a manufacturer's decision. But that decision  
20          should be in consultation with the FDA.

21          And a lot of times it just gets to be a  
22          real stickler for the members of the panel who truly

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1 understand what biostatisticians are about, and  
2 determining whether or not your results are valid,  
3 because in many cases it appears as though the results  
4 are not valid.

5 But then we approve with stipulations to  
6 try and make the information valid. So from my point  
7 of view, I think that that decision is still a  
8 manufacturers' one, but again it should be done in  
9 consultation with the FDA.

10 And I would like to ask Dr. Gutman whether  
11 or not -- or when do you encourage the manufacturer to  
12 consult FDA for selecting those appropriate  
13 statistical tests?

14 DR. GUTMAN: Well, we are trying to be  
15 more interactive. So we actually suggest -- and  
16 particularly if there are interesting outstanding  
17 issues about a particular product, we suggest that  
18 they come in early.

19 We are willing to meet with them when it  
20 is frankly just a business idea. We prefer to meet  
21 with companies when they actually have defined  
22 objectives and protocols.

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1 We are willing to do review of the  
2 protocols, including interactive review of the  
3 protocols. We prefer to review the protocols before  
4 the study has been started or completed, and we like  
5 to have guidance, because that allows us to have to  
6 meet less often, because the rules are sort of public  
7 before the game is started.

8 But we are very interactive, and so if  
9 somebody came through either with an old drug with new  
10 applications, or with a new drug, we would be  
11 interested in an early discussion about appropriate  
12 end points, design, and statistics.

13 DR. EVERETT: Okay. Well, that is  
14 basically my viewpoint on this issue.

15 DR. WILKINS: I'm Dr. Wilkins again. I am  
16 going to sort of take a simple view of looking at this  
17 question, and that is sort of what approach would you  
18 want to use for a drug that wasn't -- that doesn't  
19 belong to one of the -- as we referred to it, the NIDA  
20 five, if you want to call it that way.

21 And I think the model system that was  
22 specified on the previous slide, in terms of

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1 performance characteristics, seems a reasonable  
2 approach as a minimum criteria to shoot for. I think  
3 that is very reasonable.

4 Certainly when there are multiple  
5 metabolites present, then that becomes a complicating  
6 factor. But it seems as if the package insert  
7 labeling, and the intent of the product, is to perhaps  
8 identify a specific metabolic, and then define the  
9 cross-reactivity with a parent compound or what have  
10 you, that as long as it is clearly specified and  
11 defined in that insert what is being detected, and at  
12 what level, then I think the approach is valid, even  
13 when there are multiple metabolites present.

14 Anyway, I will see what everybody else  
15 thinks.

16 DR. KURT: Tom Kurt. I would like to  
17 comment on three areas. First, I think this is a  
18 subject of ongoing review, because, for example, the  
19 opiate level which was increased to 2,000 nanograms  
20 per ml of urine, and then the NIDA five, shows that  
21 that is a subject that is something that should be  
22 under a relative constant review or an ongoing nature.

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1           The second is that in the NIDA five we  
2           have two substances in which the metabolites are  
3           measured in THC, where you have carboxyl THC, and in  
4           cocaine, you have benzoylectnonine.

5           The FDA uses the term surrogate marker in  
6           the Center for Drugs for drugs that are metabolized,  
7           with those metabolites being surrogate markers of the  
8           drugs.

9           And I think it would be appropriate to use  
10          the term surrogate markers for drug abuse in this  
11          situation. The third is that there are substances  
12          that might be added to this list from time to time.  
13          For instance, MDMA, or metdioxymethamphetamine, or  
14          "Ecstasy" is now going into a resurgence, where that  
15          might possibly be added to the list, and that's not  
16          picked up under the methamphetamine or amphetamine  
17          testing.

18          So I think some kind of a situation where  
19          you could have a memorandum of understanding, or MOU,  
20          ongoing with SAMHSA on substances that might need to  
21          be added to the list based upon the current  
22          circumstances, such as MDMA, would be appropriate.

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1 DR. KROLL: Thank you. I am Dr. Kroll.  
2 Looking at this, I agree with the previous comments.  
3 I think if you are looking at other drugs besides this  
4 group, you have to make certain that in terms of  
5 accuracy that the methods compare with some other  
6 method, where they have a clear understanding of the  
7 metabolites involves, and the pharmacokinetics.

8 And that they can clearly establish many  
9 of the metabolites. Also, if there are a large number  
10 of metabolites, or even just a few, but they range in  
11 value from person to person, that a range of values  
12 are used for metabolites.

13 When you start looking at large classes of  
14 drugs, this actually makes it more difficult, because  
15 there are many different types of metabolites, and so  
16 they have to look at the different types of extremes  
17 in these cases, especially when answering the last  
18 part of the question, that if you pick out  
19 barbiturates, how would you pick out the cutoffs.

20 That again is really very dependent on its  
21 intended use, and what type of statement someone is  
22 trying to make, and I think that clearly has to be

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1 identified, in terms of probabilities and the outcomes  
2 of using a particular cutoff. Thank you.

3 DR. MANNO: Dr. Manno again. Like a  
4 previous panel member, I don't know where to start on  
5 this, but picking up and coming around the table to  
6 me, I would agree that the list of things on the  
7 performance of the test that we have discussed earlier  
8 -- precision, accuracy, et cetera -- seem to me to be  
9 appropriate for establishing valid cutoffs.

10 But there again we have to have an open  
11 door in establishing cutoffs so that they can be  
12 varied based on clinical experience, whether it is  
13 clinical experience in a true clinical arena, or if it  
14 is in the workplace, and what we are seeing coming out  
15 of some of the surveys that come out of SAMHSA.

16 On the second part, I think we should not  
17 make this too difficult to get the product to market  
18 so to speak when we are having to talk about detection  
19 of drugs and metabolites.

20 It has been my experience -- and I have  
21 been in the business since it started -- from a  
22 consumer standpoint in a laboratory that the companies

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1 that are serious about the business are very helpful  
2 to the consumer, in that once they will have some  
3 initial compounds, we will say, that have been checked  
4 for detection of particular things.

5 For example, again, the benzos. They will  
6 have a certain list that they have tested to start  
7 with. But as the laboratorians or the user gets into  
8 the continued use of the product, they will keep a  
9 very extensive list of products that have -- or drugs  
10 that have shown interferences or cross-reactivities.

11 And they have the help line as we call it  
12 in the lab, and they have been very -- I have had good  
13 luck with using help lines with some of the larger  
14 corporations at any rate.

15 And knowing at what concentration a  
16 product would interfere, another drug would interfere,  
17 or a metabolite might cross-react, that is not in the  
18 product insert.

19 So if we can keep those lines open with  
20 the sponsor of the product, that is very important.  
21 That is all I have at this point.

22 DR. LEWIS: Sherwood Lewis. Looking at

1 the question of what are appropriate methods for  
2 establishing valid cutoffs and assessing accuracy of  
3 these tests, and focusing simply on the question, I  
4 would say that if the appropriate methods are  
5 established for the SAMHSA five, then these should  
6 certainly be appropriate given that, yes, for  
7 barbiturates that you are going to find some  
8 distinction as to what metabolites, and the purpose to  
9 which you are putting the test.

10 But appropriate methods, I think, should  
11 in principle be the same, whether it is for the five  
12 previously discussed, or others that may come along,  
13 if I understand the question correctly.

14 DR. HENDERSON: Again, as a clinician, I  
15 don't have any comments on the laboratory tests. But  
16 certainly it seems to me that the methods for  
17 establishing cutoffs and accuracy would be very  
18 dependent on what the tests were being used for.

19 I would certainly echo one of the previous  
20 panel members in the importance -- and I think it was  
21 Dr. Kurt, of the importance of identifying the new  
22 substances that we may be testing for.

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1                   Certainly as a clinician, I have been  
2                   faced with women who have used "Ecstasy" and trying to  
3                   figure out how to test for that is very difficult, and  
4                   as we all know, if you read the paper, every other  
5                   week or every other month there are new agents out  
6                   there that people are using.

7                   So certainly the changes in what we are  
8                   testing for need to keep up to date with what is  
9                   happening, and to make it more relevant to do the  
10                  tests.

11                  DR. ROSENBLOOM: This is Dr. Rosenbloom.  
12                  I have nothing further to add. I agree very much with  
13                  Dr. Lewis' comments. And I know that there are at  
14                  least two people in the room who don't know what  
15                  SAMHSA stands for or maybe more. Does somebody care  
16                  to tell me?

17                  DR. BUSH: I will. My name is Donna Bush,  
18                  and I am from SAMHSA, and so I know what it means. It  
19                  is a five letter acronym for "Substance Abuse and  
20                  Mental Health Services Administration." Actually, it  
21                  is six letters. Since I have the microphone, may I  
22                  continue?

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1 DR. KROLL: Yes.

2 DR. BUSH: The FDA in the handout for the  
3 draft for -- not for implementation, but guidance for  
4 prescription drug use, that in that document, page 10,  
5 there is some special notes in there that the FDA put  
6 in there.

7 There is the rationale for the selection  
8 of particular cutoff when no SAMHSA cutoff is  
9 available should be described; support the cutoff  
10 selection, and must be based on sponsor studies and  
11 evaluation of scientific literature.

12 This really does put an awful lot of  
13 burden back on those who are looking to develop a  
14 product, but that burden may be very well placed, in  
15 that they need to know the literature, and they need  
16 to know the experiences of clinicians in many and  
17 varied fields, to be able to market, and to be able to  
18 develop and market a product that will be successful.

19 So they have a degree of monetary interest  
20 in this, and therefore, communication then with the  
21 FDA may be very important, because we may talk about  
22 benzodiazapines as a classic example of one size does

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1 not fit all.

2 Point-of-collection testing or immunoassay  
3 tests, liquid-based immunoassay tests, for that class  
4 of compounds, that is only one example, and the future  
5 is large in front of us. So the burden is heavy on  
6 those who are going to look to develop something  
7 applicable, again for what intended use.

8 And then again on that special notes, the  
9 fifth note down, "In all cases, cutoff concentrations  
10 should be clinically, as well as analytically, valid."  
11 And that springs immediately back into the first  
12 point, where you have to know what is going on with  
13 that particular drug.

14 How does someone set a cutoff for MDMA  
15 assays, one that was mentioned before. It is  
16 something that you wrestle with. It is not  
17 intuitively obvious. How do you look at  
18 benzodiazapines in a non-Federal workplace situation?

19 So I think it is a lot. There is no one  
20 easy answer for this, but I think that the special  
21 notes do contain very good direction for those who are  
22 interested in developing that product.

1                   And then you have got to go to the  
2 biostatisticians, and the rest of it, and back to FDA.  
3 Okay. Thank you. That's all.

4                   DR. KROLL: Thank you. Let me ask Dr.  
5 Gutman if he believes that we have adequately  
6 discussed this question.

7                   DR. GUTMAN: Yes, that's fine.

8                   DR. KROLL: Okay. Dr. Lasky has a  
9 comment.

10                  DR. LASKY: Yes. I just have one more  
11 comment, and I think I would just like to state that  
12 from a manufacturers' perspective that I agree  
13 particularly with drugs like this that there is a  
14 large burden on the manufacturer, and I also agree  
15 that much of that is where it belongs, where we are  
16 responsible for the products that we sell.

17                  The issue, I think, as Dr. Gutman  
18 mentioned before is when the negotiations actually go  
19 on. And some of the issues about the clinical  
20 cutoffs, particularly when there might be a new drug  
21 out on the street, and the metabolites and the  
22 pharmacologic activity, whether they are in fact

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1 active or inactive, may not be known.

2 So it may be that the test itself is used  
3 for determining the clinical studies. So it is really  
4 a chicken and egg sort of situation. So, we should  
5 not dismiss the fact that if the information is only  
6 analytical that that still might be very appropriate  
7 for the test to be available in commercial use.

8 And again it depends on what is stated on  
9 the label, and I think that is the key. And in a  
10 dynamic situation like drug abuse, and unfortunately  
11 too dynamic, there may be a bit of catch-up, in terms  
12 of updating labeling. It should not take too long.

13 But also what is in the literature I think  
14 is important, and I don't know if the panel is aware,  
15 but manufacturers also have a responsibility to  
16 monitor the literature.

17 And if there are issues about the  
18 effectiveness of the device of all types, then it is  
19 up to the manufacturer and the manufacturer has an  
20 obligation to follow through on that, and in fact  
21 investigate.

22 So there is a bit of cycloid issues here.

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1 Once the device is on the market, it is not left as an  
2 orphan. There is an obligation to continuously  
3 monitor how it is used and whether or not the  
4 indications are still appropriate.

5 DR. KROLL: Thank you. Any other comments  
6 from the panel?

7 (No audible response.)

8 DR. KROLL: Okay. Well, given the hour,  
9 we will now break for lunch.

10 (Whereupon, the Panel recessed for lunch  
11 at 12:03 p.m.)

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## A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:13 p.m.)

DR. KROLL: Hello. If the panel members would kindly take their seats, we can start the afternoon session, please. And this afternoon we will be discussing the topic related to over-the-counter guidance.

And to begin that discussion will be the presentation by Dr. Jean Cooper.

DR. COOPER: It is my pleasure to have the opportunity this afternoon to introduce our revised over-the-counter drugs-of-abuse guidance document. Revising this guidance was intended to, one, clarify the importance of confirming test results for drugs-of-abuse tests marketed to consumers.

Two, describe the consumer study needed to characterize performance around the cutoff. Three, establish the minimum threshold for performance for OTC products; and, four, expand the consumer survey in order to determine if the labeling communicated the limitations of the screening result. Let's review some background information.

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1           This morning we discussed study designs to  
2 characterize the performance of tests used by medical  
3 professionals. The study results are then put into  
4 the product's package insert to better assist the  
5 professional in understanding test performance and  
6 limitations.

7           The OTC guidance then describes the additional  
8 study and labeling needed before drugs-of-abuse test  
9 kits are marketed over-the-counter. The additional  
10 consumer studies are used to characterize the  
11 performance of the device in the hands of the  
12 consumers.

13           The studies are designed to evaluate  
14 consumer ability to read the package insert, perform  
15 the test correctly, and properly interpret the  
16 results. Labeling for OTC products discusses the need  
17 to confirm test results.

18           Let's discuss confirmation testing.  
19 Immunoassay based screening tests are presumptive  
20 tests. Positive tests are intended to be confirmed by  
21 another analytical method, such as Gas Chromatography  
22 and Mass Spectrometry, in order to protect individuals

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1 against false positive results.

2 The revised guidance recommends that the  
3 labeling for OTC products include a statement under  
4 the warning and precaution section. The statement  
5 reads, "This device is only the first step in a two-  
6 step process to look for the presence of drugs-of-  
7 abuse. If your result is uncertain, you must send the  
8 results of the urine sample to the laboratory to find  
9 out whether there are drugs in the sample. The  
10 laboratory test is more accurate than the home test  
11 and there is no extra cost for the laboratory test."

12 We would like your thoughts on this label  
13 statement. In support of this statement, preaddressed  
14 shipping materials for sending samples to the  
15 laboratory need to be included in the screening test  
16 kit.

17 The intent of FDA is to make the cost of  
18 confirmation testing part of the cost of the device,  
19 to increase the incentive for consumers to confirm  
20 presumptive positives. In the absence of  
21 confirmation, linking preliminary screening to true  
22 positive results, requires knowing the clinical

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1 performance of the OTC devices.

2 Linking analytical performance to the  
3 impact on clinical performance, however, is difficult  
4 to establish. Although study designs attempt to  
5 characterize performance of the device at  
6 concentrations that are challenging to the cutoff  
7 concentrations of the assay, it is not known how many  
8 samples in an OTC environment are at these  
9 concentrations.

10 It is also difficult to capture all of the  
11 physiological conditions and external interfering  
12 substances, such as medications, that could impact  
13 results. Performance around the cutoff varies greatly  
14 from one device to the next.

15 Additionally, the lot-to-lot variability  
16 in visually read unitized devices is sometimes  
17 difficult to control. There are many variables that  
18 can have an impact on false positives, as well as  
19 false negative results in the OTC environment.

20 I would like to provide you with the  
21 information we do know. Analytical performance of the  
22 devices is variable among manufacturers. In

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1 evaluating the analysis of spiked samples, we have  
2 observed that with some devices the concentration of  
3 the target acolyte must drop to 75 percent below the  
4 claimed cutoff concentration before all results are  
5 negative.,

6 In other devices, we have seen that the  
7 concentration of the target acolyte must be 25 to 50  
8 percent above the claimed cutoff concentration before  
9 all results are positive.

10 Our understanding of clinical performance  
11 of drugs-of-abuse assays is limited to information on  
12 the performance of wet chemistry assays used in  
13 reference laboratories.

14 The performance of wet chemistry automated  
15 assays undoubtedly is superior to that of unitized  
16 visually read devices. It is also unclear how the  
17 sample population evaluated in reference laboratories,  
18 predominantly work place samples and drugs of abuse  
19 clinics, relates to the samples that would originate  
20 from a consumer environment.

21 The following anecdotal data reflects  
22 results from samples originating predominantly from

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1 workplace environments. What this table reflects is  
2 that with cocaine and marijuana the screening test and  
3 the confirmation test typically relate fairly closely  
4 to each other.

5 With the other drugs-of-abuse, generally  
6 this relationship is not so strong. This data  
7 reflects the performance of wet chemistry automated  
8 assays under optimal conditions.

9 The agency believes that devices used by  
10 consumers should be as safe and reliable as possible.  
11 Sponsors of applications for OTC tests currently  
12 include the cost of confirmation testing in the cost  
13 of the initial screening test.

14 This approach removes cost barriers  
15 associated with confirmation testing, thereby  
16 increasing the chance that consumers will confirm  
17 their screening results.

18 Confirmation testing is expected to  
19 minimize the chance of individuals being falsely  
20 accused of using illegal drugs. Others, however,  
21 argue that including the cost of confirmation in the  
22 initial test cost does not compel many consumers to

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1 send the samples to the lab, and that it only adds to  
2 consumers' cost, and may therefore be preventing  
3 access to drug testing by some consumers.

4 Our intent is to balance the benefits of  
5 ensuring more accurate results to the consumer, versus  
6 the possible effects of imposing additional costs on  
7 the original purchase price. We are receptive to  
8 other approaches to establishing a responsible risk-  
9 to-benefit ratio.

10 Let's discuss the consumer study. In  
11 addition, needing confirmation testing, OTC  
12 applications include a study to determine if consumers  
13 can follow the label directions and interpret the test  
14 results.

15 The consumer study is designed to address  
16 accuracy and precision performed by consumers. A  
17 survey and labeling assessment is also given to assess  
18 label readability and to evaluate consumer  
19 understanding of results.

20 This study was described in the original  
21 guidance. The revised guidance clarifies the  
22 information needed to characterize performance around

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1 the cutoff, establishes the minimum threshold for  
2 performance for OTC products, and expands the consumer  
3 survey in order to determine if the labeling  
4 communicates the limitations of the screening result.

5 The guidance was revised to clarify the  
6 description of the consumer study design. Please  
7 comment on this design. The consumer study is to be  
8 conducted at three sites.

9 At least 200 samples per drug are tested  
10 by 200 consumers. Samples are drug-free, spiked with  
11 known amounts of drugs. Multiple drugs may be spiked  
12 in a sample to reduce the number of samples.

13 The concentration of drug in the samples  
14 is confirmed by GC/MS. The range of drug  
15 concentrations is chosen to challenge each drug cutoff  
16 as well as the high and low clinically relevant  
17 extremes of drug concentration.

18 Specifically, the testing is divided into  
19 the following format; 20 samples at a low negative  
20 concentration; and 30 samples at 50 percent above the  
21 cutoff; 50 samples at 25 percent above the cutoff; 50  
22 samples at 25 percent below the cutoff; 30 samples at

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1 50 percent below, and 20 samples at a high positive  
2 concentration.

3 Study participants are given on  
4 instruction beyond the package insert. Study  
5 participant demographics are provided in the  
6 application to demonstrate whether the participants  
7 reflect the population most likely to use the device.

8 The challenge at 25 percent above and  
9 below the cutoff is intended to determine how the  
10 SAMHSA cutoff compares with the cutoff of the product.  
11 This information also provides the reviewer with a  
12 comparison between the OTC use and professional use  
13 under the ideal analytical conditions.

14 The challenge at 50 percent above and  
15 below the cutoff is intended to determine whether a  
16 test gives too many false positives to be marketed as  
17 an OTC product. When multiple consumer study  
18 participants interpret a sample concentration as  
19 presumptively positive at 50 percent below the cutoff,  
20 it is not clear how close to background levels the  
21 test will read positive.

22 Conversely, the challenge at 50 percent

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1 above the cutoff determines if the test is likely to  
2 miss true positive samples. Correcting false readings  
3 at 50 percent above and below the cutoff might include  
4 fine tuning consumer labeling to improve interpreting  
5 test results or adjusting product release criteria to  
6 reduce misinterpreting the presence or absence of  
7 drugs.

8 Evaluating the cutoff at these drug  
9 concentrations is a revision and we would like  
10 feedback. The guidance indicates that the consumer  
11 study results are not included in the label.

12 This policy was established because of the  
13 difficulties in relaying technical information to  
14 consumers, the lack of clarity about how analytical  
15 performance relates to the device use in the overall  
16 population; and the need to encourage confirmation  
17 testing screen test positive results. We would like  
18 to hear your thoughts on this policy.

19 Let's discuss over-the-counter claims. A  
20 drugs-of-abuse test is considered over-the-counter  
21 when it is intended to be used in the home, workplace  
22 insurance, or sports settings.

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1 Issues related to consumer ability to use  
2 a test and test quality are similar in all these  
3 setting, including concerns about sample integrity and  
4 test accuracy. The need to provide assurance of test  
5 accuracy and reliability applies equally in all of  
6 these areas.

7 FDA will continue to exercise its  
8 enforcement discretion with respect to the use of  
9 these products in the law enforcement setting, because  
10 there are protections to ensure sample integrity and  
11 test accuracy that are not generally available in the  
12 home, workplace, insurance, or sports settings.

13 The additional protections include the use  
14 of rules of evidence in judicial proceedings, and the  
15 representation of the person tested through the  
16 judicial process.

17 Given that OTC claims include settings  
18 other than house use, it is important to note that the  
19 drugs-of-abuse tests are intended to detect the  
20 presence of drugs-of-abuse, or their metabolites in  
21 samples, but not whether a person is impaired.

22 Let's now go to the questions. To

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1 maximize the likelihood that confirmation testing will  
2 be performed on presumptive positive results, the FDA  
3 has been requesting that confirmatory testing be a  
4 mandatory component in the designing of the screening  
5 tests.

6 The next question, please. Are the  
7 studies and labeling guidelines as outlined in the  
8 guidances appropriate for home, workplace, insurance,  
9 sports, and other OTC settings.

10 Consider that the intended use of drugs-  
11 of-abuse tests, generally, are to indicate the  
12 presence of a drug, rather than the impairment of an  
13 individual.

14 Question 3: The FDA is suggesting that  
15 OTC devices render negligible performance error with  
16 spiked samples at concentrations of plus 50 percent  
17 and minus 50 percent of the cutoff concentration.

18 Is this reasonable. If not, not  
19 alternative performance criteria would be appropriate?

20 Next question.

21 The FDA does not encourage inclusion of  
22 performance data in OTC labeling. Do you feel such

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1 information should be included, and if so, what type  
2 of studies should be done to characterize performance  
3 well enough so that it would be meaningful to the  
4 consumer? And how should performance be relayed to  
5 consumers in the labeling?

6 The next question. Is the study design  
7 described in the guidance appropriate for  
8 demonstrating performance of the device in the hands  
9 of the lay user? Please consider sample size, use of  
10 spiked samples for consumer studies, concentration  
11 range and distribution of the samples, and size of  
12 consumer study.

13 Next. FDA is suggesting that sponsors  
14 conduct only the consumer studies described in the OTC  
15 document, when the device has already obtained  
16 prescription clearance. Are there any other studies  
17 warranted?

18 Next. Should only those devices with  
19 SAMHSA cutoffs be eligible to be cleared for OTC use?

20 Next. Visually read devices frequently  
21 render positive results well below the claimed cutoff  
22 of the assay. For instance, some sponsors might claim

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1 a cutoff of 1000 nanograms per Ml, but their test  
2 renders all positive results at 750 or 500 nanograms  
3 per Ml.

4 Should there be certain performance  
5 requirements to support a claimed cutoff  
6 concentration?

7 Now I would like to talk more generally  
8 about substance abuse. Over-the-counter alcohol tests  
9 and drug abuse tests are similar because of concerns  
10 about sample integrity, reliability, and test  
11 accuracy.

12 Confirming test results obtained in the  
13 home, workplace, insurance, or sports settings, and  
14 consumer ability to follow label instructions and  
15 interpret test results.

16 Over-the-counter alcohol tests and drugs-  
17 of-abuse tests are different because intoxication is  
18 determined rather than substance exposure. Confirming  
19 results from a test used in a bar or at a party is not  
20 practical.

21 Samples used in alcohol screening tests  
22 are generally replaced, often with another matrix, to

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1 confirm a result.

2 Time lapses between testing and  
3 confirmation may affect interpretation. The FDA  
4 currently regulates alcohol tests intended for medical  
5 use. Tests to determine chronic abuse are considered  
6 medical use.

7 Since 1992, the Department of  
8 Transportation has regulated screening tests in  
9 workplaces related to transportation, such as  
10 aviation, motor carrier, rail and mass transit  
11 industries.

12 DOT tests all of the devices that are  
13 submitted to them, and those that pass their  
14 requirements are placed in an approved device list.  
15 Jobs that are under the jurisdiction of the DOT  
16 require testing of employees that perform critical  
17 jobs to be randomly tested for acute alcohol use.

18 The tests must be performed with devices  
19 from the approved list, and they must be carried out  
20 by DOT trained personnel. The specifications for the  
21 devices are set based on on the specifications for  
22 breath analyzers and are as follows.

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1           At a cutoff of 0.02 percent; with  
2 precision /accuracy and blank reading tests being  
3 performed, and to pass this test as described the  
4 device must not have any positive readings at zero,  
5 only one false positive at 0.08, and only one false  
6 negative at 0.032.

7           The above test must be performed under the  
8 following light conditions. Under fluorescent lights,  
9 incandescent lights, mercury vapor, sodium vapor, and  
10 daylight. In total, 300 assays are performed,  
11 resulting in 3000 independent readings.

12           There is a cigarette smoke interference  
13 test that is done, and it is described in this line.  
14 All results must be negative for this test. There is  
15 a high and low ambient temperature tests. To pass,  
16 the device must have only one false positive and only  
17 one false negative under these test conditions.

18           There is a vibration test, and to pass the  
19 device must have only one false positive, and only one  
20 false negative. Based on the number of tests  
21 performed, which is 40, the concentration at which the  
22 device is expected to show no positive results within

1 a 95 percent confidence, is 0.008.

2 Similarly, the concentration at which the  
3 device is expected to show no negative results with 95  
4 percent confidence is 0.032. Home use tests, tests  
5 sold in bars, tests used in workplaces, tests  
6 performed for insurance use, and tests in sports  
7 settings, are not currently regulated.

8 Now, we will go to questions. FDA is  
9 proposing to include alcohol testing in the same  
10 category as other tests for substance abuse. Are the  
11 same types of studies appropriate for alcohol tests?  
12 Should other approaches, such as the one used by the  
13 Department of Transportation, be considered?

14 The second question. In what settings is  
15 confirmatory testing for OTC alcohol tests  
16 appropriate: home, workplace, insurance, sports,  
17 other?

18 What matrices and what time span between  
19 collection of the original sample and collection of  
20 the sample for confirmation would be appropriate?  
21 Thank you.

22 DR. KROLL: Thank you. Now we come to the

1 part in the program where we have the open public  
2 hearing, and these are people who have previously  
3 submitted their name and contacted the executive  
4 secretary.

5 And they will address the panel and  
6 present relevant information to the agenda. And I  
7 would like to ask that each speaker as they come up to  
8 state their name, and whether or not they have any  
9 financial involvement with the manufacturer of the  
10 product being discussed or with their competitors.

11 And the first person on the list is David  
12 Evans. And also each person has about 7 or 8 minutes.

13 MR. EVANS: Good afternoon. My name is  
14 David Evans, and I am the executive director of the  
15 National On-Site Testing Association. We are an  
16 industry consensus organization composed of the  
17 manufacturers, users and distributors of on-site drug  
18 and alcohol tests.

19 I am also an attorney in private practice,  
20 and I provide legal advice to corporations that do  
21 drug testing, and also to the manufacturers of drug  
22 and alcohol tests.

1 My wife and I are remodeling our house,  
2 and we live on a farm, and we have a pool in the back  
3 yard and pastures. And we are putting a new room on  
4 the back of the house, and the builder was there and  
5 asked me what I wanted for windows in the back of the  
6 house.

7 And I wanted a big picture window so that  
8 I could see the pool, and see the pastures, and see  
9 everything that is going on there. So I told him,  
10 well, I want a big picture window there.

11 So then the wife came home, and it turned  
12 out that she doesn't want a big picture window. She  
13 wants windows that are with small panes in the back.  
14 So I made my arguments to her, and then I heard what  
15 she had to say, and I said yes, dear, and we moved on.

16 Now, what was my problem? My problem was  
17 lack of jurisdiction, and I would like to bring this  
18 to your attention. I think I am in the right place.  
19 This is an advisory panel of the Medical Devices  
20 Advisory Panel, and it seems to me that the  
21 jurisdiction that you have is over medical devices as  
22 they are defined in the FDA regulations.

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1                   And the medical devices are those that  
2 deal with the diagnosis of disease or other conditions  
3 in order to cure, mitigate, treat, or prevent disease  
4 or its sequelae. So that is my humble opinion of your  
5 jurisdiction.

6                   The case law on this -- and also the  
7 regulations say -- that it is the intended use of the  
8 device is what matters. And my dad was a  
9 psychiatrist, and when I was a kid, I used to go to  
10 his office and get his tongue depressors.

11                   Now, if I took a tongue depressor and put  
12 it in the freezer with some orange juice and made a  
13 popsickle out of it, that is not a medical use. If my  
14 dad used it to treat his patients, then it is a  
15 medical use.

16                   So a tongue depressor could be considered  
17 a medical device, but not as I intended to use it, as  
18 I did from time to time. I also used to make little  
19 houses out of them.

20                   So when looking at your jurisdiction under  
21 these laws, you need to look at the intended use.  
22 Now, you may have an argument if a drug test is used

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1 to diagnose a medical condition.

2           Somebody comes into an emergency room, and  
3 they appear to be in an overdose situation, and you  
4 use a test. Even there I would assert that maybe you  
5 wouldn't want to spend your time on this issue,  
6 because hospital emergency rooms, doctor's offices,  
7 are already regulating.

8           CLIA takes care of a lot of that, and even  
9 physicians' offices in a lot of states are regulated.  
10 A lot of States have clinical laboratory laws. My  
11 good friend, Mr. Stanley, from Pennsylvania, he has a  
12 very fine clinical laboratory law.

13           And New Jersey does, and Florida does, and  
14 California. And by the way, the California laboratory  
15 office has determined that if you use an on-site test  
16 for a workplace purpose, they have no jurisdiction.

17           Pennsylvania, also, if you use an on-site  
18 test for a purely workplace purpose -- for example,  
19 whether or not to hire somebody or not, they don't  
20 have jurisdiction. If you are using it to provide  
21 treatment, then they claim that they do have  
22 jurisdiction.

1           So that I think lays out the  
2 jurisdictional issue. Now, I am just going to focus  
3 on the workplace testing, on-site workplace testing,  
4 and let's look at the reasons that the employers have  
5 given in court for having drug testing programs in the  
6 workplace, and let's see if they have anything to do  
7 with medical diagnosis or treatment.

8           And I have researched all of these, and it  
9 is in my book, and you can read them. The case law  
10 cites are in my book. To promote workplace  
11 efficiency, and to ensure the integrity of employees  
12 by prohibiting off-duty or on-duty conduct.

13           Promote public confidence in the safety or  
14 integrity of a particular job. Prevention of theft,  
15 and prevention of blackmail. That was a case in the  
16 National Treasury Employees Union versus Barrat. They  
17 were Treasury Agents, and that's why they wanted to do  
18 drug testing.

19           Prevent embarrassment to the employer. To  
20 promote a drug free society, and to gather facts about  
21 employee drug use and on company operations. Now,  
22 none of those have to do with medical diagnosis or to

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1 provide as the regulation says to cure, mitigate,  
2 treat, or prevent disease.

3 Now, what about the use of an on-site test  
4 for other purposes? Certainly for law enforcement  
5 purposes, I think you have already exempted yourselves  
6 out of that one, and I believe there is even a  
7 regulation or something to that effect.

8 Similarly, if an employer wants to use on-  
9 site testing or drug testing in general to ensure  
10 compliance with the workplace policy, the drug free  
11 workplace policy, I don't think you have jurisdiction,  
12 and the same thing with schools.

13 My daughter goes to Hunter and Central  
14 Regional High School, in Flemington, New Jersey, and  
15 they have a drug testing program for the students.  
16 The students are subject to discipline if they come to  
17 school under the influence.

18 And they are given a drug test, and the  
19 drug test is used as evidence for disciplinary  
20 purposes, and to ensure compliance of school rules.  
21 Again, there I don't think you would have  
22 jurisdiction.

1           The same thing with athletics; to  
2 determine whether or not somebody can participate in  
3 athletics, and not whether they get treatment, but to  
4 determine whether they can participate in athletics or  
5 not.

6           And these are really conduct issues, and  
7 compliance issues, and not health issues, okay? And  
8 also the Courts that have looked at this issue have  
9 said that if you declare that an on-site test or drug  
10 testing in employment are medical examinations, you  
11 are going to have direct conflict with Congress on the  
12 Americans With Disabilities Act.

13           Now, the reason that Congress exempted  
14 testing for illegal use of drugs is because they did  
15 not want drug addicts who are under the influence at  
16 work, and because of a drug test to be able to claim  
17 that they are subject to protection under the  
18 disability discrimination laws.

19           So this is going to cause a conflict with  
20 the ADA. Congress has spoken on this issue, and a  
21 recent Supreme Court case that the FDA lost trying to  
22 regulate cigarettes, the Supreme Court said that you

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1 must look at the intent of Congress before the FDA can  
2 take an action.

3 And you also have to look to see if there  
4 is any other existing regulations that would provide  
5 protections before you can take action or exert your  
6 authority, no matter how good the cause.

7 And I believe that you are all people of  
8 good faith, and I have heard nothing here other than  
9 that you want to protect people, and you want to do  
10 the right thing, and you want to make sure that these  
11 tests are accurate.

12 We also share those goals, but again it is  
13 a question of the jurisdiction. We believe that  
14 having to impose OTC requirements on all these uses  
15 for on-site tests will be extremely burdensome on our  
16 industry, and it will be extremely burdensome on  
17 employers, and it will be burdensome on athletic  
18 events, and insurance companies, and law enforcement  
19 if that goes down.

20 So that is the reason that we are opposed  
21 to it. I would also urge you to look at the  
22 protections that are already in place. Multiple

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1 States have employment drug testing laws. And 7 to 12  
2 million people are now going to be regulated under the  
3 SAMHSA regulations.

4 They have done a very fine job, and they  
5 are already permitting on-site testing, at least in  
6 the last draft that we saw, and they have a final  
7 draft to go through.

8 And what they are doing is that they are  
9 putting their trust in the manufacturers, and saying  
10 the manufacturers will train the users. This is a  
11 model with the Federal Department of Transportation  
12 that it has used for several years, and it has been  
13 successful, and we have not had any real problems.  
14 Thank you very much.

15 DR. KROLL: Thank you. Our next speaker  
16 is Bob Aromando.

17 MR. AROMANDO: Thank you very much. My  
18 name is Bob Aromando, and I am an independent industry  
19 consultant, and I do some consulting for some of the  
20 special interest parties that would be adversely  
21 affected should these regulations become a reality.  
22 So I do make that statement quite freely up front.

1                   So I would like to thank everybody here  
2 for this opportunity to address this esteemed panel on  
3 the topic of the over-the-counter screening tests for  
4 drugs-of-abuse.

5                   Initially when I heard about this meeting,  
6 I was prepared to testify on the issues surrounding  
7 accuracy, reliability, safety, and effectiveness to  
8 this panel.

9                   However, I was very surprised to learn  
10 that the OTC draft guidance document has the potential  
11 to implement FDA oversight to the workplace,  
12 insurance, and sports drug testing markets, well  
13 outside and beyond any realm of medical diagnostic  
14 assessment, and therefore outside the oversight of the  
15 FDA when you look at the markets that we just  
16 mentioned utilizing an on-site drug test.

17                   Let's remind the members of this advisory  
18 panel and the audience here today that the mission of  
19 the FDA according to the FDA Modernization Act of  
20 1997, and that is posted on the website, is to  
21 promptly and efficiently review clinical research,  
22 protect the public from ensuring that foods are safe,

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1 and ensure reasonable safety and effectiveness of  
2 devices intended for human use.

3 And according to the FDA growing  
4 responsibilities for the year 2000 and beyond, the  
5 FDA, in quotes, "review or scrutinize products that  
6 are designed to treat human conditions or diseases."

7 Nowhere in there is it to be interpreted  
8 or stated that the FDA must now render oversight to  
9 corporate hiring practices and business management,  
10 criteria that effects inclusion and exclusion of  
11 insurance policy applicants, and criteria for  
12 participation in structured sports.

13 Absolutely nowhere can it be even implied  
14 that the FDA has any authority over there not  
15 medically related areas. So why aren't were here  
16 today discussing FDA's possibility to regulate drug  
17 testing in the workplace, insurance, and sports  
18 markets.

19 My testimony here today contains  
20 compelling arguments and justifications to modify  
21 and/or eliminate completely major components of the  
22 over-the-counter draft guidance for pre-market

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1 notifications in order to continue to permit the  
2 commercial sale of on-site drug tests, by the way,  
3 which have already been cleared by the FDA for  
4 professional use to the workplace, insurance, and  
5 sports testing markets.

6 The Food and Drug Administration is making  
7 two stretch assumptions relative to the OTC user of a  
8 drug test. One, the FDA assumes that concerns related  
9 to OTC use of a drug test are similar in workplace,  
10 insurance, and sports settings.

11 And, two, the FDA assumes that there  
12 should be consistency in its regulation, if any, of  
13 drugs-of-abuse screening tests used in the home,  
14 workplace, insurance, and sports testing settings.

15 Panel Members, let me assure you that  
16 under no conditions whatsoever are the concerns  
17 similar in these markets. As an example, in the  
18 workplace setting, a drug test is used exclusively to  
19 assess compliance to a corporate drug-free workplace  
20 program.

21 It is not used for medical treatment  
22 purposes or disease management, or diagnosis of

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1 disease. Corporate entities and businesses in general  
2 utilizing drug testing simply do so to ensure they  
3 recruit and hire only those candidates that are drug  
4 free, which is very consistent with any drug free  
5 workplace program.

6 In fact, the U.S. Government implemented  
7 such a drug-free workplace program in the late 1980s  
8 under then President Reagan, and that program is still  
9 in existence today, and has absolutely nothing to do  
10 with the diagnosing of disease, nor the management and  
11 treatment of disease.

12 It is simply a program that drug test  
13 eligible employee candidates intended for hire and  
14 nothing more. In an insurance setting, a drug test is  
15 also simply a means by which an underwriter excludes  
16 or includes an individual from subscribing to some  
17 form of insurance policy.

18 In fact, the Supreme Court of the State of  
19 New York has previously ruled overwhelmingly that  
20 insurance type testing is not considered a medical  
21 test for diagnostic purposes, and as such would be  
22 exempt from the New York State laboratory statute.

1 That is case law.

2 In a sports setting, again we have a  
3 situation whereby as an example the NCAA will drug  
4 test athletes to assess compliance and/or drug use  
5 status to determine whether or not a policy has been  
6 violated and nothing more.

7 As another example, and I mention back to  
8 David Evans' Huntering Central High School in New  
9 Jersey, implemented on-site random drug-testing of  
10 student athletes simply to assess compliance to the  
11 school's anti-drug policy and nothing more.

12 Now in an OTC or consumer setting, you are  
13 likely to have a parent purchase a drug test because  
14 they suspect that their child may be using drugs. As  
15 a parent myself, with two children, this would allow  
16 me to get my children into treatment faster, with the  
17 intent of a more effective rehabilitation outcome.

18 Here, I grant you, you have oversight.  
19 The use of a drug test in an over-the-counter setting  
20 has clear medical related concerns, and as such should  
21 be within the oversight of the FDA.

22 The use of a drug test in workplace,

1 insurance, and sports, carries no true diagnostic  
2 implications whatsoever. When performed in the  
3 management of probation, parole, prison, drug and  
4 alcohol rehabilitation, compliance to school policies,  
5 clearance for a life insurance policy, or management  
6 of workplace policies, drug abuse screening only  
7 provides detection of drug or alcohol use.

8 It does not assess disease, immediate  
9 impairment, or other health related diagnosis  
10 requiring medical judgment or treatment. Drug abuse  
11 testing in these situations is also qualitatively  
12 different from testing for purposes of treatment or  
13 diagnosis.

14 This is because the individual being  
15 tested is fully aware of what the outcome of the test  
16 should be. The principles of diagnosis are then  
17 irrelevant for this type of testing. As such, the FDA  
18 must defer oversight of workplace, insurance, and  
19 sports testing settings.

20 In the past, an attempt to regulate  
21 workplace drug testing under CLIA '99 met with  
22 immediate objections, and ultimately was exempted and

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1 placed in moratorium by then Secretary Sullivan.

2 Thus, in permitting this exemption, HCFA  
3 recognized the need for testing, that has as its  
4 purpose the uncovering of behavior that the U.S.  
5 Congress and every State Legislature recognizes to be  
6 sufficiently dangerous to society and its members, to  
7 warrant such conduct being deemed illegal.

8 The purpose of drug abuse testing in the  
9 workplace is to identify behavior that unquestionably  
10 is illegal and clearly constitutes a danger to the  
11 workforce collectively and its individual members.

12 Furthermore, the FDA cannot assume a role  
13 of selective oversight relative to the workplace  
14 setting simply because the test format in question is  
15 that of a point-of-care platform and not lab based.

16 Currently, a number of drug testing  
17 reference labs in this country running millions of  
18 drug tests utilize generic home-brew assays made from  
19 FDA clear products, and absolutely no oversight is  
20 enforced or even considered.

21 To even consider oversight of an on-site  
22 point-of-care drug test in a workplace setting, while

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1 completely ignoring the practice of diluting drug  
2 testing re-agents, is blatant prejudice and bias in  
3 favor of lab-based testing.

4 This would be viewed clearly as a means to  
5 position manufacturers of point-of-care drug tests at  
6 a competitive disadvantage. In conclusion, the FDA  
7 must and should limit its oversight authority  
8 specifically in those areas where a drug test is  
9 utilized for diagnosis of disease, for treatment  
10 and/or cure, and in those situations where medical  
11 treatment is required.

12 Within the confines of workplace,  
13 insurance, and sports settings, that only utilize a  
14 drug test to assess compliance to policy, the FDA is  
15 clearly outside the perimeters of its legislative  
16 charge.

17 I would like to thank the panel for this  
18 opportunity to voice my concerns, and I hope that the  
19 messages that I have provided in this forum allow for  
20 an informed decision to be made. Thank you.

21 DR. KROLL: Thank you. Our next speaker  
22 is LuAnn Ochs.

1 MS. OCHS: I'm LuAnn Ochs, and I am with  
2 Roche Diagnostics Corporation, and I am a regulatory  
3 manager there. I am a scientist and not an attorney,  
4 and so I am going to leave the legal issues to the  
5 attorneys, and take a different vain here and address  
6 the guidance document itself.

7 First of all, I would like to compliment  
8 the FDA for continuing to produce guidance documents  
9 and for promoting good guidance practices. As a  
10 member of industry, we are very happy to have guidance  
11 documents, and they allow us to participate in FDA's  
12 new paradigm for product approval, the abbreviated  
13 510(k).

14 In case you are not aware, manufacturers  
15 are now able to achieve 510(k) clearances through  
16 certification of conformity to recognized standards,  
17 or FDA's published guidance documents.

18 This abbreviated 510(k) program brings  
19 much needed efficiencies to the 510(k) process,  
20 benefiting both the FDA and industry. Because of  
21 these mutual benefits, we appreciate the opportunity  
22 to work with the agency in the development of

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1 guidance.

2           Regarding the specific guidance for ODC  
3 drug products, with only a few minor comments that we  
4 will send in, we agree that this guidance is very good  
5 for obtaining clearances for home use drugs-of-abuse  
6 testing products.

7           Parts of this guidance may also be  
8 appropriately applicable to the other testing venues  
9 as well; workplace testing, insurance, testing, and  
10 sports settings testings.

11           If the attorneys are able to substantiate  
12 that DATs in these settings are indeed subject to FDA  
13 regulation, then Roche would like to offer these  
14 comments on the guidance document.

15           The guidance document should clearly split  
16 apart the regulatory requirements for home testing,  
17 from workplace, insurance, and sports settings. There  
18 are some clear differences in the needs of home users,  
19 versus the other testing settings.

20           Certainly there are labeling differences  
21 between these settings. All users need to know how  
22 to perform the tests and how to interpret the results,

1 and If the result is indeterminate, then they must be  
2 instructed in the meaning of that result, and the need  
3 for a more accurate confirmatory test.

4 But then what? For example, home users  
5 need additional instruction and information referring  
6 them to their health care professionals for  
7 appropriate counseling and/or treatment.

8 Let's look at the requirement for  
9 confirmatory testing. Obviously, this testing is  
10 needed. We manufacturers agree that the accuracy  
11 around the cutoff needs to be improved.

12 Perhaps new technologies will some day  
13 reduce the rates of cross-reactivities and  
14 interferences. And perhaps then we can achieve Dr.  
15 Kroll's requested 99.99 percent accuracy.

16 Cutoff levels are set to identify the  
17 drug, while avoiding cross-reactivities. We  
18 understand that Dr. Cooper wants to protect innocent  
19 people from being labeled as drug users. That  
20 protection mechanism is already in place.

21 The confirmation testing already offers  
22 that protection. Also, bear this in mind. There are

1 no legal levels for drugs-of-abuse. Ethanol testing  
2 was mentioned this morning.

3 Unlike ethanol, where a level of  
4 impairment has been determined, no level of cocaine,  
5 for example, is legal. Presumptive positive results  
6 are due to either the presence of the drug or the  
7 presence of an interference.

8 Interferences can and will produce false  
9 results no matter what the cutoff. That's why these  
10 tests must be confirmed. However, there is no such  
11 thing as a false positive result when the drug is  
12 present.

13 It is not okay to have a drug present at  
14 a level below the cutoff. It is still illegal. Yes,  
15 we have to protect people from being labeled positive  
16 when no drug is present. But we do not have to  
17 protect the real drug abusers. We must identify them.

18 This is the inherent difference between  
19 these tests and diagnostic tests. These people know  
20 that they have taken the drug, and we are trying to  
21 identify that drug's presence. Please remember that  
22 confirmation testing is already required by agencies

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1 that oversee Federal workplace drug testing.

2 It is mandated by many States, and it is  
3 good practice for everyone else who does this kind of  
4 testing to avoid litigation. The guidance document  
5 requires that manufacturers establish a mechanism for  
6 lay users to obtain confirmatory tests.

7 While we agree that this is needed, we are  
8 concerned that in practice that it may be difficult  
9 to achieve. By Regulation 21 CFR 801.109, lay users  
10 cannot order confirmatory tests on their own.

11 In some States, medical laboratory tests  
12 can only be ordered by a licensed health care  
13 professional. I have with me an excerpt from the  
14 Illinois compiled statutes, the Illinois Clinical  
15 Laboratory and Blood Bank Act.

16 And it says that a clinical laboratory  
17 shall examine specimens only at the request of a  
18 licensed physician, a licensed dentist, a licensed  
19 podiatrist, a therapeutic optometrist, a licensed  
20 physician assistant, an advanced practice nurse, or an  
21 authorized law enforcement agency.

22 In Illinois, manufacturers cannot order

1 these tests, and although manufacturers can attempt to  
2 set up relationships with reference laboratories to do  
3 the confirmatory testing, for some States this  
4 mechanism will not work.

5 The home-use intended use is clearly a  
6 medical use of the test. The same is not true,  
7 however, for workplace settings. Workplaces can set  
8 up relationships with reference labs because the test  
9 is not being used for medical purposes.

10 At Roche, we have found that our workplace  
11 customers usually already have relationships with  
12 reference laboratories. Often they are locked into  
13 using particular laboratories, and would not be able  
14 to use our certified laboratory as required by the  
15 guidance.

16 For the customers who don't have access to  
17 a reference lab, Roche Diagnostics already is  
18 implementing a program to provide that access. We  
19 would prefer to offer this program as an optional  
20 service to our customers, and not have it mandated by  
21 regulation.

22 We are concerned that if the FDA expands

1 their oversight to include workplace, insurance, and  
2 sports settings, then these tests will automatically  
3 become considered as medical tests, preventing our  
4 customers from ordering the necessary confirmation  
5 testing in some States.

6 Certainly the FDA does not intend to  
7 restrict the current access to DAT testing in that  
8 manner. We again ask the FDA to focus this guidance  
9 to separately address the needs of the home-users and  
10 the differing needs of the other settings.

11 Thank you for hearing our concerns today.  
12 We will be sending these and other comments to the  
13 guidance document in writing, and I will be happy to  
14 answer any questions.

15 DR. KROLL: Thank you. The next speaker  
16 is Carl Mongiovi.

17 MR. MONGIOVI: Good afternoon. I am Carl  
18 Mongiovi, and I am the vice president of Phamatech,  
19 Incorporated. I do have some monetary interest in  
20 this. They pay me sometimes enough.

21 Pardon me also if my voice is a little  
22 waver. I have been in Mexico and San Diego, and I am

1 here in the last three days. So I am a little tired,  
2 but we felt that this was important.

3 I would like to give you a little  
4 background. Phamatech was the first company to get an  
5 approval for over-the-counter screening devices. That  
6 was in October of 1998. We are currently in over  
7 30,000 stores.

8 Our level of sales is approximately 18,000  
9 devices per month, and because of this intimate  
10 knowledge, we have learned a substantial amount in the  
11 last two years, and some of this information I would  
12 like to pass along.

13 When we did our original submission, we  
14 ran over 4,700 tests, with 300 and some participants,  
15 and I realize that is a tremendous amount. It was  
16 done to draw attention to the fact that we felt that  
17 we could do it, and we wanted to be the first.

18 We ended up getting an overall accuracy  
19 with that test of 96.6 percent, and we were surprised  
20 by that. We had looked at participants who were in  
21 mental health institutions, drug rehab centers, and we  
22 took some Ph.Ds to see if we could throw them off.

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1 Still, the number came out to almost 97  
2 percent. I heard it said earlier that in the  
3 workplace that the manufacturer trains the technician,  
4 and indeed that is the case for corrections, law  
5 enforcement, and several other arenas.

6 It's that which makes the OTC test for  
7 home use so different from the others. We don't go to  
8 everyone's house to teach them anything. We give them  
9 a directional insert.

10 The target audience for lay people are  
11 individuals that have little or no experience in  
12 diagnostic testing, other than possibly pregnancy  
13 tests or glucose tests.

14 They seem to have very little patience and  
15 they don't seem to have a lot of time to read the  
16 directions. Something that we thought that we had  
17 covered very well was the study we produced to do this  
18 with so many numbers, and we thought we took in all  
19 the relevant factors, including education, sex, race,  
20 English as a second language, education, regional  
21 diversity.

22 We forgot one and that was stress, and we

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1 are finding that parents do the darneest things  
2 sometimes, and they don't often read and they are  
3 impatient.

4 I found out about this meeting Friday two  
5 weeks ago, and I was in Latin America all last week.  
6 I pulled up information and this is one days worth of  
7 confirmation tests that our laboratory did for us, and  
8 I just made copies of them, and took with me on my  
9 trip.

10 And I would like to just sort of tell you  
11 what I see. There were 62 samples; 34 positive for  
12 THC, and the high was 780 ng/ml. We had four  
13 cocaines, and the highest of those was 11 6,000  
14 ng/ml. We had three MDMA's, which we could not get,  
15 except that our confirmation laboratory tests that for  
16 us.

17 It is becoming an ever increasing problem,  
18 and we are finding a huge number of these samples. We  
19 had eight multiple drugs, and none of them had more  
20 than three drugs in an individual sample. But a lot  
21 of multiple drugs; five methamphetamine/amphetamines.

22 I believe it is very important for anyone

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1 to get a result and be able to do something with it.  
2 confirmation testing is necessary. It is not just  
3 that, yes, he is positive for THC. Was he positive  
4 for THC at 25 ng/ml, or 50 ng/ml, or was it 780 ng/ml.

5 Certainly the clinical implications are a  
6 little bit different. We know that our tests are not  
7 100 percent accurate. The test is to be used in the  
8 home. It is not for DOT, and not DoD, and the donor  
9 and the person that are running this test have the  
10 right to expect an accurate result.

11 And the only way they are going to get an  
12 accurate result is with confirmation. False results  
13 of any kind are going to override any good that we do  
14 with this test. And any incidents of false positives  
15 is going to seriously weaken this emerging category.

16 It is crass to talk about money, but that  
17 is the bottom line. If we cannot create a product  
18 that gives an accurate result, it will fail. It will  
19 be off the shelves and this whole thing will go away.

20 We feel that confirmation testing is  
21 necessary. We feel that the performance criteria that  
22 the test is judged by should be no less than what we

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1 see in the clinical lab.

2 Indeed, I would offer that and perhaps an  
3 over-the-counter test, only be a test that has been  
4 slightly modified from the clinical laboratory, so  
5 that there is enough data to show that it will work.

6 And finally we found that with  
7 confirmation testing we get to close the cycle. There  
8 is a need for individuals to be given an opportunity  
9 to find substance abuse counselors in their area, and  
10 the only way they can find out about that is to call  
11 up for that anonymous result.

12 When they call up, we can simply ask for  
13 a zip code, and that closes the circle. Thank you  
14 very much. If there are any questions, I would be  
15 happy to answer them.

16 DR. KROLL: Thank you. The next speaker  
17 is Naresh Jain.

18 DR. JAIN: Good afternoon, ladies and  
19 gentlemen. I am a scientist, and probably looking at  
20 the audience and the members, I am probably the oldest  
21 person standing here.

22 And naturally with age comes some

1 experience, and experience is that I have been in this  
2 field for over 35 years. I see one of my students is  
3 sitting as a panel member, and I know that I am a  
4 forensic scientist for 35 years, and for the last 30  
5 years, I have been doing nothing but testing drugs-of-  
6 abuse.

7 I was the Chief of Toxicology for L.A.  
8 County in 1970, and I started a laboratory, and I am  
9 now the director of a fairly larger drug testing  
10 laboratory specializing in drug testing for law  
11 enforcement agencies.

12 And our contracts includes the California  
13 Department of Corrections, and then send about 2,000  
14 or 3,000 urine samples a day. We have the Federal  
15 Bureau of Prisons contract, and the California  
16 Department of Mental Health, and we do a lot of job  
17 seekers, and pre-employment, DOT, and all that.

18 And the reason that I am here is primarily  
19 -- and I am surprised that I am here speaking to this  
20 panel for confirmation tasking. This is like  
21 reinventing the wheel.

22 I mean, we have taken for granted that a

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1 scientist, that whatever test we put on the market, it  
2 should be accurate, and it should be reliable. If we  
3 are not doing that, then we are in the wrong business.

4 The nature of all of these tests, over-  
5 the-counter drug tests, are based on immunoassays.  
6 And all immunoassays, if you read just basic  
7 chemistry, basic science, will cross-react with high  
8 end of concentrations with some molecules which are  
9 completely unrelated to the drug.

10 And of course with structurally similar  
11 substances, they will react. What is this argument,  
12 and it is hard for me to fathom, and when people come  
13 here and say, oh, we do this -- and on insurance  
14 testing, which I have heard so much words just now.

15 It so happens that two weeks ago, I took  
16 an insurance policy, and the doctor came home, and he  
17 said that one of the requirements was cocaine and  
18 marijuana tests, and he pulled out his kit, and put my  
19 hand in it.

20 And should I rely on that test? I mean,  
21 it has to be confirmed, and so basically what I am  
22 saying is that these screening tests are like API

1 grouping systems. They can eliminate a suspect, but  
2 for confirmation, you need DNA testing, and that is  
3 the best analogy that I can give.

4 Then we have these -- with the nature of  
5 the technology that we have, all the over-the-counter  
6 medications. You know, dietary supplements,  
7 containing pseudoephedrine and ephedra, all of these  
8 will give a false-positive test.

9 Then we come down to narcotics. A lot of  
10 people use pain killers on prescription, such as  
11 oxycodone, vicodin, and all those things. They will  
12 give a false-positive for morphine, because none of  
13 the immunoassays, or over-the-counter drug tests can  
14 distinguish between those two.

15 Then as I said, we get a lot of probation  
16 department samples from paroles, and a lot of these  
17 units have their -- they do on-site testing before  
18 they send the samples to us.

19 We have no control where they get these  
20 samples, where they get the kits. Some are from Roche  
21 and some are from Phamatech, and some are from  
22 different manufacturers. We have nothing to do with

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1 that.

2 And we found from the prison population  
3 and paroles that we were getting a high percentage of  
4 THC, and could not understand what was happening.  
5 Then further research showed that a lot of these  
6 paroles had AIDS.

7 And they were receiving this medication  
8 called sustiva, and that was giving a cross-reactivity  
9 with the THC agent. So, I mean, this is such a basic  
10 thing to go into this thing.

11 So confirmatory testing, the question with  
12 that was whether it should be limited to GC/MS. No,  
13 it should not be limited to GC/MS. Anything  
14 scientifically accepted. GC/MS is the gold standard,  
15 and LC/MS would be equally good.

16 Something which is accepted by the peers  
17 in the scientific community as giving reliable and  
18 accurate tests. I mean, the GC/MS is very good, and  
19 LC/MS would be good, and triple quot would be even  
20 better.

21 But anything that is acceptable to the  
22 general scientific community. And then another

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1 question that comes is that like you may get  
2 methamphetamine/amphetamine test, and we would not  
3 know. I don't think any test is available for MDMA,  
4 or MDA, or MDEA.

5 Only the confirmation will tell whether it  
6 is methamphetamine or anything. Then we come to where  
7 if a parent finds that their child is taking a drug.  
8 Okay. And now the child says, well, dad, I am not  
9 going to use any more.

10 Well, that's true, and so we test him a  
11 week later, and again it shows positive. Is he  
12 telling the truth? Maybe. So confirmation testing  
13 will show whether the level of concentration is going  
14 down or not.

15 I mean, how can we in the year 2001 debate  
16 this issue that confirmation testing is not -- it  
17 should be an integral component of any over-the-  
18 counter drug kit, and this should be so mandatory that  
19 no manufacturer is allowed to sell any product which  
20 can give false and misleading results.

21 Now, coming to anything that is necessary  
22 and useful; necessary because it can eliminate unfair

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1 accusation and punishment; and useful because it can  
2 help both the parent and the child establish a  
3 dialogue and maybe form a statement.

4 And if I have a few more minutes just to  
5 partly discuss this?

6 DR. KROLL: Can you wrap it up in 30  
7 seconds?

8 MS. JAIN: No. I just wanted to say that  
9 because of the spiked urine, that I have some ideas,  
10 because I have been in this field for a long time.  
11 Somebody thought of pooling the samples like we do,  
12 because should I review the samples, you are altering  
13 the metrics, because when you test something, you want  
14 to make sure there are metabolites present.

15 And that's because there are a lot of  
16 other drugs, and that is a true test. What we do is  
17 when we take and pool samples, one set will contain  
18 10,000 anograms, and sometimes there is 2,000  
19 anograms.

20 If you pool them together, you can come  
21 out to a very close concentration at a cutoff level  
22 without any dilution, and which will give the true

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1 metabolites, and other things. And with alcohol, be  
2 careful, because the 15 minute wait period if it is  
3 saliva testing. Thank you very much.

4 DR. KROLL: Thank you. The next speaker  
5 is Carl Good. And please remember to limit your  
6 comments to seven minutes, and tell us your financial  
7 affiliations.

8 DR. GOOD: As you said, my name is Carl  
9 Good, and I am the vice president of research and  
10 development at Avitar Corporation, and I have a  
11 financial investment there, and I own a few mutual  
12 funds, and I don't have much idea what they own, but  
13 there could be other aspects.

14 I would like to say that we really  
15 appreciate the opportunity of speaking before this  
16 group, and also would like to say that we very much  
17 appreciate the guidance documents that have been  
18 generated, and the benefit that I think that they  
19 provide to all parties concerned.

20 My background isn't legal at all, and I  
21 know that there were some issues raised as far as  
22 jurisdiction in the legal area, and I will leave those

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1 to others who are better informed.

2 What I would like to talk about a little  
3 bit today are a couple of technical aspects that have  
4 to do with testing, and our focus as a corporation is  
5 primarily on industrial and forensic insurance and  
6 sports testing, and secondary education testing.

7 And in these market places one has the  
8 opportunity for more extensive training, and  
9 certification of testers within that environment. We  
10 as a company strongly support the requirement for  
11 confirmatory testing.

12 However, including the cost of  
13 confirmatory testing, and the price of the screening  
14 test, can create difficulties. With all tests  
15 positive or negative to be confirmed, then the cost of  
16 this confirmation testing using GC/MS and other  
17 sophisticated procedures would cause the price of the  
18 consumable to be prohibitively high, and discourage  
19 folks from taking advantage of these drug testing  
20 opportunities.

21 It is also in conflict with current  
22 laboratory testing in which only positives are

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1 confirmed. If only positives are confirmed, then the  
2 test may again result in high prices due to the  
3 attempt to compensate for worst-case situations.

4 We would like to propose that it might be  
5 possible to provide each individual being tested with  
6 something perhaps that I incorrectly call a "Miranda  
7 Rights" card, so that anyone being tested -- and again  
8 our focus is primarily on the industrial environment -  
9 -- would be given a card saying that you have the  
10 right to confirmatory testing, and it should be borne  
11 by the organization that is performing the testing.

12 This way it would minimize the costs since  
13 most tests will be negative, and focus primarily on  
14 confirmatory testing and the positives, assuming that  
15 few people would ask that their negatives tests be  
16 confirmed.

17 I also would like to talk a little bit  
18 about perhaps a more technical area. Our focus is  
19 primarily oral fluids testing, which gives the  
20 advantage of direct observation of the testing  
21 process, unlike most urine testing situations, either  
22 laboratory based or over-the-counter.

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1           And also by that process in using oral  
2 fluids, reduces the opportunities for substitution or  
3 adulteration of the sample. And substituted or  
4 adulterated samples really have a quality of zero.

5           In the proposed guidelines, there is a  
6 section where the individuals who would be typical  
7 customers or typical people operating the tests would  
8 be asked to look at standard samples, and we believe  
9 that oral fluids testing, where your concentration of  
10 drug is much lower, that these ranges of plus or minus  
11 50 percent can be too tight.

12           For example, a cutoff perhaps for opiates  
13 might be in the 10 nanogram range, and so you would be  
14 looking at differences in a qualitative over-the-  
15 counter visually read test of only perhaps a 5  
16 nanogram difference.

17           Whereas, if you are looking at cocaine and  
18 urine, you are looking at 300 nanograms, and that is  
19 plus or minus 150 nanograms for the plus or minus 50  
20 sample.

21           And for opiates it is a level of 2,000,  
22 and it would be plus or minus a thousand nanograms.

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1 And so we would hope that this type of constraint on  
2 samples to be tested by users in that portion of the  
3 guidance be considered to be widened somewhat for  
4 these kinds of samples. Thank you very much.

5 DR. KROLL: Thank you. The next speaker  
6 is Ken Berger.

7 MR. BERGER: Good afternoon. I am the  
8 vice president of regulatory affairs and quality  
9 systems for Lifepoint, Incorporated, Ontario,  
10 California. We will shortly be commercializing a  
11 rapid, on-site product that will simultaneously test  
12 for both alcohol and drugs in saliva.

13 The Lifepoint test system consists of a  
14 small portable instrument, and a disposable cassette.  
15 By testing a few drops of saliva, the system can  
16 provide results for up to 10 analytes in under 5  
17 minutes.

18 The specimen and collection, processing,  
19 analysis and interpretation, is completely automated,  
20 with no user intervention. Additionally, the system  
21 is self-calibrating, and automatically quality  
22 controls the instrument and the cassette.

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1           As applied to testing for substances-of-  
2 abuse, the Lifepoint product brings the advantages of  
3 observable, non-evasive, collection as we just heard,  
4 and quantitative legally defensible results.

5           This technology should prove to be  
6 evidential for alcohol, and be significantly more  
7 sensitive and specific than current on-site or lab  
8 based urine immunoassay drug tests.

9           The test is completely automated to  
10 minimize operator error. In addition, we anticipate  
11 significant cost savings and operational improvements  
12 for testing substances of abuse in the workplace,  
13 insurance, and sports.

14           We are convinced that saliva is a drug  
15 test specimen represents a viable alternative for drug  
16 testing programs. The use of saliva, rather than  
17 urine, makes it possible to address a number of  
18 burdensome issues that have plagued drug testing for  
19 years.

20           The collection of saliva is non-evasive,  
21 and unlike urine, few people find it offensive to  
22 provide a saliva sample. Saliva also makes it

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1 possible to conduct and observe collection every time  
2 without requiring anyone to watch a donor urinate.

3 This significantly reduces the opportunity  
4 for adulteration or substitution, again as we just  
5 heard. Because the saliva's window is a detection of  
6 several hours, depending on the drug, it makes for an  
7 excellent indicator of under-the-influence status.

8 This makes it particularly effective as a  
9 more accurate post-accident, reasonable suspicion  
10 test, and even fit for duty testing. Additionally,  
11 all urine and saliva-based drug tests are recent use  
12 tests, and as such have the capability to be used for  
13 preemployment, random, and return to duty, testing.

14 Saliva has already been validated and  
15 approved in many States has a viable specimen for use  
16 in the criminal justice system. Law enforcement  
17 officials are specifically allowed by law to use  
18 saliva as a specimen for DUI drug testing purposes in  
19 9 States, while 10 other States allow the use of other  
20 bodily substances besides breath, urine, and blood.

21 Lastly, several participants in the  
22 European-funded Rosita Project have published the

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1 results of their studies, and have defined the perfect  
2 on-site drug test as a saliva-based, instrumented for  
3 objectivity and elimination of user interpretation  
4 panel tests, with results in 5 minutes.

5 Interest in the use of saliva for drug  
6 testing purposes is growing rapidly, and the guideline  
7 should not only reflect this, but also be careful not  
8 to inadvertently restrict or discourage the use of  
9 saliva.

10 This is especially true at a time when  
11 adulteration and substitution problems associated with  
12 urine testing are beginning to impact the integrity of  
13 the drug testing process overall.

14 Furthermore, the development of simple,  
15 easy to use, drug testing products, such as the  
16 Lifepoint test system, should enhance substance abuse  
17 detection and allow for more reliable, accurate, and  
18 faster testing methods without increasing the costs of  
19 such testing.

20 There is no real attempt to include these  
21 new and improved technologies. The draft guidelines  
22 focus on current urine drug tests. Also, while we

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1 acknowledge the need to set guidelines for OTC  
2 products and environments where there are casual, and  
3 frequent, and inexperienced users, such as the home,  
4 the application of these guidelines to more routine  
5 professional use in the workplace, sports, and  
6 insurance is not appropriate.

7 Drug testing in these environments is  
8 conducted by trained professionals under the guidance  
9 of SAMHSA, DOT, the International Olympic Committee,  
10 the NCAA, and others as we have heard today.

11 Additionally, the guideline proposed by  
12 the FDA is inconsistent and disruptive to these  
13 current practices, and will add uncertainty and costs  
14 to already established processes.

15 For example, how and when a confirmation  
16 testing is required, when confirmation testing is  
17 required as defined in these environments, the FDA  
18 requirement for automatically including the  
19 confirmation test in the pricing process of an initial  
20 test is confusing, and inconsistent with accepted  
21 protocol.

22 It is critical, therefore, that the FDA

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1 take into consideration the newer technologies and  
2 products that will soon be available. These newer  
3 technologies and products will revolutionize substance  
4 abuse testing practices, and finally provide the  
5 ability to obtain lab quality results easily, quickly,  
6 and cost effectively, on-site by non-technical users.

7 It is critical, moreover, that the FDA  
8 take into consideration the guidance that already  
9 exists for workplace, insurance, and sports. We  
10 believe that creating duplicate requirements on the  
11 user and the manufacturer by FDA, in conjunction with  
12 the proposed DOT and SAMHSA guidelines will have  
13 significant, undesired effects, on drug testing in  
14 general.

15 There will be increases in costs, and  
16 corresponding decreases in the amount of testing being  
17 done. It has been validated numerous times that  
18 testing routinely for drugs is the best deterrent of  
19 drug use.

20 We firmly believe, therefore, that by  
21 melding the FDA guidelines with those of SAMHSA and  
22 DOT, this will further promote public health and

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1 safety.

2 We also strongly recommend that the FDA  
3 consider that these environments are separate and  
4 distinct from home OTC. Lastly, and most importantly,  
5 although I am not a lawyer, the FDA's charter, as  
6 authorized by law, and not by regulation as we heard  
7 earlier, 21 U.S.C, paragraph 393, is to promote and  
8 protect the public health by regulating devices  
9 intended for the use and the diagnosis of disease, and  
10 other conditions, or in the cure, mitigation,  
11 treatment, or prevention of disease, and that is 21  
12 U.S.C. 321(h).

13 The results of tests in the workplace,  
14 sports, and insurance are not used for diagnosis of  
15 disease or other conditions, or in the cure,  
16 mitigation, treatment, or prevention of disease.

17 Drug testing in these environments  
18 therefore appears to fall outside the legal charter of  
19 the FDA. Thank you for your time.

20 DR. KROLL: Thank you. The next and final  
21 speaker is Tony Toranto.

22 MR. TORANTO: Ladies and Gentlemen,

1 representatives of the FDA, and distinguished  
2 panelists, thank you for holding today's forum, and  
3 for enabling me to address this audience.

4 My name is Tony Toranto, and I am the  
5 proud president and chief executive officer of  
6 Guardian Angel, an amazing company hailing from the  
7 great State of California.

8 Today I will tell you about Guardian Angel  
9 and our mission, and then I will focus on three issues  
10 presented to the panel by the FDA. One, whether  
11 alcohol tests should be in the same category as the  
12 various tests for drugs-of-abuse, including the  
13 appropriate standards.

14 Two, whether the study design in the FDA's  
15 draft guidance for drugs-of-abuse is appropriate for  
16 alcohol tests; and, three, whether confirmation  
17 testing is appropriate for alcohol tests.

18 I said before that I am the proud  
19 president and CEO of Guardian Angel, and in my shoes  
20 you would be, too. Guardian Angel has a simple  
21 mission; to be the great company that stops drunk  
22 driving. To repeat that, Guardian Angel's mission is

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1 to be the great company that stops drunk driving.

2 In the United States, people drink and  
3 subsequently get behind the wheel an estimated 2.5  
4 billion times each year. These occasions lead to over  
5 1.5 million DUIs, and one million alcohol related  
6 injuries, and 16,000 alcohol related deaths.

7 But who are these people that are getting  
8 behind the wheel after drinking? You may be surprised  
9 to know that many of them are social drinkers. Many  
10 of them are no different from you, or from me, or from  
11 our friends.

12 They may have two drinks with dinner, or  
13 maybe three, and then think they are okay to drive.  
14 That's where Guardian Angel steps in. We have  
15 developed a product that is a simple alcohol test, and  
16 this is it. It's small. It fits right in your  
17 wallet, and there is a small test strip, like a strip  
18 of lintless paper.

19 The user simply inserts the test strip  
20 into his or her mouth, and the test strip changes  
21 color to give an estimate of the user's blood alcohol  
22 content. It is pretty amazing.

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1           Now, knowledge is power, and Guardian  
2 Angel gives people empowering information. That's  
3 what we are about, giving people empowering  
4 information to make more informed decisions before  
5 getting behind the wheel.

6           The intended use of our product, and  
7 everything that Guardian Angel does, is focused on  
8 providing people with that empowering information.  
9 The need for products like ours is manifest, and it is  
10 with that background in mind that I address the first  
11 of the three issues that I mentioned earlier.

12           Should alcohol tests like ours be included  
13 in the same category as other tests for drugs of  
14 abuse. What analytical studies are appropriate, and  
15 what standards, such as DOT standards, should be  
16 applied.

17           To be very clear, we are not the same as  
18 a test for heroin, or cocaine, or marijuana for that  
19 matter, and we never will be. We are different, and  
20 if regulated -- and of course you have heard arguments  
21 suggesting that we should not be regulated. We should  
22 be subject to different studies and standards if

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1 regulated.

2           The first and most obvious reason for this  
3 is that we do not test for an illegal substance.  
4 There is a huge different between helping law abiding  
5 users to test their alcohol level before driving on  
6 the one-hand, and testing law breakers for the  
7 presence on the other.

8           And there is a huge difference between  
9 what we do and testing alcohol for some medical  
10 purpose, like when a patient comes into an emergency  
11 room.

12           The basic message here is that we should  
13 not treat an apple like an orange. Further weight for  
14 this is evident by comparing the historical  
15 progression of tests for drugs-of-abuse to the  
16 historical progression of alcohol tests like ours.

17           Historically, many tests for cocaine,  
18 heroin, and other drugs-of-abuse were first  
19 prescription devices, which are not being tested and  
20 adapted for OTC purposes. Our products simply do not  
21 evolve that way. We are an OTC product first and  
22 last.

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1           Again, products like ours are just a  
2 different kind of cat. We should not treat an apple  
3 like an orange. The different studies and analytical  
4 standards that apply to products like ours are well  
5 articulated.

6           For years the Department of Transportation  
7 has published standards for alcohol tests. These  
8 standards are the valuable model used by makers of  
9 products like ours. These standards are high  
10 standards based on sound methodology.

11           They are already in place and have  
12 withstood the test of time. The DOT standards should  
13 be the model applied to products like ours. There  
14 simply is no need to reinvent the wheel.

15           The second issue that I will address is  
16 the appropriateness of the study design set forth in  
17 the guidance for products like ours. The FDA poses a  
18 question about the use of spiked samples, and the  
19 answer here is straightforward.

20           The DOT approved spiked samples under its  
21 standards, and the FDA already allows spiked samples  
22 for prescription testing of alcohol. So clearly

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1 spiked samples are appropriate for studying tests like  
2 ours.

3 The FDA also poses a question about the  
4 appropriate concentration range and distribution for  
5 studying tests like ours. The model in the guidance  
6 for drugs-of-abuse should not be applied to products  
7 like ours. We are different for all the reasons that  
8 I already said.

9 The DOT model should apply, and the DOT  
10 model already sets forth concentration ranges and  
11 distributions. Lastly on this issue, the FDA poses a  
12 question about the appropriate size of the study,  
13 including the sample size.

14 The design set forth in the guidance for  
15 drugs-of-abuse contains 6 different cells, and it  
16 requires 200 subjects. The DOT model, which is the  
17 right model for us, requires only two cells, plus a  
18 zero concentration control cell.

19 As a result, we suggested only a third of  
20 as many subjects should be required. The third and  
21 final issue that I will address is the appropriateness  
22 of confirmation testing for products like Guardian

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1 Angels.

2           Simply put, for us confirmation testing  
3 makes no sense. Our intended use is to empower people  
4 with information about their alcohol level on the spot  
5 so that they can make more informed decisions about  
6 drinking and driving on the spot.

7           This is not like testing for the presence  
8 of heroin. For our intended use, confirmation testing  
9 at a later point makes no sense at all. It is neither  
10 appropriate nor practical.

11           If there were circumstances where a user  
12 wanted confirmation, labeling should take care of it.  
13 Labeling should advise the user to apply a different  
14 assay, and other approaches just don't make sense.

15           In closing, Ladies and Gentlemen, remember  
16 who we are and what we do. Guardian Angel is the  
17 great company that stops drunk driving. Our mission  
18 is noble, and our product important, and our reasoning  
19 sound.

20           The DOT model is the right one to apply,  
21 and there is no need to reinvent the wheel. The  
22 agency and this distinguished panel should work hand-

1 in-hand with Guardian Angel to encourage these types  
2 of products. It is the right think to do. Thank you  
3 for your time.

4 DR. KROLL: Thank you. Now, I am going to  
5 go to the open committee discussion. First what I  
6 would like to do is ask Mr. Gutman to give us a  
7 comment or opinion about some of the legal aspects  
8 that have been brought up here, in terms of how our  
9 panelists want to discuss or not discuss them.

10 DR. GUTMAN: Sure. I would request that  
11 the panel actually take the legal issues off the  
12 table. You actually weren't assembled here for legal  
13 advice. We probably would have constituted a  
14 different panel had we been interested in discussing  
15 legal issues.

16 So I would ask you to focus on the science  
17 and public health. That's not to suggest that legal  
18 issues aren't important, but they are not relevant  
19 today.

20 DR. KROLL: Okay. Thank you. And now  
21 what I would like to do is per our discussion is if  
22 Dr. Cooper could put some of the questions back up on

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1 the board here for us to consider.

2 DR. COOPER: There are a total of 10  
3 questions, which is quite a bit more than this  
4 morning, and so we were going to try to see if we  
5 could group some of the questions to try to cover the  
6 topic to be efficient.

7 The drugs-of-abuse questions will be the  
8 first eight questions, and then the two following  
9 questions will be on alcohol. Some of the questions  
10 that you answer initially may help with answers  
11 further down. But that is going to somewhat depend on  
12 the answers you give.

13 So I think we perhaps ought to start with  
14 number one of the eight for the drugs-of-abuse.

15 DR. KROLL: Okay.

16 DR. COOPER: Do you want me to read the  
17 question?

18 DR. KROLL: Why don't you read the  
19 question for us.

20 DR. COOPER: Okay. to maximize the  
21 likelihood that confirmation testing will be performed  
22 on presumptive positive results, FDA has been

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1 requesting that confirmatory testing be a mandatory  
2 component and design of the screening test. Are there  
3 other approaches that might be equally effective.

4 DR. KROLL: All right. I was going to  
5 start to my right, but since Dr. Rosenbloom is  
6 temporarily out, I am going to go to the other side of  
7 the room and ask Dr. Lasky to begin.

8 DR. LASKY: Okay. Thank you. Actually,  
9 I have two concerns about the results of this  
10 question, if indeed the confirmation testing was a  
11 requirement. One is that I was thinking about the use  
12 of other home tests, and what the instructions are  
13 when the result is provided to a lay user, like  
14 cholesterol testing.

15 And there the instructions are to consult  
16 a physician for further workup and counseling, et  
17 cetera, et cetera. And although certainly drugs-of-  
18 abuse testing have different social connotations, I  
19 don't see where there should be anything other than  
20 that sort of recommendation.

21 The other concern that I have is if a  
22 confirmatory testing was a mandatory component of the

1 design of the screening test, then the device becomes  
2 not only the initial device, the over-the-counter  
3 test, but also the confirmatory test.

4 And that opens from a regulatory  
5 standpoint a whole other can of worms. If I were to  
6 develop such a test, would then my confirmatory test,  
7 say GC/MS or whatever it happened to be, would that be  
8 subject to FDA clearance, and would I have to provide  
9 labeling, and all other kinds of information to the  
10 agency, even though I have no intent of putting that  
11 device into interstate commerce.

12 It will just reside in my own reference  
13 laboratory, or even more troublesome, in terms of  
14 regulation, if it is a laboratory that I contract  
15 with. So I think that is just extremely difficult,  
16 and opening a Pandora's Box, and frankly I don't think  
17 it is necessary if there is appropriated advice in the  
18 initial labeling of the over-the-counter test kit.

19 DR. KROLL: Okay. We will go to Mr.  
20 Reynolds.

21 MR. REYNOLDS: When I looked at this  
22 question, the first comment that came to my mind was

1 who was this really intended for. You know, we have  
2 had some of the industry people make a big distinction  
3 between an at-home test, as opposed to the test which  
4 may be used in the workplace.

5 I could see where possibly you might have  
6 a manufacturer selling a kit who might have some  
7 influence perhaps in the work setting, but in a home  
8 setting, for instance, I really don't know how you  
9 would enforce something like this.

10 Now, if a parent decides that a positive  
11 is a positive, then what does the manufacturer of that  
12 kit do? So, I am not really sure how you go about  
13 implementing this.

14 DR. BUSH: Donna Bush. Historically, two  
15 tests tend to give you a much better result than just  
16 one. When you have a screening device such as what we  
17 are talking about here, immunoassay-based, they may in  
18 fact rule out negatives.

19 If they are so prepared, you can rely on  
20 the negative results. But clearly the positive result  
21 needs further work, needs further analysis. So in the  
22 past, ideas have been floated about constructing a kit

1 that would have the ability -- if you get a screening  
2 test result, then have the capability within that kit  
3 to immediately send that specimen on for confirmation  
4 to another site.

5 That is inherent, because then it is up to  
6 the user. If the user reads that package insert and  
7 decides not to send it in, that is there decision.  
8 But clearly the counseling and the information  
9 provided in that package insert tells the individual  
10 that more testing is in fact necessary.

11 And I see at this point in time, or at  
12 this point in time, I am not sure that I see another  
13 approach that is equally effective. Confirmation  
14 tests is essential. So, thank you.

15 DR. EVERETT: This is James Everett.  
16 Clearly as a physician and a scientist, confirmatory  
17 testing is absolutely necessary. You can't put, or  
18 perhaps if you recognize the danger of putting these  
19 type tests in the hands of laymen, and they are not a  
20 hundred percent accurate, the resulting effect could  
21 be disastrous.

22 The industry mentioned the cost. It is

1 strictly up to the individual whether they want  
2 confirmation or not, but if a significant number of  
3 people do not send in for confirmation, plus the  
4 negative ones have already paid for it, and then they  
5 don't know it, then the cost in essence is offset.

6 So the amount of cost is irrelevant. The  
7 important thing is the public and the safety. The  
8 information we review for approval of medical devices  
9 is tremendous. It is a lot of information and for us  
10 it can be difficult to interpret.

11 Kindly the FDA provides experts to come in  
12 and explain that information to us. The layman will  
13 not have that assistance in understanding exactly  
14 what a positive test really meant, or what the meaning  
15 of it really is.

16 So the only true answer is to have the  
17 experts decide whether this is a truly positive  
18 sample, or as opposed to a truly negative one. But in  
19 essence, with every other analytical test we perform  
20 as experts, we always have what is called a gold  
21 standard for confirmatory tests. There is no need to  
22 remove that expertise from the layman as well.

1 DR. WILKINS: Diana Wilkins. I wanted to  
2 say that I agree with both Dr. Bush and Dr. Everett,  
3 and with their comments about the confirmatory  
4 testing. And I would just like to make one other  
5 additional comment about that.

6 That while I realize that it doesn't  
7 increase the cost of the product, one concern I have  
8 is that with the increasing use of what you might  
9 refer to as unregulated products, unregulated  
10 medications, or supplements, et cetera, by consumers,  
11 without an avenue that clearly makes it apparent to  
12 the consumer that that sample or that specimen is  
13 presumptive, I am concerned that without requiring  
14 confirmatory testing that we could end up in a  
15 tremendous problem with other products that we or the  
16 manufacturers don't anticipate a problem right now,  
17 but could be.

18 You have an anticipated testing, and  
19 whether this cross-reacts with a home-use device or  
20 something, and that is a concern to me. I think if  
21 anything unregulated product use is certainly on the  
22 rise, and I don't think that is going to go away.

1           And without the ability to confirm the  
2 presence of that substance in the urine, I think we  
3 are misleading the consumer.

4           DR. KURT: Tom Kurt. I certainly have  
5 been giving consideration to my fellow panel members,  
6 and I would like to comment on some things that would  
7 be just a little bit different.

8           First, I was concerned about the consumer  
9 pre-marketing testing of a kit that the consumers be  
10 a broad range of the population as a whole, instead  
11 all of them being college graduates; that there would  
12 be an educational level that would be polled among  
13 them.

14           Perhaps some of them might be visually  
15 impaired, and perhaps some of them might be older, et  
16 cetera. Perhaps some of them might even be  
17 artificially put under stress to see how they function  
18 under the conditions of performing the test.

19           And in confirmation testing obviously  
20 alcohol testing is quite different than doing  
21 confirmation on drugs-of-abuse, where GC/MS, of  
22 course, is a preferred confirmation.

1 But I would like to point out that Donna  
2 Bush pointed out at a previous panel meeting that the  
3 emit tests, or tests of such a nature, are used as a  
4 stand alone test in different situations, such as  
5 parole programs, employee action programs, methadone  
6 clinics, et cetera, on a sort of a serial basis to see  
7 whether a person is compliant.

8 And I think that in certain situations  
9 where you have such tests performed under a very  
10 creditable auspices such as a -- and let's say in this  
11 city, Georgetown University Hospital, I would not  
12 necessarily question the result of an emit test  
13 performed under those auspices, even though a GC/MS  
14 might be preferred.

15 I wouldn't necessary say that the GC/MS is  
16 absolutely necessary under those circumstances, unless  
17 it falls under the DOT perview. I would like to  
18 comment also on the situation of consumers using  
19 testing in situations where you have sports use, home  
20 use, clinics. I mean, in an non-clinical use under  
21 non-professional review.

22 I would say "caveat emptor" or let the

1 buyer beware; that if such ever occurs, let such kits  
2 be properly labeled that the user or the buyer be  
3 forewarned, and that any positive tests should be  
4 consulted with the appropriate medical person, such as  
5 the family physician, et cetera, with such a positive  
6 test.

7 DR. KROLL: Dr. Manno.

8 DR. MANNO: You are skipping.

9 DR. KROLL: I'm passing.

10 DR. MANNO: Just simply at this time  
11 addressing one, I concur with Dr. Bush, Dr. Everett,  
12 Dr. Wilkins, on their comments. It seems to me that  
13 I have been here before when we first discussed  
14 whether or not guidelines should be developed.

15 And I think the concern then was the  
16 misleading of the consumer on the OTC type product,  
17 and the education of the consumer. So I really think  
18 that in order to additionally strength the family  
19 structure in an adversarial situation between a parent  
20 and a child, I think that for use in this environment  
21 that confirmatory tests have to be available.

22 They absolutely have to be available, and

1 like Dr. Bush, at this point in time, I just don't see  
2 any other way going about making that available than  
3 what we already have. Thank you.

4 DR. LEWIS: Sherwood Lewis. I certainly  
5 agree with the others, as far as the need for the  
6 confirmatory testing. I do have a question which  
7 comes as a result of the thought on my part that what  
8 does this say about the confirmatory testing of  
9 negative results.

10 If, for example, the cost is built into  
11 the test, should the user insist that a confirmatory  
12 be conducted even though the test is negative, and say  
13 that they know about the cutoffs, and the sensitivity  
14 around the cutoff and so forth, and say I know this  
15 should be positive, even though it turns out negative,  
16 and I want a confirmatory test.

17 Is that though built into the FDA's  
18 approach to the labeling and marketing of the product.  
19 Thank you.

20 DR. GUTMAN: I will respond to that.  
21 There is no question that the configuration can be  
22 gained, and that is someone who has a negative result

1 and has high anxiety could pretend that it is  
2 positive, and mail it in and have it confirmed under  
3 this algorithm.

4 That's not the intent and I would guess  
5 that is not a common practice, but it certainly is a  
6 possible practice. So there is no intention if you  
7 were really concerned about false negatives that this  
8 might be bad.

9 There is actually no intention to capture  
10 false negatives here. The intention is to make sure  
11 that a false positive does not create a false label.  
12 And just to clarify, we obviously can't go into the  
13 home with a shotgun and make anybody do anything.

14 What is on the table here is the notion  
15 that by having this design and cost built into the up-  
16 front review or clearance of the product, that it will  
17 reduce a barrier and make appropriate behavior more  
18 likely.

19 We obviously can't actually force anybody,  
20 and then can run the test and use it to diagnose brain  
21 cancer if they want.

22 DR. HENDERSON: I have a couple of

1 comments. One, the notion that the FDA doesn't have  
2 jurisdiction over a test that is used in the home is  
3 a little concerning to me, because I would assume that  
4 all consumers would have a right to expect that a  
5 product that they buy is safe and reliable.

6 And if the FDA were not to certify that or  
7 assure that, I am not sure who would. So I certainly  
8 think that the FDA has a role in that.

9 DR. GUTMAN: No, I didn't mean to suggest  
10 that we wouldn't --

11 DR. HENDERSON: No, no, no. The industry  
12 is suggesting that the FDA doesn't have any perview  
13 over the regulation of such a device.

14 DR. KROLL: I think we would want to skirt  
15 around this issue. We are now dealing with the legal  
16 aspects.

17 DR. HENDERSON: Okay. The other thing is  
18 that if such a device as a screening test was decided  
19 to be really a medical test, and therefore something  
20 that we could look at, I certainly think that after  
21 the screening for the confirmatory, in looking at and  
22 paying for it, health care insurance.

1                   If it was decided that we were using this  
2                   at home to diagnose drug addiction, or use of drugs,  
3                   and they needed to have treatment afterwards,  
4                   certainly it would be something that health care  
5                   insurance would be interested in, and perhaps would  
6                   help to flip some of the bill for the confirmatory  
7                   test.

8                   I also agree that if we do provide this  
9                   for home use that there should be some incentive to  
10                  follow up with confirmatory testing, and certainly  
11                  building the cost of that into it does decrease a  
12                  barrier, and would help to increase the use of  
13                  confirmatory testing.

14                  DR. ROSENBLOOM: Rosenbloom. It is hard  
15                  for me to imagine not having confirmation of all  
16                  positives, not just those at the cutoff. But any  
17                  positive.

18                  I think with the negatives that one would  
19                  have to consider the quality control that is applied  
20                  at the point of contact in sports applications and  
21                  other applications.

22                  But for the individual user, I would think

1 that they would be well advised to not just have  
2 cutoff positives confirmed, but to have any positive  
3 confirmed, because that's where you are likely to see  
4 the most false negatives, are those that are below the  
5 cutoff and considered negative under those  
6 circumstances.

7 DR. KROLL: Okay. Thank you. I am going  
8 to ask Dr. Cooper if we could go to question number  
9 two, and if there are any other questions she thinks  
10 that we can group together.

11 DR. COOPER: I think that there is enough  
12 distinction between the two questions that we need to  
13 make this a stand alone question. Are the studies and  
14 labeling guidelines as outlined in the guidance  
15 appropriate for home, workplace, insurance, sports, or  
16 other OTC settings.

17 Consider that the intended use of drug  
18 abuse tests generally are to indicate the presence of  
19 drug rather than impairment.

20 DR. KROLL: Okay. Thank you. Why don't  
21 we begin with Dr. Rosenbloom.

22 DR. ROSENBLOOM: What I just said. I

1 think I have pretty much addressed that. I think that  
2 we need QC in those places where they are doing  
3 numerous tests to confirm that negatives in general  
4 are true negatives, and that any positive, not just  
5 those at the cutoff, but that any -- unless it is  
6 confirmed that there is a base line, and of course  
7 that is a negative.

8 But that the zero point is really -- that  
9 there is some reaction, but it is present in all  
10 specimens. But that anything that is positive, and  
11 not just those considered at the cutoff, needs to be  
12 confirmed.

13 DR. HENDERSON: I agree.

14 DR. KROLL: Dr. Henderson.

15 DR. LEWIS: Sherwood Lewis. I agree  
16 generally that there is one thing that has been  
17 throughout the documents that I have been reading and  
18 what has been presented, a term, which I guess goes  
19 under labeling, which describes the presumptive result  
20 as being uncertain.

21 And I think that this would create a real  
22 problem for the lay user, where instead of using that

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1 word presumptive, uncertain is the term that I have  
2 seen used throughout. And I just wonder if that is an  
3 appropriate term to describe the positive test result  
4 in a screening modality.

5 DR. MANNO: Dr. Manno. The main thing on  
6 question two that gives me deep concern is the  
7 application of the OTC product to anything that  
8 follows the words appropriate for home.

9 I think that we have got guidelines for  
10 workplace, and I think insurance is not for treatment.  
11 Sports is not for treatment, and so on, and so I think  
12 this needs to be limited to home use.

13 DR. KROLL: All right. Thank you. Marty  
14 Kroll. I was looking at the labeling guidelines, and  
15 I didn't see a separation come out for these different  
16 entities.

17 And I would think that they would actually  
18 be used differently in each place, and I think maybe  
19 there could be some language that would address that.

20 DR. KURT: Tom Kurt. I would like to  
21 comment that I think that any consumer use test,  
22 whether at home or in the sports arena setting, should

1 have a built-in confirmation as part of the cost of  
2 that test, so that the person does not necessarily  
3 misjudge what that result is, or is unnecessarily  
4 penalized in a situation of determining what the  
5 preliminary, or presumptive, or initial test is, I  
6 would consider that a probable positive result, but  
7 not necessarily a certain, with near medical certainty  
8 in the result.

9 I think that there should be differences  
10 in the labeling guidelines, depending upon the  
11 circumstances of the distribution of the kid. There  
12 should be an 800 number available for the appropriate  
13 parties to call, and that the people should be advised  
14 to consult their immediate medical advisors.

15 And that there might be some quality  
16 control built into such disseminated kits by including  
17 on a randomized basis a card, for instance, every 10  
18 to 20 kits to have the person send in to see their  
19 response to doing the test, and the results that they  
20 obtained.

21 DR. WILKINS: Dr. Wilkins. I agree with  
22 both Dr. Kroll and Dr. Manno regarding the labeling

1 guidelines and the issues in my mind become most  
2 important in the issue of home use, because there  
3 isn't oversight at some other level.

4 At least with workplace testing and sports  
5 testing, there are other agencies that set criteria,  
6 et cetera, for the type of testing to some degree.  
7 But I think where it becomes very critical is for the  
8 at-home use, and I think that somehow the labeling  
9 guidelines, or the guidance provided for that, should  
10 be separated out for those purposes.

11 DR. EVERETT: James Everett. This is  
12 clearly an over-the-counter device, and the decision  
13 to use it in the home, at work, or in some other  
14 environment, the rules in essence should not change.  
15 It becomes more imperative perhaps, of course, if you  
16 use an over-the-counter device and take it to work,  
17 and the thing turns out to be positive, and not the  
18 employee has no recourse.

19 Those types of activities become very  
20 important and ensures in essence that you have a need  
21 to make sure that the test is reading accurately or  
22 correctly.

1 To have this device and not have a  
2 background mechanism to make sure that the device is  
3 correct ensures that people will be injured at all  
4 ages -- children, adults, and those who are somewhat  
5 in between being an adult and a child.

6 These are usually the kids in the early  
7 20s, and the important thing about having a test to  
8 confirm your answer is to ensure that you are  
9 proceeding on correct information. Anything else is  
10 truly presumptive.

11 And that opens the door to danger,  
12 misdiagnosis, misuse, and perhaps abuse of these types  
13 of kids. So again trying to decide what the rules  
14 should be based on where the test is being used  
15 employees somewhat of a fallacy.

16 And that is that the test is more accurate  
17 in one environment than another, or that it is  
18 somebody else's responsibility to make sure that the  
19 test is accurate.

20 The rules for determining whether it is  
21 accurate or not should be based on how the test  
22 performs, and not so much whether it is in the hands

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1 of the employer, versus the hands of the parent.

2 Whether this test is going to be accurate  
3 for urine or saliva should be the same in either  
4 environment. So again I don't think we should alter  
5 the rules for playing this particular game based on  
6 who is doing it, whether we are expecting the employer  
7 to pick up the responsibility for the accuracy or the  
8 manufacturer.

9 Clearly the manufacturer should absorb  
10 some of that responsibility, and this is a way to  
11 ensure that that happens.

12 DR. BUSH: Donna Bush. I strongly concur  
13 with Dr. Everett and his review of the applicability  
14 in all arenas of an accurate test, because a result of  
15 the test is a result of the test, and is a result of  
16 the test, no matter how and where you apply it.

17 We spoke earlier in the day about the  
18 quandary of no result at all, versus an incorrect  
19 result, which is worse. And that applies in whatever  
20 scenario the testing is performed.

21 So I believe equal weight, equal  
22 applicability for accurate and reliable result,

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1 screening, confirmation, initial test, followed by  
2 confirmation, is a necessity.

3 Also, I think a question was asked are the  
4 studies and labeling guidelines as outlined in these  
5 guidances, and I do want to specifically take a look  
6 at what Dr. Cooper had presented concerning the  
7 consumer study designs and I concur with them. That  
8 is a very good and nicely done approach. Thank you.  
9 That's all.

10 MR. REYNOLDS: Stan Reynolds. I agree  
11 basically with Dr. Bush and Dr. Everett, in that  
12 either the test works or doesn't work. It is that  
13 simple, regardless of the setting. And also Dr.  
14 Lewis' comment that I really don't like that term  
15 uncertain.

16 I think that particularly for consumers  
17 for at-home use that that is a confusing term, and  
18 should come up with something better, whether it is  
19 presumptive positive, or whatever the term is, but I  
20 really don't like that term uncertain.

21 DR. LASKY: Fred Lasky. First, I would  
22 like to qualify what I had mentioned earlier, because

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1 as people are going around the table, I recognized  
2 that everybody was avoiding my comment. I certainly  
3 agree that confirmatory testing in drug analysis is  
4 essential.

5 I was addressing some of the regulatory  
6 quagmire that might follow in the event that  
7 confirmatory testing was a required follow-up to an  
8 over-the-counter test. So please be assured that I  
9 agree that in an environment like this that confirming  
10 a drug test is important and is in the best interests  
11 of everyone.

12 I would like to now comment on the  
13 question asked about the -- to consider that the  
14 intended use of the drugs-of-abuse test generally are  
15 to indicate presence of a drug.

16 In fact, I have serious reservations about  
17 that statement because it is in fact the intended use  
18 under different settings that I think is really the  
19 issue that we really need to be troubled about,  
20 because uncertainly certainly is a fact of life, and  
21 to minimize that uncertainly is going to depend on how  
22 the test is intended to be used.

1 For example -- and we are leaving the  
2 legal issues aside, and so we are talking about the  
3 workplace, and insurance, and sports, and other things  
4 like that.

5 But I want to say right up front that I am  
6 not sure that that is within the realm of what we were  
7 talking about. But that being said, let me go on. If  
8 a pilot in the plane that I am going to take back to  
9 Rochester, New York, had a presumptive positive screen  
10 test, I would want to be sure that he was off or out  
11 of the cockpit.

12 However, if an insurance company is using  
13 the same drug test, and is going to prohibit me from  
14 getting a new insurance policy, I would want to be  
15 sure that it was a hundred percent sure that that same  
16 test would be positive only 100 percent of the time  
17 when in fact somebody -- I was going to say I, but  
18 somebody had in fact taken or abused the drug.

19 So here again it is the intended use that  
20 we really have to be so careful about, and how the  
21 labeling has to be put forward clearly and  
22 unequivocally, and I think it depends upon the setting

1 and the facts.

2 Also, it has to be imminently clear when  
3 this box or kit is picked up by a physician or an  
4 insurance company, or somebody in the workplace, that  
5 they understand clearly what the limitations are. I  
6 don't think one size will fit all in this case.

7 DR. KROLL: Dr. Rosenbloom.

8 DR. ROSENBLOOM: I am really confused. I  
9 don't see a dimes worth of difference between those  
10 two situations, except in terms of timing. I want  
11 that pilot not flying until the test is confirmed.

12 I don't give a damn whether you get your  
13 insurance today or a week from now. Other than the  
14 timing, I think that both of those tests demand  
15 confirmation equally. I don't see the difference.

16 DR. KROLL: Okay. Let me thank the panel  
17 for their comments. I would like to take a short  
18 break now.

19 (Whereupon, the panel recessed at 3:06  
20 p.m., and resumed at 3:26 p.m.)

21 DR. KROLL: I would ask the panel members  
22 to resume their seats, please. I would like to

1 reconvene now. In the interest of -- or someone asked  
2 me if we could discuss the questions concerning  
3 alcohol testing now because someone has to leave, and  
4 wanted to listen to them, and I said we could probably  
5 do that, and we will start with them.

6 And then we will return to the ones  
7 dealing with the other types of drugs.

8 DR. COOPER: All right. What we are going  
9 to do is present question one and question two for  
10 alcohol, and have the comments be collectively for  
11 question one and question two, rather than do them as  
12 two separate questions.

13 The FDA is proposing to include alcohol  
14 testing in the same category as other tests for  
15 substance abuse. Are the same types of studies  
16 appropriate for alcohol tests and should other  
17 approaches, such as the one used by the Department of  
18 Transportation, be considered.

19 And the question that we are combining  
20 that with is in what setting is confirmatory testing  
21 for OTC alcohol tests appropriate, at home, workplace,  
22 insurance, sports, other.

1                   What matrices and what time span between  
2 collection of the original sample and collection of  
3 the sample for confirmation would be appropriate.  
4 Thank you.

5                   DR. KROLL: Okay. These are on page 13 of  
6 the handouts. You can review what the actual  
7 questions are there. I would like to ask that in the  
8 interest of time can people please keep their comments  
9 succinct, but if you do have something that you want  
10 to say, please say it. So let me go to Dr. Lasky.

11                  DR. LASKY: I don't have any comment on  
12 this part.

13                  MR. REYNOLDS: I have no comment at this  
14 time either.

15                  DR. BUSH: Donna Bush. DOT models work  
16 well. Actually, when we are taking a look at point of  
17 collection testing in the SAMHSA workplace arena, the  
18 Federal workplace, we are looking at the NHTSA,  
19 National Highway and Traffic Safety Administration,  
20 way of approving and testing on their own separate and  
21 independently the test devices for breath alcohol.

22                  Well, we are looking at that model and

1 later on our point of collection testing, urine drug  
2 testing and oral fluid drug testing, possible assay  
3 kits.

4 And so there is a model out there that  
5 works well for taking a look at evaluating devices, as  
6 well as implementing cutoffs, and confirmation,  
7 screening and confirmation, and DOT has a good model  
8 in their workplace program also.

9 DR. EVERETT: James Everett. I agree in  
10 the sense that I don't run into the same problems, and  
11 other physicians that I know, we don't tend to run  
12 into the same problems with alcohol as we run into  
13 with the other types of drugs.

14 So I don't think it is necessarily needed  
15 to include it in the same type testing and impose the  
16 same type criteria.

17 DR. WILKINS: Diana Wilkins. I also agree  
18 with Dr. Bush's comments, and Dr. Everett's comments,  
19 and I think we definitely should consider other  
20 approaches, such as the DOT model, because I think at  
21 least there we have some basis or some reference  
22 point, some experience to go on particularly for

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1 alcohol.

2 So I think that that is a reasonable  
3 approach to take.

4 DR. KURT: John Kurt. I agree with Donna  
5 Bush's point that NHTSA and DOT have long established  
6 the kind of program review devices used in alcohol  
7 testing.

8 I think it would be helpful for the FDA to  
9 have sort of editing privileges of labeling, or input  
10 on the labeling of such devices, but not necessarily  
11 take the lead, because the lead is already well  
12 established.

13 DR. KROLL: Martin Kroll. I am going to  
14 try to answer the things in question two. First of  
15 all, I think for confirmatory testing there, I think  
16 that where it is going to be used for some type of  
17 purpose, like where a punishment is attached, think  
18 there should be some type of confirmatory testing.

19 I think if you are looking at somebody who  
20 is at a bar or some in the home, and decides or is  
21 trying to decide whether or not they have drunk too  
22 much to drive, I don't think that needs confirmatory

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1 testing.

2 I think they need to look at that and say  
3 what goes over a certain amount over the certain limit  
4 and that could be set fairly low, and that they would  
5 say it is better for me not to drive, and try to deal  
6 with that.

7 But in other places, the workplace or  
8 sports, or insurance, I think that needs to be handled  
9 differently, because the consequences are more severe.

10 DR. MANNO: Barbara Manno. I agree with  
11 all the comments so far. I would add one more just  
12 general comment to the whole area of alcohol testing.  
13 I heard one of the sponsors plead for not including  
14 other drugs-of-abuse.

15 I don't see where the inclusion of alcohol  
16 in any way in a drug kit that has other drugs of abuse  
17 in it for over-the-counter testing precludes in any  
18 way a single test unit that may be out there, just  
19 purely to see if you have had too much to drink to  
20 drive.

21 But I would think that we should use that  
22 DOT, or at least consider what is there already as a

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1 pattern to follow. There is a good knowledge base  
2 there.

3 DR. LEWIS: Sherwood Lewis. I have  
4 nothing to add.

5 DR. HENDERSON: Cassandra Henderson. I  
6 don't either.

7 DR. ROSENBLOOM: Arlan Rosenbloom. I  
8 agree that a parsimonious approach and the most  
9 efficient would be to use established guidelines, and  
10 that alcohol is a very different testing issue, and  
11 database -- and a well established database compared  
12 to the other substances.

13 DR. KROLL: Thank you. I would like to go  
14 to Dr. Gutman and ask him if there are any more  
15 questions that we have related to this issue.

16 (Brief Pause.)

17 DR. KROLL: All right. Let's go back to  
18 the other drug tests, and I believe that takes us to  
19 questions 3 and 4; is that right?

20 DR. COOPER: Actually, I believe it is  
21 going to be 3 and 8. We are combining our cutoff  
22 questions. The FDA is suggesting that OTC devices

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1 render negligible performance error with spiked  
2 samples that concentrations of plus 50 percent, and  
3 minus 50 percent of the cutoff concentration.

4 Again, these are drugs-of-abuse questions.  
5 And is this reasonable. If not, what alternative  
6 performance criteria would be appropriate.

7 And visually read devices frequently  
8 render positive results well below the claimed cutoff  
9 of the assay. And the caveat is should there be  
10 certain performance requirements to support a claimed  
11 cutoff concentration.

12 DR. KROLL: All right. Let's start with  
13 Dr. Rosenbloom.

14 DR. ROSENBLOOM: Can you start with  
15 somebody who is registering faster than I am?

16 DR. KROLL: Dr. Henderson.

17 DR. HENDERSON: Again, I'm still focusing  
18 on negative results. I certainly think that devices  
19 that are read, if they are less likely to render a  
20 positive result because of the cutoff, I would argue  
21 that the cutoff should be moved so as to render it  
22 much less likely that you are going to get a false

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1 negative than a false positive.

2 So I would argue that the devices, the  
3 concentrations, the cutoffs, would be changed so that  
4 the spread between what is acceptable and what the  
5 sponsors might produce on their data, would actually  
6 be tightened to increase the likelihood that they are  
7 not going to identify somebody as being positive when  
8 in fact they may well in fact be negative.

9 So I am really concerned about the false  
10 negatives.

11 DR. ROSENBLOOM: I guess I would say the  
12 same thing, which is what I have been saying right  
13 along, is that any positive, even if it is below the  
14 cutoff, should be emphatically stated as requiring  
15 confirmatory testing before it is assumed to be  
16 negative; just as positive requires confirmatory  
17 testing before a label is placed.

18 DR. LEWIS: Sherwood Lewis. I think that  
19 for the reasons already given that the plus 50 percent  
20 and minus 50 percent are pretty broad, and could be  
21 tightened up for the reasons mentioned.

22 DR. MANNO: I kind of feel like the 50

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1 percent value is rather tight for this also. If they  
2 are going to stay there, there needs to be some  
3 discussion on the labeling, and the percent of the  
4 time that you would expect to have a frank positive  
5 and one is that you might consider making a suggestion  
6 that when it is negative, they might want to test on  
7 another day and another time.

8 I am not selling over-the-counter drug  
9 testing kits, but I am thinking about the practical  
10 application in the home setting. And in terms of  
11 question number 8, I am going to pass on that  
12 temporarily.

13 DR. KROLL: All right. Martin Kroll. I  
14 am a little concerned on question three whether plus  
15 or minus 50 percent, and that seems a little liberal  
16 to me. I mean, I just imagine that could be a bit  
17 tighter. You need something that is like a plus or  
18 minus 25 percent, or plus or minus 30 percent.

19 There could be a lot of values that fall  
20 within that range and that may in part depend somewhat  
21 on the actual drug that is being looked at. And on  
22 question eight, I didn't exactly understand this

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