

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

CLINICAL CHEMISTRY AND
CLINICAL TOXICOLOGY DEVICES PANEL
OF THE MEDICAL DEVICES ADVISORY COMMITTEE
OPEN PUBLIC SESSION

Thursday, September 25, 1997

Holiday Inn - Bethesda
8120 Wisconsin Avenue
Bethesda, Maryland

The meeting in the above-entitled matter
convened, pursuant to notice at 9:00 a.m.

PANEL MEMBERS PRESENT:

HENRY NIPPER, Ph.D., Chairperson

JOANN BOUGHMAN, Ph.D.
BARBARA GOLDSMITH, Ph.D.
ROBERT REJ, Ph.D.
THOMAS KURT, M.D.
BEVERLY HARRINGTON-FALLS, M.D.
SHERWOOD C. LEWIS, Ph.D.
DAVID SOHN, M.D.
BARBARA R. MANNO, Ph.D.
BENJAMIN GERSON, M.D.

JAMES EVERETT, M.D., Ph.D.
THEODORE TONG, Pharm.D.
ROBERT HABIG, Ph.D.
ELLEN S. ROSENTHAL, M.S.

C O N T E N T S

AGENDA:

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Adjournment	

1 P R O C E E D I N G S

2 DR. NIPPER: In the interest of keeping our
3 schedule, I'd like to urge the spectators and panel to take
4 their seats so we can begin.

5 MS. LAPPALAINEN: Good morning and welcome Panel
6 Chairperson , members and consultants. I am Sharon
7 Lappalainen, Executive Secretary of the Clinical Chemistry
8 and Clinical Toxicology Devices Panel of the Medical Devices
9 Advisory Panel Committee.

10 The committee is here today to provide advice and
11 recommendations to the Agency regarding over-the-counter
12 drugs of abuse testing systems and to comment on a draft
13 points to consider document for these products.

14 Single copies of the draft points to consider
15 document entitled points to consider for approval of home
16 drugs of abuse test kits are available in the hand-out
17 materials that are provided at this meeting.

18 The Clinical Chemistry and Clinical Toxicology
19 Devices Panel last met on March 20th and 21st of this year.
20 At that meeting, the panel deliberated upon a pre-market
21 notification for an over-the-counter device that measures
22 for tosamine for the management of diabetes mellitus. The
23 FDA has since cleared this device to market.

24 In addition, the panel deliberated upon the issues

1 surrounding self-monitoring of blood glucose systems. Based
2 upon the panel's deliberations, and upon comments received
3 from industry, academia, and the public, FDA will make
4 available in the future a revision of the current guidance
5 document entitled review criteria for the assessment of
6 portable blood glucose monitoring, in vitro diagnostic
7 devices, using glucose oxidase, dehydrogenase, or hexokinase
8 methodology.

9 At this time, I would like to read the conflict of
10 interest statement into the record. Conflict of interest
11 for the Clinical Chemistry and Clinical Toxicology Devices
12 Panel meeting, September 25, 1997. The following
13 announcement addresses conflict of interest issues
14 associated with this meeting, and is made part of the record
15 to preclude even the appearance of an impropriety.

16 To determine if any conflict existed, the Agency
17 reviewed the submitted agenda and all financial interests
18 reported by the committee participants. The conflict of
19 interest statutes prohibit special Government employees from
20 participating in matters that could affect their or their
21 employer's financial interests.

22 However, the Agency has determined that
23 participation of certain members and consultants, the need
24 for whose services outweighs the potential conflict of

1 interest involved, is in the best interest of the
2 Government. A waiver has been granted to Ms. Ellen
3 Rosenthal for her financial interest in the firm at issue
4 that could potentially be affected by the committee's
5 deliberations. The waiver permits this individual to
6 participate in all general matters before the committee.

7 Copies of this waiver may be obtained from the
8 Agency's freedom of information office, Room 12A-25 of the
9 Parklawn Building.

10 We would like to note for the record that the
11 Agency took into consideration a certain matter regarding
12 Dr. Barbara Goldsmith. Dr. Goldsmith reported interests in
13 a firm's at issues on matters not related to what is being
14 discussed today. Since these matters are not related to the
15 specific matters before the committee, the Agency has
16 determined that she may participate in the committee's
17 deliberations.

18 In the event that the discussions involve any
19 other products or firms not already on the agenda for which
20 the FDA participant has a financial interest, the
21 participants should exclude themselves from such involvement
22 and their exclusion will be noted for the record.

23 With respect to all other participants, we ask in
24 the interest of fairness that all persons making statements

1 or presentations disclose any current or previous financial
2 involvement with any firm who's products they may wish to
3 comment on.

4 Now I will turn the meeting over to our
5 Chairperson, Dr. Henry Nipper.

6 DR. NIPPER: Thanks. I am Henry Nipper and I'm
7 affiliated with Creighton University. I'd like to go around
8 the room again and have the panel introduce themselves to
9 those people in the audience. We're glad to have Dr. Robert
10 Habig with us today. We'd like Dr. Habig to start with
11 introducing himself, and we'll proceed around the room to
12 Ms. Rosenthal.

13 DR. HABIG: Good morning. I'm Robert Habig. I am
14 the Director of Corporate Regulatory Affairs at Becton
15 Dickinson and Company. I am the non-voting industry
16 representative on this panel.

17 DR. TONG: Good morning. I'm Ted Tong. I'm a
18 member of the FDA Non-Prescription Drug Advisory Committee.
19 I'm here this morning and afternoon as a consultant to the
20 panel. I'm a Professor of Pharmacy Practice, Pharmacology
21 and Toxicology at the University of Arizona in Tucson,
22 Arizona.

23 DR. GERSON: Benjamin Gerson. I'm on the faculty
24 of the Boston University School of Medicine.

1 DR. MANNO: Barbara Manno. I'm from the Louisiana
2 State University Medical Center in Shreveport, Louisiana.
3 I'm a Professor in the Department of Psychiatry and Co-
4 director of the Clinical Toxicology Lab of the University
5 Hospital at that facility. I am a consultant to the
6 committee and I am a forensic toxicologist.

7 DR. KURT: Good morning, I'm Tom Kurt. I'm a
8 Medical Toxicologist and a Professor at the University of
9 Texas Southwestern Medical Center in Dallas. I'm also a
10 former FDA medical officer.

11 DR. HARRINGTON-FALLS: Good morning. I'm Dr.
12 Beverly Harrington-Falls, Ob-Gyn with Cornerstone Health
13 Care in High Point, North Carolina and a panel member.

14 DR. GUTMAN: I'm Steve Gutman and I'm the Director
15 of the Division of Clinical Laboratory Devices.

16 DR. BOUGHMAN: Joann Boughman, Professor and
17 Geneticist at the University of Maryland. Also Vice
18 President for Academic Affairs and Dean of the Graduate
19 School and a regular panel member.

20 DR. EVERETT: I'm James Everett, physician and
21 Medical Director at Morehouse School of Medicine in Atlanta,
22 Georgia.

23 DR. LEWIS: Good morning, again. I'm Sherwod
24 Lewis, Director of Toxicology at the Office of the Chief

1 Medical Examiner, State of Connecticut.

2 DR. REJ: Good morning, I'm Bob Rej. I'm on the
3 faculty of the School of Public Health, the State University
4 of New York at Albany, and Director of Clinical Chemistry,
5 Toxicology and Hematology at the New York State Department
6 of Health in Albany. I'm a regular voting member of this
7 panel.

8 DR. GOLDSMITH: Good morning, I'm Barbara
9 Goldsmith. I'm a voting member of this panel. I'm also the
10 Associate Director and the Interim Director of the
11 Department of Laboratory Medicine at St. Christopher's
12 Hospital for Children in Philadelphia and an Associate
13 Professor of Pathology and Laboratory Medicine at Allegheny
14 University of the Health Sciences.

15 DR. SOHN: Good morning, I'm David Sohn. I'm
16 Associate Laboratory Director and Director of Toxicology and
17 Forensic Toxicology at Beninger & Schlesinger Medical
18 Laboratories in New York City.

19 MS. ROSENTHAL: Good morning, I'm Ellen Rosenthal.
20 I'm an engineer. I'm the consumer representative to this
21 panel.

22 DR. NIPPER: Thank you. As you can see, we have a
23 wide variety of experience and affiliations on the panel and
24 consultants today.

1 It's time now to call for speakers to the open
2 public session. At this time, we will hear from public
3 attendees who have contacted the executive secretary prior
4 to the meeting. These people, who will address the panel
5 and present information, will do so relevant to the agenda
6 of the meeting.

7 At this time, we will remind speakers that they
8 will be asked to state whether they have any financial
9 involvement with manufacturers of any products being
10 discussed or with their competitors. If you, somehow or
11 other, forget to do that, please don't be offended if I
12 interrupt and ask you to tell us that.

13 At this point, the first speaker on the list is
14 Vana Smith whose affiliation is stated as Abbott
15 Laboratories. Ms. Smith?

16 MS. SMITH: I represent a manufacturer of drug
17 testing products. We are a leading manufacturer of both
18 drug testing reagents and instruments. We are also a
19 leading manufacturer of rapid diagnostics used by consumers,
20 hospital laboratories and physician's offices.

21 On the basis of our years of experience in these
22 areas, we would like to offer our recommendation to the
23 committee concerning the labeling for the home use drug test
24 and recommend that confirmation is needed for a lay user to

1 be able to interpret and understand any positive drug
2 testing result.

3 To address the question in the points to consider,
4 can the product be labeled in such a manner that a lay user
5 will have net beneficial information from the use of the kit
6 in the over-the-counter setting? We believe this is more
7 than an issue of labeling. The complexities in the
8 interpretation of drug testing may be extremely difficult to
9 explain with labeling.

10 When a non-drug user is drug tested, the
11 laboratory confirmation procedure provides assurance they
12 will not be falsely accused of being a drug user.
13 Protection from that false accusation and the consequences
14 to their family and their livelihood is what gives the non-
15 drug user assurance that it's a quality drug testing program
16 and reliable.

17 Outside the DHHS programs confirmation is not
18 required. As such, the interpretation of drug screening
19 results can often be problematic. As you know, cross
20 reactive substances can be found in many over-the-counter
21 drugs and health food supplements. Due to the controversial
22 nature of drug testing, rumors and half-truths about drug
23 testing abound in society, propagated by word of mouth, the
24 local newspaper and the Internet.

1 In my own seven-and-a-half years supporting drug
2 testing products for Abbott Laboratories, I cannot count the
3 number of times that I have dealt with questions regarding
4 poppy seeds, prescription drugs, health food supplements and
5 the like, even from the laboratory professional.

6 Interpretation of unconfirmed positive results and
7 cross reactivity can be difficult today, but would be
8 extremely challenging for the lay user. When using a simple
9 over-the-counter diagnostic product, such as a pregnancy
10 test, the lay user knows what to do if the test is positive.
11 In most cases, that means self-referral to their family
12 physician. However, the lay user will need substantially
13 more guidance than labeling to interpret a home drug
14 screening result.

15 In order for a lay user to obtain beneficial
16 information from a home use drug test, confirmation of the
17 result is necessary.

18 To summarize, we would recommend that in a home
19 drug testing model, confirmation is required for a lay user
20 to be able to interpret and understand any positive drug
21 testing result. Thank you.

22 DR. NIPPER: Thank you. We have about a minute
23 for questions of this speaker from the panel, if there are
24 any.

1 [No response.]

2 DR. NIPPER: Seeing no questions, thank you, Ms.
3 Smith. I appreciate our first speaker staying within the
4 five minute limit. I'm not sure whether the personnel who
5 are handling the visual aids are going to use the timer
6 that's up there to help me keep on track, but I sure would
7 appreciate if you would.

8 Our next speaker, I hope I get the first name
9 right, Niquette Hunt. Please correct me if I make a
10 mistake.

11 MS. HUNT: Niquette, so you're pretty close.

12 DR. NIPPER: It's easier than I thought, thank
13 you.

14 MS. HUNT: Good morning. My name is Niquette Hunt
15 and I'm from ChemTrak, the manufacturer of Parent's Alert
16 Home Drug Test Service, the one originally developed by
17 Sunny Cloud, who you'll hear from right after me.

18 Earlier this year, Parent's Alert and ChemTrak
19 joined forces to make our product available to a broader
20 national audience. We believe that quality tests, used
21 correctly, are a critical component in helping parents stand
22 between their children and drugs. As such, they should be
23 accessible to all families.

24 However, as a manufacturer, we have the

1 responsibility to provide the best test service possible,
2 adhering to the highest standards. In this case, this
3 includes the gold standard lab test, which is currently
4 GC/MS, followed by informative results reporting.

5 We support the points to consider document as it
6 relates to rapid tests, as it establishes strict guidelines
7 for these tests that we believe will benefit consumers.
8 Because parents have a right to expect that the product they
9 bring into their homes are reliable and don't open more
10 questions in the family unit than they answer.

11 The fact is, drug use among kids continues to
12 rise. That sounds scary, but how does it affect you and me?
13 Families just like yours and families just like mine?
14 Unfortunately, good children from good homes who live in
15 nice neighborhoods use drugs. The problem is not one
16 limited to the inner city. 60 percent of the problem occurs
17 in suburbs, many of them affluent suburbs. And it gets
18 worse, unfortunately, particularly among younger children.

19 Consider these statistics: one out of every four
20 nine to 12 year-olds were offered drugs last year. 24
21 percent of all 12-year-olds have a friend or classmate who
22 used LSD, cocaine or heroin. The greatest increase in drug
23 use comes between the sixth and seventh grades. In most
24 cases we're talking about 11 and 12-year olds here.

1 But there is good news. Children who learn about
2 the risks and consequences of drug use from their parents
3 are half as likely to try drugs. That's half as likely.

4 We believe that prevention is the answer to our
5 nation's drug problem, and prevention begins at home, in the
6 family, with proactive parents. Parents who are willing to
7 take the steps necessary to stand between their children and
8 drugs. And that's where we believe a home drug test service
9 can play a role.

10 We believe that there are three important elements
11 that should be included in every test service: educational
12 materials, professional counseling, and an accurate test.
13 Specifically, educational materials give parents a better
14 understanding of the drug problem and the risks their
15 children face.

16 Second, trained counselors offer parents a
17 perspective about the overall drug problem, their child's
18 specific results, and can give referrals to local resources
19 if necessary.

20 The third piece is a drug test that includes both
21 screening and confirmation, using the most technically
22 accurate methods available.

23 We also believe that this test should be done in
24 labs approved by SAMHSA, the Substance Abuse and Mental

1 Health Services Administration, because of SAMHSA's high
2 standards. Each sample should also be checked for additives
3 or dilutants to ensure that it wasn't tampered with. And
4 after testing, each result should receive a final check from
5 a scientist to ensure accuracy one last time before it goes
6 to the parents.

7 Designed with these elements in place home drug
8 test services can make a difference. They can help parents
9 stand between children and their drugs. We've seen it
10 happen through Sunny Cloud and the numerous parents she's
11 helped with her test service.

12 Based on our current understanding of rapid in
13 vitro home drug devices, we have some concerns about using
14 these devices in the homes. Specifically, can these tests
15 provide confirmed results as accurate as those provided by
16 the GC/MS? Can these devices be labeled in such a way to
17 help parents understand the difference between a screening
18 test and a confirmatory test, and the need to follow up the
19 first with the second?

20 Are these tests able to detect attempts to skew
21 results? Or are they able to differentiate between illegal
22 drugs and common over-the-counter medications?

23 Once parents have their screening results, will
24 they be motivated to seek out the vital confirmatory testing

1 and importantly, delay their reactions while they wait for
2 these confirming results? Can these tests provide parents
3 with enough perspective around the test results to minimize
4 chances for misinterpretation?

5 We do not believe it is responsible to accept and
6 support rapid tests until these questions have been
7 answered. Because at the end of the day, our only goal is
8 to provide parents with high quality products. Products
9 that, in this case, will help them truly stand between their
10 children and drugs.

11 Thank you very much for your attention.

12 DR. NIPPER: Thank you. Your time is up because
13 the little light blinked. I appreciate your presentation.

14 Our next presenter is Sunny Cloud. Ms. Cloud,
15 welcome to the panel.

16 MS. CLOUD: Thank you very much, I appreciate it.

17 My name is Sunny Cloud. I am the founder of
18 Parent's Alert and a consultant for ChemTrak in California.

19 I appreciate the opportunity to address the panel
20 today. I'm a single mother of teenage sons and the founder
21 of Parent's Alert, as I mentioned. Parent's Alert is a
22 complete home collection drug test service.

23 I also was an ostrich, with my head in the sand. L
24 Let me explain.

1 Several years ago, I came home unexpectedly one
2 day to find my son smoking marijuana in our living room. I
3 was completely shocked. Up to that moment, I never even
4 considered that my kid would ever use drugs. He was a good
5 kid. He made decent grades and he had nice friends. He
6 wasn't like those other kids, the ones that use drugs. Or
7 so I thought.

8 That was my mistake. The truth is, he was exactly
9 like many of the other kids and I was exactly like most of
10 the other parents. We all had our head in the sand.

11 I reacted the way most parents react when the
12 well-being of their child is threatened. I took him to a
13 doctor, in this case the emergency room, for a drug test.
14 That experience proved to be costly and embarrassing for
15 both of us.

16 Then I attended counseling sessions with my son.
17 It was there that I had an interesting thought. We parents
18 are expected to get our kids help for drug abuse only after
19 the use has been discovered. We have to react to a bad
20 situation. Why can't we be more proactive and hopefully
21 prevent the abuse in the first place?

22 So I began to look around. I found two examples
23 in our society that had shown success in reducing drug use,
24 the workplace and the military. These two examples shared a

1 common denominator, they both drug tested. I set about
2 learning as I could about what was going on in the testing
3 industry.

4 I learned about various types of tests being used
5 in the workplace, and laws governing those workplace
6 testings. I learned that the very best test, the gold
7 standard of all tests, is the GC/MS. I also learned about
8 rapid test in vitro screens that some employers are using.

9 In the workplace, these screens are very helpful.
10 They're effective because if a screen comes up positive the
11 employer, by law, has to forward the specimen to a SAMHSA
12 approved lab for the GC/MS confirmation. Those results are
13 then reviewed by a scientist, forwarded to a medical review
14 officer, and only then are they forwarded on to the
15 employer.

16 An idea began to form. If parents had access to
17 the very same types of tests used in most of the workplaces,
18 we might be able to stand between our kids and drugs. And
19 our kids could use the test as an excuse to say no. A child
20 could say my parents have a drug test at home, I can't.
21 That could be a very effective deterrent to peer pressure.

22 Parent's Alert was born. I set up a program to
23 offer parents the capability of drug testing their child in
24 the privacy of the home. The service incorporated the most

1 accurate and reliable test with assurance of professional
2 review of all results. You know, it isn't easy to decide to
3 bring a drug test into your home. But one thing is for
4 sure, to protect your child and your relationship with your
5 child, the test you use must be the right one.

6 Ignoring warning signs of drug use, sticking your
7 head in the sand, can be a dangerous approach for parents to
8 take. Parents need to expect that if they do decide to use
9 a drug test in their family drug policy, it's a reliable
10 test.

11 I'm just a mom. Some of you probably have kids,
12 too. We all face the same problems. For example, what
13 would you do if during the height of the cold and flu season
14 your teenager come home a little hyper, maybe seems a little
15 spacey one day. You get concerned and you pull out a
16 dipstick or a slide test. After a few minutes, the strip
17 shows positive for amphetamines.

18 You panic. You remember she went to a party two
19 nights ago and came in past curfew. You ask her and she
20 says she's been taking Sudafed for a head cold. What would
21 you believe? How can you know for sure? Would you, the
22 concerned parent, be able to hold your reaction for several
23 days while a confirmatory test is being run? I don't think
24 I could and I've been through it before.

1 I've spoken to thousands of parents around the
2 country over the last few years. Know how many of them have
3 questioned the reliability of a drug test they've purchased
4 from Parent's Alert? Not one. They take it for granted?
5 Why? In my opinion that when you learn that your child has
6 a positive test result, there are so many other things going
7 on in your mind, it doesn't even occur to you that the test
8 might be wrong. With all the other issues involved at that
9 time, aren't we parents entitled to at least that? I can't
10 imagine a worse thing than to confront your child on the
11 basis of just a screening test, only to have your child be
12 innocent.

13 I'm here today because I want to be sure that
14 parents can depend on the results they get from any drug
15 test they may use. So they can use the test productively to
16 build trust with their children rather than break it down by
17 taking a chance of accusing them unfairly.

18 Drugs are everywhere. I'm afraid for our
19 children. We parents need every tool we can get to help
20 keep our kids off drugs, or identify a potential drug
21 problem early, to get help as soon as possible. But the
22 tools must be reliable. The results must be as certain as
23 possible.

24 I ask the members of this panel, and people in

1 this hearing today, if it was your child, would you want a
2 test that gave a screening result at home which would
3 require you to hold your reaction for several days? Or
4 would you prefer a definite answer with the assistance of
5 trained personnel to help you understand these results?

6 I think the answer is obvious. Let us ensure that
7 only accurate, reliable and understandable home drug tests
8 are made available to parents. Our kids deserve it.

9 Thank you.

10 DR. NIPPER: Thank you, Ms. Cloud. Since the time
11 has elapsed, we'll hold questions until the end. Thank you.

12 Our next speaker is Dr. Howard Taylor from Sensor
13 Technologies. Dr. Taylor?

14 DR. TAYLOR: Good morning. My name is Dr. Howard
15 Taylor. I'm a Ph.D toxicologist, board certified by the
16 American Board of Forensic Toxicology, and also the American
17 Board of Clinical Chemistry with a specialty in toxicology.

18 I've been active in the field of drug testing for
19 over 15 years, with experience as a responsible person in a
20 SAMHSA certified laboratory. And I also serve as inspector
21 for the National Laboratory Certification Program, which is
22 the group which certifies SAMHSA laboratories for Federal
23 workplace testing.

24 Earlier this year, the FDA proposed guidelines for

1 testing in the over-the-counter or home drug testing
2 environment. Those requirements were one, testing in a
3 SAMHSA certified laboratory. Two, use of an FDA approved
4 immunoassay technology with confirmation by GC/MS. Three,
5 use of a unique identifier of a sample.

6 These protocols mirror the requirements for
7 workplace drug testing, to ensure the accuracy and
8 reliability of testing. These components are essential to
9 the quality of workplace testing and over-the-counter drug
10 testing requires these same standards to guarantee the
11 accuracy of testing. Anything less is providing a
12 disservice to the public.

13 The Drug Testing Advisory Board, DTAB, which
14 advises SAMHSA for Federal workplace drug testing is
15 wrestling with many issues related to the accuracy of on-
16 site testing devices. I would like to submit to the FDA a
17 copy of a summary of those issues entitled factors required
18 for reliable workplace drug testing discussed at the recent
19 DTAB meeting. And also, a copy of Dr. Robert Willette's
20 presentation, testing for alcohol and drugs, on-site
21 approaches.

22 It is well known that false positives from
23 structurally similar compounds are produced if using
24 immunoassay as a stand-alone test.

1 How would a parent handle a false positive from an
2 on-site test device? Would the parent send the specimen on
3 for GC/MS confirmation? Would the child or donor have been
4 falsely accused as a drug user?

5 The proposed draft document points to consider for
6 approval of home drug tests, dated August 25, 1997 and later
7 revised on September 16, 1997, asks two key questions. Can
8 the lay user obtain acceptable analytical results? Two, can
9 the product be labeled to assure that net beneficial
10 information is attained from the use of the kit in the OTC
11 setting?

12 If on-site immunoassays are used, I believe the
13 answer to the first question is no. If on-site devices are
14 currently not acceptable for Federal workplace drug testing
15 programs, and top scientists in the country have questions
16 relating to the accuracy and reliability of these devices as
17 described above, how can the lay user obtain acceptable
18 analytical results?

19 The answer to the second question is more complex.
20 How does a parent reverse damage done by a false positive
21 on-site device? Since the positive predictive value is
22 significantly lower in an on-site device versus a test
23 performed in a SAMHSA lab, the public will be at significant
24 risk. On-site devices may be appropriate for the OTC

1 environment at some point in the future, once these issues
2 are addressed for Federal workplace drug testing programs to
3 ensure the same quality of testing which is currently
4 performed in a SAMHSA certified lab.

5 I urge the FDA to maintain the highest quality of
6 testing possible in the over-the-counter and home testing
7 environment by relying on the currently most accurate and
8 reliable techniques available which are testing in a SAMHSA
9 certified lab and assuring the public of the same quality
10 standards currently used in the workplace testing.

11 Thank you.

12 DR. NIPPER: Thank you very much. There's about a
13 minute left for questioning from the panel, if there is any?

14 [No response.]

15 DR. NIPPER: Seeing none, thank you, Dr. Taylor.

16 Our next presenter is Robert Aromando, Jr. from
17 Roche Diagnostic Systems.

18 MR. AROMANDO: Good morning, Mr. Chairman.

19 Roche Diagnostic Systems, a subsidiary of Hoffman-
20 LaRoche, is dedicated to improving human health care by
21 developing, manufacturing, and marketing diagnostic test
22 kits, reagents and analytical instrumentation used in
23 hospitals, clinical laboratories, physicians offices, and in
24 alternate sites as required to screen for substance abuse.

1 The field of toxicology and specifically drug
2 abuse testing is a specialty in which RDS has over 20 years
3 experience. Both Hoffman-LaRoche and RDS are strong
4 proponents of a drug-free America and believe drug testing
5 plays a vital role in the responsible management of the
6 problem of drug abuse in our environment.

7 There's no doubt that drug use in this country has
8 reached epidemic proportions. Recent surveys indicate that
9 teenage drug use, in particular, is escalating at alarming
10 rates. A survey conducted in 1996 by the University of
11 Michigan among 50,000 students showed marijuana use among
12 10th graders increased from 17.2 percent to 20.4 percent.

13 The Pride Survey, conducted also in 1996 polled
14 129,000 students in 26 states. The study showed more
15 students reported getting "very high, bombed or stoned"
16 during the past school year. And 18.3 percent of the
17 students reported using an illicit drug weekly or more.
18 This increase in drug use by teenage students has forced
19 educational institutions to revise their anti-drug programs
20 to now include some form of drug testing.

21 The majority of parents support school drug
22 testing programs where appropriate and believe a higher
23 level of success in solving the problem of drug abuse can be
24 accomplished through at-home testing with results

1 immediately available. This would afford parents the
2 opportunity to deal directly with the problem in confidence
3 and, more importantly, within the confines of the home and
4 the family.

5 A test result under this circumstance would
6 optimize the rehabilitation process with immediate
7 intervention because it quickly addresses and overcomes the
8 denial phase of drug addiction.

9 Current tests approved by the FDA do not allow for
10 immediate assessment of an individual's drug use status.
11 Rather, a hair or urine sample is sent to the lab for
12 processing, which may take several days for a result to be
13 completed.

14 Roche offers a number of drug testing products
15 based on various technologies for the detection of illicit
16 drug use. Among our product lines include Ontrack TesTcup
17 which utilizes a simple yet proven technology, similar to
18 many home urine pregnancy tests.

19 Ontrack TesTcup provides an immediate result
20 within three minutes, highly accurate, qualitative
21 assessment of whether the testing subject has ingested any
22 of five illicit drugs with a simple yes or no, positive or
23 negative result, and requires minimal operator skills and
24 interpretive judgment. TesTcup combines the specimen

1 testing collecting and testing for multiple drugs into a
2 single device.

3 Three versions of TestCup have received clearance
4 from the U.S. Food and Drug Administration for commercial
5 distribution as a medical device, and utilize cutoff
6 detection levels identical to those mandated to those by
7 SAMHSA.

8 Roche believes that the Ontrack TestCup can play
9 an important role in helping parents detect and address
10 teenage drug use in a safe and effective manner.

11 Roche also clearly supports the need for FDA
12 supervision and regulation of products offered for at-home
13 screening of drug abuse. In fact, Roche applauds the FDA's
14 recent draft of points to consider for approval of home
15 drugs of abuse test kits, which suggests that marketing of
16 such a test may be permitted utilizing a 510(k).

17 We strongly feel that products such as TestCup
18 which have already undergone the scrutiny of the FDA for use
19 by professionals should not be held to standards of a pre-
20 market approval submission.

21 We feel this way for the following reasons: the
22 Ontrack TestCup is not unlike home pregnancy kits or home
23 glucose tests, both of which are currently regulated by the
24 pre-market notification, i.e. 510(k), regulations rather

1 than a pre-market approval process.

2 When performed in a management of probation,
3 parole, prison, drug and alcohol rehabilitation or
4 management of workplace policies, drug abuse screening
5 provides detection of drug or alcohol use. It does not
6 assess disease, immediate impairment, or other health
7 related diagnosis requiring medical judgment or treatment.

8 Drug abuse testing is also qualitatively different
9 from testing for purposes of treatment or diagnosis. This
10 is because the individual being tested is fully aware of
11 what the outcome of the test should be. The principles of
12 diagnosis are there. They are therefore irrelevant for this
13 type of testing.

14 The Ontrack TestCup has already undergone FDA
15 scrutiny and review of its safety and efficacy several times
16 in the last three years. Although the intended audience for
17 an OTC product is non-technical, the current users of
18 TestCup have similar levels of technical skills. TestCup is
19 marketed to criminal justice agencies, workplace,
20 educational institutions, and drug treatment centers. The
21 actual operators of these tests do not typically have
22 laboratory skills or training.

23 Also, users of home pregnancy or glucose tests
24 fall into the same category as the intended home users of

1 TesTcup.

2 The FDA's concern over the safety and efficacy of
3 TesTcup in the hands of a home user can be wholly addressed
4 through a special clinical trial with a sample of the target
5 audience. Roche has offered to do such clinical trial and
6 stands ready to work with the FDA to establish a mutually
7 agreed upon study protocol. However, the pre-market
8 approval process is not necessary to achieve this objective.

9 The PMA regulations require the manufacturer to
10 submit extensive and detailed records on manufacturing and
11 quality control. There is no logical reason to require such
12 information for products utilized by one user but not
13 another, particularly when the products used for both are
14 identical in manufacturing design, processes, and controls.

15 To impose PMA categorization of TesTcup for the
16 OTC market will merely delay the availability of this needed
17 product to parents and cause undue and unnecessary expense
18 to the manufacturer without any resulting benefit to the
19 public or the regulatory agencies.

20 The FDA's position to regulate pre-reviewed
21 products, such as Ontrack TesTcup, via the PMA regulations
22 is particularly irksome in light of the exception and
23 exemption granted by the Agency to a provider who has
24 undergone absolutely no review or approval for safety and

1 efficacy.

2 The point-of-care Saliva Alcohol Test marketed by
3 Sunny Cloud, in fact, was cleared via a 510(k) process not
4 PMA. It seems that if the FDA's concern was truly with the
5 American public, political compromises such as this one
6 would not be acceptable.

7 Today, as we speak, parents may obtain drug
8 testing results on their children from a supplier who has
9 filed no data, manufacturing or clinical, to support their
10 presumption of safety and efficacy for use by anyone,
11 whether professional or non-technical.

12 However, at the same time we are here discussing
13 whether a product which has undergone review by the FDA
14 three times in the last three years, and has each time been
15 deemed safe and effective, should be required to comply with
16 unduly stringent and non-value added regulatory
17 requirements.

18 To reiterate, Roche is not here proposing that our
19 product be excluded from review and regulation, as Sunny
20 Cloud and her testing currently are. We have proposed and
21 stand by our offer to work closely with the FDA to design a
22 clinical study which would prove that Ontrack TestCup can be
23 used safely and effectively by a typical consumer. We are
24 merely requesting that unreasonable and onerous regulatory

1 requirements not be imposed without any concomitant benefit
2 to the American public.

3 We request the FDA permit Roche to submit a 510(k)
4 amendment of its current filing with the appropriate
5 clinical data, labeling, and other reasonable information to
6 support OTC use of Ontrack TestCup.

7 Thank you.

8 DR. NIPPER: Thank you very much. May I reiterate
9 to speakers to please remain within the five minute time
10 frame?

11 Our next speaker is Dr. David Evans of the
12 National On-Site Testing Association.

13 MR. EVANS: Good morning, I'm David Evans. I'm an
14 attorney, not a doctor. I thank you for the promotion,
15 though.

16 I have submitted written testimony and I don't
17 want to go over my written testimony. I'd like to just
18 clear up some points that have been raised by some of the
19 earlier speakers.

20 Let me first of all tell you who the National On-
21 Site Testing Association is. We are an association of the
22 consumers, manufacturers, and distributors of on-site
23 alcohol and drug tests. As far as drug tests go, we only
24 recommend drug tests that have been cleared by the FDA. All

1 of our members use FDA cleared drug tests.

2 We are in favor of good standards, good drug
3 testing standards. We are in favor of good science. And I
4 think you will find that anybody that's a member of NOTA
5 that is a manufacturer has the science to back up their
6 product.

7 I'm also a parent. I would urge you, before you
8 make a decision about this, to go to schools like I do and
9 talk to kids about drug abuse and find out what's going on.
10 It is worse than it was in the '60s. Take my word for it.

11 I have talked to ninth graders in my county about
12 marijuana and cocaine and other issues. When I go and give
13 the talks, I only talk to them about scientific studies that
14 have been done and give them good information. I've come
15 away profoundly depressed about what I've seen.

16 So get some information, get some education on
17 that issue before you make a decision about this issue.

18 On-site tests that are cleared by the FDA meet the
19 scientific standards. Dr. Taylor talked earlier about how
20 HHS is not approving them for use in Federal drug testing
21 programs. That's absolutely untrue.

22 If you'll read the regulation, he'll see that the
23 only requirement for an initial immunoassay screen is a test
24 that's been cleared by the FDA. What's confusing him is

1 that all of the tests on the Federal level have to be done
2 in a laboratory. A laboratory can use--a SAMHSA laboratory
3 can use one of our on-site tests as the initial immunoassay
4 screen. It's perfectly legal.

5 Half of the hospitals in the United States that
6 are doing drug testing of patients are using on-site tests.
7 So if it's good enough for half the hospitals, it's good
8 enough for the Federal Government.

9 What we're talking about right now, with HHS, is
10 to allow on-site testing be done outside of a laboratory
11 setting, and they are giving it a very serious
12 consideration. They have set up standards for us to meet,
13 and we feel we can meet all those standards. And we feel
14 ultimately that on-site testing will be approved.

15 What do we recommend about over-the-counter use?
16 We are concerned about the impact that this will have on
17 consumers, and particularly on parents. I guess I differ a
18 little bit from Ms. Cloud in that I would like to trust
19 parents more to make good decisions about their children. I
20 feel parents need information.

21 You know, if my kid was on Sudafed, I'd want to
22 know that. If a drug test would show that to me, I'd like
23 to know that. Prescription drugs can be abused, non-
24 prescription drugs can be abused. Most kids are using

1 marijuana and cocaine. The chance of a false positive on
2 marijuana and cocaine on an on-site test is pretty small.

3 I'd like to know everything my kids are doing.
4 Any drug that goes in their body, I'd like to know about it.

5 I think parents can be trusted. I think if you
6 give them clear guidelines, this is one of the things that
7 NOTA recommends, is that they should be informed through a
8 clear package insert, written for the seventh grade reader,
9 providing them with information on what does a negative
10 result mean. Instead of a positive result, I think we would
11 want to call it an indeterminate result, meaning that you
12 should get further information before you talk to your child
13 about it.

14 We recommend an 800 hotline number that parents
15 can call in, where they can get information, where they will
16 be referred to a local physician. A physician who, by the
17 way, is experienced in substance abuse problems. They can
18 be referred to a local substance abuse professional. And
19 they can get other information on what the test actually
20 means.

21 We do recommend confirmation. Not all parents,
22 though, are going to be able to pay the amount of money that
23 is going to be necessary to do all of that. That's why we
24 like the idea of on-site tests because at least they will

1 give you a negative right away. And in most cases, it's
2 going to be negative.

3 A parent can spend a couple of dollars, get a
4 negative result, get the peace of mind. If you have to send
5 everything to a laboratory before you get an answer, it's
6 going to be more expensive. I don't know what Ms. Cloud's
7 tests cost, but there are a lot of parents that even can't
8 afford \$25, \$30, \$35. Some of these on-site tests go for a
9 couple of dollars and at least will give you a negative
10 result. Then if it's indeterminate, the parent then can
11 decide whether to spend the extra money in getting a GC/MS
12 confirmation.

13 We are in favor of education. We have found that
14 employers are having no trouble using on-site tests. They
15 are used in hundreds of workplaces around the United States.
16 We're not seeing court cases develop with people being
17 falsely accused. They're used in hundreds of probation and
18 parole offices around the United States. Again, we're not
19 seeing a whole bunch of false accusations coming up.

20 The most common response when somebody gets a
21 positive on an on-site test is what do you think it is? You
22 got me. Admission right on the spot. That is the most
23 common response that people get. If an employer then wants
24 to go out and get the test confirmed, by all means. But

1 there is ample case law now showing that if somebody admits
2 to it, then that is confirmation in itself.

3 I've kept to my time limit. I'll be happy to
4 respond to any questions the panel may have either now or
5 this afternoon. Thank you.

6 DR. NIPPER: We do have about a half a minute
7 left. Are there any questions?

8 [No response.]

9 DR. NIPPER: Thank you, Mr. Evans.

10 Our next presenter is Dr. Henry Wells and Diane
11 Boice-Yorck. I'm not sure who's going to do the first part?
12 Okay, you didn't flip a coin? Okay.

13 MS. BOICE-YORK: I'm Diane Boice-York and this is
14 Dr. Henry Wells and we are employees of American Bio Medica
15 Corporation. I'm going to read our presentation and he's
16 going to be here with me if there are any questions.

17 We, at American Bio Medica Corporation, developer
18 of the Rapid Drug Screen test, support the proposed draft
19 points to consider for approval of home drugs of abuse test
20 kits. We stand ready to meet or exceed all regulations as
21 proposed, confident that we can provide fast, accurate tests
22 for home use that will be easy for all to use and
23 understand.

24 We will provide the initial test for screening, as

1 well as a mechanism for low cost laboratory confirmation, as
2 your draft suggests. The screening device will include our
3 easy-to-follow directions and result guides and all sales
4 will be supported by our competent customer service staff,
5 ready to field any and all questions.

6 We have also addressed the matter of adulteration
7 of the urine sample by developing a simple adulteration test
8 designed to determine the presence of adulterants such as
9 acids or bases, aldehydes or dilution.

10 We wish to note, however, that we believe the
11 Substance Abuse and Mental Health Services Administration
12 recommendation for confirming 30 to 40 percent of all
13 negative test results, as referred to in Section I.A.6,
14 accuracy by comparison studies, is excessive. It is the
15 opinion of our clinical staff that confirmation of 10
16 percent of all negative results is adequate.

17 It is also the opinion of our staff that all
18 screening results should be classified negative or
19 indeterminate, in need of laboratory re-analysis, as opposed
20 to positive or negative.

21 Speaking not only as an American Bio Medica
22 Corporation employee but also as a parent facing the daily
23 trials of raising teenagers in the '90s, I implore you to
24 move forward with over-the-counter drug test sale

1 regulations. I have used the tests. I know how simple they
2 are to use and to read. Let's get them in the homes and
3 take yet another step in the march against drug abuse.

4 And I'd like to add one other thing that wasn't
5 part of my prepared speech, but listening to everyone speak,
6 I just wanted to share something that happened in my past.
7 Everyone is concerned about parental reaction to a drug
8 test. Last winter I was faced with a 16-year-old daughter
9 who was exhibiting bizarre behavior, losing weight rapidly
10 and went from a high honor student to a failing student.

11 Working at this facility, I was able to bring home
12 a drug test. I put it in the middle of the table and I said
13 Amanda, we have to talk. It's time for the truth. We never
14 had to use that test. In my case, the problem turned out to
15 be an eating disorder.

16 But it was that test that was the catalyst that
17 opened up the communication that finally revealed what the
18 problem was. I think many parents would be happy to have
19 such a catalyst to open up the communication between their
20 children and themselves. Thank you.

21 DR. NIPPER: Thank you. We have a few minutes for
22 questions, if there are any.

23 [No response.]

24 DR. NIPPER: Thank you very much for your

1 presentation.

2 MS. BOICE-YORK: Thank you for the opportunity to
3 speak.

4 DR. NIPPER: Our next presenter is Sue Stevens
5 from CASCO Standards.

6 MS. STEVENS: Good morning. I'm Suzanne Stevens
7 from CASCO Standards and we are a manufacturer of on-site
8 drug of abuse testing. I'd like to say that primarily my
9 comments have been incorporated in the statement that was
10 prepared by NOTA, since we are members of the National On-
11 Site Testing Association. But I would like to make a few
12 points that were included in the NOTA statement.

13 On-site screens for drugs of abuse are a simple,
14 easy to use test for the presence of drug or drug metabolite
15 in a urine sample. They are currently in use in workplace,
16 treatment centers, correctional institutions, and hospital
17 laboratories where results are relied upon as the basis of
18 many critical decisions.

19 The reliability of these results of screening
20 tests is comparable to the automated laboratory methods that
21 are currently being used in the SAMHSA certified lab. This
22 is supported by many papers that have been published in the
23 clinical literature and clinical journals. Many of the on-
24 site drug screens are currently cleared for in vitro

1 diagnostic use by the Food and Drug Administration. As
2 such, they are manufactured to the highest quality standards
3 to ensure accuracy and reproducibility of the results.

4 In addition to the quality that is built in from
5 the manufacturing site, there is almost in most of these
6 tests a process control such as you would see in a home
7 pregnancy test, which insures the user that the process has
8 run smoothly and correctly, such that they know that they
9 have proceeded correctly and followed the package insert
10 instructions.

11 In conclusion, I would just like to say that the
12 availability of rapid and reliable drug screens may be a
13 valuable tool in the struggle for a drug-free society. As a
14 parent that has also faced the issue of drug abuse by my
15 children, if I had had the ability to do the confrontation,
16 I think it would have made my decision and my life and my
17 children's life much easier, as well.

18 We do recommend the confirmation of presumptive
19 positive or indeterminate results because we know that there
20 may be the possibility for some interaction of over-the-
21 counter medications. I, too, would like to have had that
22 backup feeling that I could have had the ability to have
23 that at my disposal.

24 Thank you very much for your attention and the

1 opportunity to speak this morning.

2 DR. NIPPER: Thank you. Are there any questions
3 that the panel has for Ms. Stevens? Dr. Sohn?

4 DR. SOHN: Since we have time, could you please
5 tell us the analytes for which your screen screens?

6 MS. STEVENS: We have the microline screen for
7 drugs of abuse is currently available in many
8 configurations. The drugs that are available are the so-
9 called NIDA five, which is cocaine, opiates,
10 methamphetamines, cannabinoids, which is marijuana, and PCP.
11 We also offer tests for benzodiazepines, amphetamines, which
12 are the diet drugs, over-the-counter, we separate the two
13 from the abused methamphetamine and amphetamine.
14 Benzodiazepines and barbiturates.

15 DR. NIPPER: Thank you. Are there any other
16 questions from the panel from Ms. Stevens?

17 [No response.]

18 DR. NIPPER: Thank you, Ms. Stevens.

19 Our next presenter is Sandy Dews from Drug Test
20 Resources International.

21 MR. EVANS: Mr. Chairman, she had a family
22 emergency and will not be able to attend today and sends her
23 regrets.

24 DR. NIPPER: Thank you. I'm sorry for her

1 emergency.

2 The next person on the list is
3 Dr. Richard Roblin, Point of Care Technologies,
4 Incorporated. I hope I got your last name correct, Doctor.
5 Is it Roblin?

6 DR. ROBLIN: Roblin.

7 DR. NIPPER: Well, I had two choices and I made
8 the wrong one.

9 DR. ROBLIN: You're forgiven. Mr. Chairman,
10 members of the panel, my name is Dr. Richard Roblin. I'm
11 the Chief Scientific Officer at Point of Care Technologies,
12 Incorporated, located in Herndon, Virginia. I'm here today
13 to discuss the draft points to consider for approval of home
14 drugs of abuse test kits dated as revised September 16,
15 1997.

16 We are very much an interested party in the
17 outcome of your deliberations and in the guidelines to be
18 presented in the final points to consider document. Point
19 of Care Technologies is an emerging company whose focus is
20 the development and marketing of reliable, efficient, and
21 disposable screening and diagnostic products for use in the
22 home and at the point-of-care.

23 We believe strongly in developing products that
24 give individuals immediate, accurate and cost effective

1 information to help them make informed choices about
2 personal health issues. We are developing a program that we
3 believe will meet the needs of consumers who desire a drugs
4 of abuse screening test in the home with external laboratory
5 confirmation of positive or indeterminate screening test
6 results. The final guidelines in this points to consider
7 document will directly impact our ability to commercialize
8 such products for use in the home.

9 We would like to focus attention today on four
10 aspects of granting clearance to in vitro drugs of abuse
11 tests used in the home, as detailed in the draft points to
12 consider document. First, we endorse the concept that any
13 home drugs of abuse test might meet FDA criteria for safety
14 and efficacy. We believe that such products should give
15 consistent results when used as directed and that the
16 product's instructions should lead to reliable usage by a
17 reasonably defined average consumer.

18 That this approach can work successfully is
19 demonstrated by the widespread use of and reliable results
20 from in vitro home diagnostic tests for pregnancy. After
21 more than 10 years of use by consumers around the world,
22 home pregnancy tests have become valued products that
23 provide quick, affordable, and reliable information.

24 Second, we believe that home drugs of abuse test

1 products should include a direct and simple step to obtain a
2 confirmatory laboratory test in the event of a positive or
3 indeterminate screening test. They should also include a
4 wide variety of information resources that will encourage
5 and enable consumers and parents to respond constructively
6 to the test results with the aid of trained health
7 professionals. Thus, our planning for this area envisions a
8 program that is far more than just the physical means to do
9 the test.

10 Third, we support FDA's position on the
11 desirability of demonstrating that lay users can obtain
12 acceptable analytical results and adequate understanding of
13 the relevant drugs of abuse testing concepts. We agree that
14 that this could be assessed through an in-home testing study
15 and a consumer survey. We believe that it would be most
16 appropriate in a regulatory submission to compare the
17 results of the test as performed by average consumers with
18 the results of the same tests when performed by
19 professionals.

20 Finally, however, we believe that the current
21 guidelines draft should be more specific regarding the
22 definition of a statistically adequate number of consumers
23 who represent the target population. The diversity of the
24 American population, with regard to age, education, race and

1 regional variation makes the definition of an in-home test
2 group a topic on which reasonable statisticians may differ.

3 For a small company like ours, the substantial
4 costs of such an in-home trial require that an understanding
5 be reached in advance with the FDA that the study population
6 chosen would be considered statistically adequate. Since
7 other companies may be in the same position, would it not be
8 more cost effective for FDA to convene a group of
9 statisticians, perhaps with outside consultants, and define
10 and publish the characteristics of an acceptable population
11 sample for the purposes of this in-home drugs of abuse
12 testing study?

13 In conclusion, if a home drugs of abuse testing
14 program satisfies the conditions detailed in the draft
15 guideline, we believe that the American public will be able
16 to use such products safely and effectively. We hope that
17 these guidelines can be agreed on and promulgated in final
18 form soon, so that products of this time can be cleared by
19 the FDA and commercially marketed as quickly as possible.

20 Mr. Chairman and members of the panel, as parents
21 and family members, we're all aware of the terrible toll
22 from drug abuse in our schools, our workplaces and our
23 neighborhoods. By acting together in a timely and
24 expeditious manner, we can provide American consumers with

1 another important tool to fight the increasing use of drugs
2 in our country, particularly among our young people.

3 Thank you.

4 DR. NIPPER: Thank you, Dr. Brown. I think your
5 time is up and we'll reserve questions until the end if we
6 still have town. Our next speaker is Dr. Michael Wandell.
7 I'm sorry, I've gotten it out of whack, here. Our next
8 speaker is Dr. Brown. I apologize to Dr. Roblin and Dr.
9 Brown for making my notes in the wrong place.

10 Dr. Brown is affiliated with Personal Health and
11 Hygiene, Incorporated.

12 DR. BROWN: Thank you very much for having me.

13 I represent Personal Health and Hygiene and Dr.
14 Brown's Home Drug Testing System which to date, I believe,
15 is the only over-the-counter home drug testing system
16 approved by the Food and Drug Administration.

17 My position is somewhat mixed. I've been
18 listening to the presentations and there seems to be, in my
19 opinion, an over-emphasis on the testing, given the fact
20 that whether you're using an enzyme test at home or you're
21 using a GC mag spec, none of them are perfect. However, I
22 think we are obliged, by virtue of our responsibility to
23 look after the welfare of the consumer and adhere to their
24 sense of safety and effectiveness, to go with the best

1 that's available.

2 Right now, I would have to convey my opinion that
3 the laboratory testing, which uses the GC/MS as part of the
4 analytical process, is the best that we have available. I
5 think it is deceptively simple to believe that a substance
6 abuse problem and the analysis via an on-site test that
7 gives an immediate response appropriately addresses the
8 problem. It is just not that simple.

9 We believe that the FDA standards that we had to
10 adhere to, which forced us to look at all the various
11 options and consider even the most extreme theoretical
12 facets of substance abuse and a parent's reaction to finding
13 out that their test results, either positive or negative,
14 are important. However, once again, I do not think that
15 testing in and of itself is sufficient. I do believe that
16 there has to be a nurturing of the general population, at
17 this point, to make them more responsible, as it were, with
18 respect to taking on the whole issue of substance abuse and
19 assuming a responsibility for their children's involvement
20 and being aware of what sorts of things that they should be
21 attuned to with regards to their respective child's
22 involvement with substance abuse.

23 I don't think that a quick and easy two minute
24 analysis is going to do anything to encourage parents and

1 the lay population to start to assume the kind of
2 responsibility that I think only comes about with their
3 being more involved, having material, literature, as well as
4 the kind of professional support that we advocate is
5 necessary in order to start to make some inroads in terms of
6 this whole problem of substance abuse.

7 So in that respect, since I recognize that the on-
8 site test may very well not be perfect and at the same
9 standard that laboratory tests are, and that they may have
10 some value in that their better than just espousing slogans
11 and cliches, I don't think that at this particular time,
12 given the state of affairs with regards to the problem of
13 substance abuse and where we need to go in general, that the
14 emphasis should be placed on an on-site test. I think
15 there's an over-emphasis on testing at the expense of the
16 other components which are necessary for us to feel
17 responsible that we've done the right thing for the
18 interests of the general population and those parents and
19 individuals who are truly concerned about trying to
20 effectively address this problem.

21 Thank you.

22 DR. NIPPER: Thank you, Dr. Brown. We do have a
23 minute or so of Dr. Brown's time for questions, if there are
24 any? Dr. Sohn?

1 DR. SOHN: For the record, sir, would you indicate
2 those analytes for which you test?

3 DR. BROWN: Marijuana, cocaine, amphetamines,
4 methamphetamines, codeine, morphine, heroin, and PCP.

5 DR. SOHN: Thank you, sir.

6 DR. NIPPER: Thank you, Dr. Brown.

7 I see a person who wants to speak from the public
8 and I'm going to ask you to defer comments until after the
9 presentations.

10 Dr. Wandell, I will now call you to the podium and
11 I apologize again for my getting things out of order.

12 DR. WANDELL: Thank you. My name is Michael
13 Wandell. I'm Vice President and Chief Scientific Officer of
14 Home Access Health Corporation. On behalf of Home Access
15 Health Corporation, I'm pleased to be here today to
16 participate in this important discussion of the scientific
17 and regulatory issues regarding consumers drugs of abuse
18 test systems.

19 Home Access Health believes that the performance
20 standards should be established and maintained for all drugs
21 of abuse reagent systems destined for consumer use. Point-
22 of-care drugs of abuse test systems which provide results
23 directly to the consumer without professional intervention
24 or by a chemical confirmation be marketed only after

1 thorough review of a pre-market approval application, and
2 that the 510(k) track is appropriate for consumer use point-
3 of-care drugs of abuse test systems which require and
4 include medically directed interpretation to obtain results.

5 For those unfamiliar with Home Access Health, we
6 are currently the only manufacturer approved to offer a home
7 HIV-1 test system for consumer purchase over-the-counter.
8 The Home Access HIV-1 Test System provides consumers all the
9 materials needed to collect a dried blood spot sample, ship
10 it to a certified laboratory for analysis in a pre-
11 addressed/pre-paid mailer, receive their results and
12 emotional support by telephone from certified counselors 24
13 hours a day, seven days a week, and as appropriate, to be
14 referred to a health care professional in their locale.

15 Approved for marketing by the U.S. Food and Drug
16 Administration in July 1995, the Home Access HIV-1 Test
17 System is based upon the company's consumer telemedicine
18 platform which integrates home specimen collection
19 technologies, overnight shipment, processing in a certified
20 laboratory with FDA-approved--or in some cases released--
21 reagents and automated database compilation of user-reported
22 health factors with round-the-clock access to medically
23 directed and supervised counselors or other health
24 professionals.

1 To the lay person, the Home Access Health
2 telemedicine platform enables the consumer to conveniently
3 and confidently access medical testing services without the
4 necessity of visiting a doctor's office. Thereby, it
5 represents a significant breakthrough in health care
6 delivery. By providing the user with laboratory quality
7 diagnostic analysis for serious medical conditions, combined
8 with professional interpretation, it offers the individual
9 unprecedented control of their own personal health and well-
10 being.

11 Home Access Health believes that the products
12 being discussed here today, for home specimen collection and
13 testing of dependent minors for drugs of abuse, represent
14 methodologies which demand an approach similar to that
15 previously demonstrated as safe and effective for diagnosis
16 of HIV-1 infection. Home Access encourages the advisory
17 panel to consider, in conjunction with the scientific review
18 criteria for the assessment of in vitro diagnostic devices
19 for drugs of abuse testing, the benefits of products that
20 are made available under the auspices of medical oversight.

21 Integration of all of the system components, each
22 with its own quality control checks, reduces the possibility
23 of improper collection, analysis, or interpretation, as well
24 as increasing the potential for delivery of appropriate

1 health educational messages and/or health professional
2 referrals.

3 In consideration of point-of-care or instant test
4 products for home use, Home Access supports the
5 establishment of reasonable criteria for analytical
6 performance. In addition, we support the requirement of
7 prospective clinical studies designed to demonstrate
8 substantial equivalence with established laboratory methods,
9 with a condition of 510(k) release that post-marketing
10 surveillance studies be conducted to verify such performance
11 in actual use.

12 Given compliance to reasonable performance
13 standards of the reagent systems, that is sensitivity,
14 specificity, precision and accuracy, compliance to quality
15 systems regulations in all components of production, medical
16 oversight of the interpretation of results and the
17 appropriate counseling regardless of those results, these
18 products appear to raise no different or additional
19 questions of safety and efficacy.

20 In summary, one, Home Access Health Corporation
21 supports the Agency in establishing performance standards
22 for all drugs of abuse reagent systems destined for consumer
23 use.

24 Two, it also supports the notion that point-of-

1 care drugs of abuse tests, which provide a result directly
2 to the consumer without professional intervention or
3 biochemical confirmation, be marketed only after a thorough
4 review of pre-market approvals or product development
5 protocols.

6 And three, that Home Access Health endorses the
7 510(k) as the appropriate regulatory track for consumer
8 point-of-care drugs of abuse test systems which require and
9 include medically directed interpretation to yield results
10 and provide guidance to consumers for appropriate use of
11 those results.

12 DR. NIPPER: Thank you. I think we have a couple
13 of seconds for questions, if there are any.

14 [No response.]

15 DR. NIPPER: Seeing none, thank you, Dr. Wandell.

16 Our last speaker on the list is Dr. Stuart Bogema
17 from Forensic Testing, Incorporated.

18 DR. BOGEMA: Good morning. My name is Dr. Stuart
19 Bogema with Forensic Testing, Incorporated, a consulting and
20 research firm. I'm here today at the request of Roche
21 Diagnostic Systems. I have worked as a clinical and
22 forensic toxicologist in the field of substance abuse
23 testing for 20 years now. I am also board certified in both
24 forensic toxicology and clinical chemistry toxicological

1 chemistry.

2 I have been a laboratory director and responsible
3 person at two SAMHSA certified laboratories over the last
4 five years and am very familiar with laboratory testing for
5 substance abuse.

6 I have also been actively involved for the last 10
7 years in research related to on-site testing. Starting back
8 in about 1986, I have followed the development of these on-
9 site testing products, immunoassays, closely. In the past,
10 I have worked for a company that both operated a certified
11 laboratory and manufactured immunoassays for on-site use.
12 And there are a number of such companies today that are in
13 both the laboratory and manufacturing or distribution side
14 of drug testing.

15 I have, over the years, performed a number of
16 independent studies of on-site immunoassay drug testing
17 devices for the detection of the five drugs stipulated by
18 the Department of Health and Human Services and the
19 Department of Transportation in urine. These studies, in my
20 opinion, have shown that there are devices that are
21 comparable to the laboratory screening tests for drugs of
22 abuse.

23 I support the points to consider for approval of
24 home drugs of abuse test analytical characteristics and I

1 suggest that the FDA 510(k) clearance process can meet these
2 evaluation criteria. Further, I suggest that the
3 requirements for meeting these criteria be determined and
4 published to aid manufacturers in knowing what will be
5 needed for approval on the analytical performance side. My
6 independent studies have shown that some devices can meet
7 these criteria and some devices, at this time, cannot.

8 I also agree that confirmation testing of non-
9 negative or indeterminate results must be included in such a
10 system of drug testing available directly to consumers.

11 I have kept my remarks relatively brief. Any
12 questions?

13 DR. NIPPER: Thank you, Dr. Bogema. Are there any
14 questions from the panel for Dr. Bogema?

15 [No response.]

16 DR. NIPPER: Hearing none, thank you very much.

17 At this point, there was a gentleman from the
18 audience who raised his hand to make a comment or ask a
19 question. You are recognized, sir. Would you please come
20 to the podium and tell us who you are? And remember the
21 admonition to tell us if you have a financial involvement
22 with the manufacturers of any products being discussed, or
23 with their competitors. Thank you.

24 MR. MORRIS: Good morning, and thank you for the

1 opportunity to address this panel and the public.

2 My name is Thad Morris and I'm the President and
3 Chief Executive Officer of World Wide Medical Corporation.
4 My company develops, markets and manufactures a wide variety
5 of diagnostic testing products, primarily of the rapid
6 immunoassay types that we're talking about today. In fact,
7 we have about 14 FDA approved products that we sell to the
8 hospitals, emergency rooms, physicians office, and a variety
9 of markets that we've heard from the speakers earlier.

10 A couple of comments that struck me from the
11 presenters, and also I think of the concerns of all of us,
12 and I might remind the panel--or at least advise the panel
13 and the public--I recently received a report on my desk that
14 said--that you could buy--that was assessing the world and
15 global market for rapid diagnostic testing products such as
16 we're talking about today.

17 In that study it said, and for the first time in
18 history, the rapid test for the measurement of drugs of
19 abuse now outnumber pregnancy testing in the total market
20 share. The company was Find SVP. 25 percent of all rapid
21 tests performed in this particular study were testing for
22 drugs of abuse. I think that does a couple of things.

23 It says one thing about the widespread use of
24 these products, as well as the magnitude of the problem that

1 we're facing.

2 The idea that all of the tasks that we've talked
3 about, have talked about from one biased point of view or
4 another, that they should be run by GC/mass spec, when in
5 fact all of the products that we've heard and talked about,
6 the initial screening test usually is an immunoassay,
7 whether it's on an instrument or a rapid device. And then
8 with the protocol as deemed by the consumer or the user,
9 whoever that consumer or user might be.

10 So I'd like to make those points for the panel and
11 thank you for the opportunity of speaking.

12 DR. NIPPER: Thank you. Are there any questions
13 of the speaker from the panel?

14 [No response.]

15 DR. NIPPER: Hearing none, I'd like to open the
16 rest of the time we have for any questions we have of
17 speakers that we, for interests of time, did not get to
18 question, or any comments from the panel at this point.

19 I'd like to begin at this point with my right-hand
20 side of the table and start with Ms. Rosenthal to see if she
21 has any questions of anyone. And we'll move around the
22 table and end up with Dr. Habig.

23 I'd like to interrupt you for--I did tell myself
24 not to forget this and I wanted to mention that, even though

1 there have been many hooks laid out for us as a panel today,
2 that deal with social and family issues, that the social and
3 family issues of the use of these projects are outside of
4 the purview or the review authority of the FDA, and that I
5 would like to ask the panel to remember that in their
6 deliberations and questions.

7 Whether we personally agree with that approach or
8 not, those are the rules of the game that we're working
9 under today. I believe that we will then be able to focus
10 on the questions that we will be asked to deal with later
11 this afternoon.

12 Now, I apologize for pulling back.

13 MS. ROSENTHAL: I think I'll pass right now. I
14 have some questions but I have a feeling they'll come up in
15 our discussion.

16 DR. NIPPER: Thank you. Dr. Sohn?

17 DR. SOHN: I believe I asked two of the presenters
18 just the scope of analytes that they are screening for. I'd
19 certainly like to ask Mr. Aromando to verify that and
20 perhaps Ms. Hunt to tell us what analytes she screens for.

21 MR. AROMANDO: Dr. Sohn, just for the record, the
22 TesTcup product that we were talking about will screen for
23 the SAMHSA five, which would be amphetamines, cocaine, THC,
24 opiates, and PCP.

1 DR. SOHN: Thank you, sir. Ms. Hunt or Sunny,
2 either one?

3 MS. CLOUD: The Parent's Alert program has a teen
4 specific drug panel that tests for amphetamines,
5 barbiturates, cocaine, marijuana, benzodiazepines, opiates,
6 LSD, and Ecstasy, and all of the metabolites that go with
7 them.

8 DR. SOHN: Thank you.

9 DR. NIPPER: Thank you, Ms. Cloud. Any other
10 people you'd like to ask that question of, Dr. Sohn?

11 DR. TAYLOR: Since the question was being asked of
12 all the other speakers, I might say that our company also--

13 DR. NIPPER: Please identify yourself.

14 DR. TAYLOR: I'm Dr. Howard Taylor, Sensor
15 Technologies Corporation. We also have a test that is
16 performed in a laboratory and tests for the NIDA five,
17 barbiturates, benzodiazepines, propoxyphene and methadone
18 are included on our panel. I want to add that, to clarify
19 that for you, as well.

20 DR. SOHN: Thank you.

21 DR. WELLS: I'm Dr. Wells from American Bio
22 Medica. Our products also screen for the SAMHSA five, that
23 just about everyone else has.

24 DR. SOHN: Thank you.

1 MS. SMITH: Van Smith, Abbott Laboratories. Our
2 are the laboratory instruments. We have the NIDA five,
3 methadone, propoxyphene, the same.

4 DR. NIPPER: Thank you. Dr. Goldsmith?

5 DR. GOLDSMITH: I have no questions at this time.

6 DR. NIPPER: Dr. Rej?

7 DR. REJ: I'll defer my questions.

8 DR. NIPPER: Dr. Lewis?

9 DR. LEWIS: I have no questions.

10 DR. NIPPER: Dr. Everett?

11 DR. EVERETT: No questions.

12 DR. NIPPER: Dr. Boughman?

13 DR. BOUGHMAN: I have no questions, but as a
14 member of this panel, having been through several public
15 sessions, I would just like to compliment our speakers on
16 their thoughtful and useful testimony this morning. I think
17 you've focused in on several very important issues. I'd
18 like to thank you.

19 DR. NIPPER: Dr. Harrington-Falls?

20 DR. HARRINGTON-FALLS: Taking into consideration
21 your admonition about the social concerns, I still have a
22 question for David Evans. This is just for my personal
23 information.

24 A parent trying to get a child to give a urine

1 sample, how would that legally compare to someone trying to
2 obtain some type of sample from anyone else, in a search and
3 seizure type of --

4 MR. EVANS: If I got your question properly here,
5 what are the legal issues involved in a parent trying to get
6 a urine specimen from the parent's child, as opposed to an
7 employer or somebody else trying to get a urine specimen
8 from somebody else.

9 Well, first of all, the constitutional rights that
10 a person has to be free from an unreasonable search and
11 seizure only apply when the Government is attempting to do a
12 search. The United States Supreme Court has determined that
13 a drug test is a search.

14 So the constitutional protections would only apply
15 when the Government, in the form of an employer, some
16 regulatory agency, probation, parole, corrections wants to
17 do a drug test on you. At that point, of course people who
18 have convicted of crimes have a diminished expectation of
19 privacy, and would have diminished rights in this area.

20 But if it was a Federal employer, for example,
21 wanting to do a search on you, then you would get into a
22 whole range of protections that would be required under the
23 law.

24 As far as a parent goes, there may be of some

1 variance on individual states, but I'm not aware of any law
2 that would forbid or limit a parent's right to mandate that
3 a child get a drug test. I mean, parents have the right to
4 order medical treatment for their children, and certainly
5 this would be well within a parental right. Now whether or
6 not you can get the kid to do it or not, is more an issue of
7 parental control and discipline and relationship with the
8 child.

9 I think we can trust parents. Parents, in
10 general, have difficulty facing this issue. They are only
11 brought to facing it when they are really compelled to. At
12 least that's been my experience. Again, this is from years
13 of trying to get parents involved in school anti-drug
14 programs. It's very hard to get people to focus on.

15 So if a medical test or a test like this can be
16 used to provide clear evidence to the parent, to overcome
17 the child's denial, and overcome the child's ability to talk
18 their parent out of something--and I've got two kids, I know
19 it's real tough--it would be helpful.

20 I think we can trust parents to make the right
21 decision. Give them the information and they'll make the
22 right decision. They love their children, we assume, and
23 would want to do the right thing, and would not falsely
24 accuse them.

1 DR. HARRINGTON-FALLS: Thank you.

2 DR. NIPPER: Thank you. Dr. Kurt?

3 DR. KURT: I will defer any comments to later in
4 the session.

5 DR. NIPPER: Dr. Manno?

6 DR. MANNO: I have no questions at this time.

7 DR. NIPPER: Dr. Gerson?

8 DR. GERSON: No questions at this time.

9 DR. NIPPER: Dr. Tong?

10 DR. TONG: I'd like to ask one question. We've
11 had an opportunity to hear the industry discuss the product.
12 I want to know, is there an industry standard that makes
13 available for access for people who use the home kits for
14 information? Is that something that's available now, when
15 one uses a home kit? Where one can get access to
16 information?

17 DR. NIPPER: Do you want to direct that to any
18 particular individual?

19 DR. TONG: I just want to see if there's any
20 response from them.

21 DR. NIPPER: I saw Ms. Cloud's hand go up first.

22 MS. CLOUD: I'm not sure I understand your
23 question.

24 DR. TONG: I hear that there are products out

1 there and I just want to know if there's an industry
2 standard to have access, like a phone number or a place that
3 a user of a home kit can have access to, to call--

4 MS. CLOUD: It's not an established standard
5 within the industry. It's a very young and new industry. I
6 think that if we're going to do this we need to do it right,
7 though. And I think parents need to have access, not only
8 to scientific evaluation of the results, but I think more
9 importantly, as Dr. Brown pointed out, it's not about drug
10 testing. It's part of a whole program or service that
11 really is trying to enable parents to fight these drugs in
12 the privacy of the home.

13 That would include access to an 800 number. In
14 our particular situation, speaking to a licensed counselor,
15 to interpret the results, explain the test, and offer as
16 much information as possible. We're more of a resource than
17 a testing situation.

18 DR. NIPPER: Thank you. I saw another hand go up
19 behind Ms. Cloud, before I call on you, sir.

20 MR. MORRIS: Thad Morris, with World Wide Medical.

21 In terms of an industry standard, I think today
22 each individual company purporting to sell a particular
23 product that heretofore has no regulation chooses to do what
24 they feel is best in order to sell and promote their

1 products. So at a minimum, you'd like to have an address
2 and a phone number to contact.

3 But as far as an industry standard, within the
4 diagnostic arena, there certainly is and we all provide
5 those things.

6 DR. NIPPER: Thank you. Was that Dr. Wandell's
7 hand?

8 DR. WANDELL: Yes. Dr. Wandell, Home Access
9 Health.

10 I don't believe there are industry standards for
11 most over-the-counter diagnostic products. There are 800
12 numbers for pregnancy test kits, for fertility, for glucose
13 monitoring. For all of those, there are 800 numbers.

14 What Home Access Health does, in terms of
15 providing an 800 number, we also provide licensed counselors
16 who not only interpret the results, but also give emotional
17 support and referrals to physicians in the locale of the
18 individual in the case of HIV testing. Presumably in the
19 case of drug testing, this same model could be used.

20 DR. NIPPER: Thank you. Dr. Habig?

21 DR. HABIG: I might provide just a little bit of
22 response to Dr. Tong. The FDA labeling regulations for
23 cleared and approved devices require that the manufacturer
24 name and address or the distributor name and address be on

1 the package. So at the minimum, you could write.

2 But most diagnostics companies also provide 800
3 numbers. It is not a requirement for that, but it is a
4 generally accepted around the industry position. I think
5 it's probably market-driven, compared to being any
6 regulation driven.

7 I do have a specific question that relates to the
8 announcement for this meeting and how FDA handles the
9 invitation for open public presentations, which we heard.
10 Typically, FDA puts a notice in the Federal Register and
11 invites people to put their name in so they can present. In
12 this case, I'm wondering, can the panel know whether FDA
13 specifically invited people to come? Specific individuals
14 or companies. Or were the people who were here this morning
15 all responding simply to the announcement in the register?

16 MS. LAPPALAINEN: This is Sharon Lappalainen,
17 executive secretary. I did not specifically send out
18 invitations to the industry to invite them to come and
19 speak. The people who did come and speak contacted me via
20 telephone, presumably because they either got it off the
21 hotline number or the Internet or from the Federal Register
22 notice.

23 DR. HABIG: Thank you. That was my only question.

24 DR. NIPPER: Dr. Gutman?

1 DR. GUTMAN: I believe we also made a deliberate
2 effort to get this into the--I don't know if it was in both
3 the gray or the orange sheet, but I think it was in one or
4 the other. We did try to make the invitation as broad as
5 possible.

6 DR. HABIG: If I may, this is Habig again. The
7 reason for my question was to wonder whether FDA
8 specifically invited individual companies to present,
9 perhaps because they would support an FDA position. Hearing
10 that that did not happen, that satisfies my curiosity.

11 DR. NIPPER: Thank you, Dr. Habig.

12 At this point, we've reached almost the end of the
13 time, according to my Radio Shack watch, and the end of the
14 list that we had. I've got about 30 or 45 seconds if
15 anybody else in the audience wishes to have a final comment?

16 [No response.]

17 DR. NIPPER: Seeing no hands, I'd like to adjourn
18 us for a 15 minute break. We will reconvene at 10:45, as
19 promptly as I know how to make it, for some presentations to
20 the panel by the Agency. Thank you.

21 [Recess.]

22 DR. NIPPER: I'd like to call the session to
23 order. I'd like the public to please take their seats, the
24 panel members to rejoin the head table, please.

1 Our first presentation after the break is Dr.
2 Alfred Montgomery, who's the Acting Branch Chief of
3 Clinical Chemistry, Toxicology and Hematology in the
4 Division of Clinical Laboratory Devices. Dr. Montgomery, I
5 didn't know you were a veterinarian?

6 DR. MONTGOMERY: Yes, by training. Surprise,
7 surprise. Yes, sir.

8 DR. NIPPER: That's good.

9 DR. MONTGOMERY: Thank you very much, Dr. Nipper.
10 Good morning, Dr. Nipper, ladies and gentlemen of
11 the panel, invited guest speakers and distinguished
12 audience.

13 Today we address the very timely topic of over-
14 the-counter drugs of abuse test systems. Before we move any
15 further, I would like to inform the panel of a couple of
16 recent regulatory developments of interest. We've begun an
17 initiative in the form of a pilot program to utilize
18 recognized standards in the review process for eventual
19 certification. Teams have been appointed to coordinate
20 standards activities, make standards more accessible to the
21 Center and the industry and modify 510(k) guidances to
22 incorporate the assessed standards.

23 Also, a new paradigm is being assessed to
24 reclassify devices, so only Class II devices will be subject

1 to pre-market notification. Class I devices will be exempt.
2 And Class III devices will be either PMA or product
3 development protocols.

4 We're also pilot testing actual product
5 development protocols as an alternative to the PMA process.
6 This process is based on early consultation with FDA and
7 device development where a testing plan is acceptable to
8 both parties. This process minimizes the risk that a
9 sponsor will un-knowingly pursue the development of a device
10 that FDA won't approve.

11 Four divisions are in various stages with PDPs
12 from device manufacturers and ODE has assembled core review
13 teams for these new PDPs.

14 A team is planning a workshop to present these
15 concepts to interested parties on October 22nd at the
16 Washington Renaissance. I've just barely scratched the
17 surface of some of the positive re-engineering initiatives
18 underway by the Center, but for the sake of time, I'm going
19 to move on and return to the topic of discussion on our
20 agenda.

21 What scientific criteria should FDA consider for
22 the approval of over-the-counter drugs of abuse test kits?
23 It should be stated that FDA has no position on this subject
24 at this time. It should also be stated from the outset that

1 DCLD has been approached by several manufacturers asking
2 what kinds of data would support such a pre-market
3 submission.

4 We came to the conclusion that we needed the
5 advice of this committee. The Safe Medical Devices Act of
6 1990 provides for panel involvement to, among other things,
7 ensure internal consistency in decision making and clarify
8 the review process.

9 A number of issues will be discussed, including
10 performance characteristics and labeling considerations for
11 the end user. So we need your advice in the review of the
12 draft points to consider for approval of home drugs of abuse
13 test kits, and what if any entails the adequacy of
14 directions for use in the labeling for the device as it
15 relates to the indications for use. Are there any special
16 labeling requirements?

17 FDA recognizes that there are interested
18 manufacturers at various stages of R&D and we welcome
19 manufacturers to share those views, as they already have, on
20 this important topic and explain how they see this issue.

21 We've added to the expertise of the panel by
22 adding additional consultants, Drs. David Sohn, Benjamin
23 Gerson, James Everett, and Barbara Manno, who are qualified
24 in the field of clinical toxicology and other applicable

1 areas. Dr. Steve Gutman, our Director of Clinical
2 Laboratory Devices will give us the history and background
3 of the devices, and present focused questions that will help
4 in the deliberations today.

5 We also invited Dr. Donna Bush from the Substance
6 Abuse and Mental Health Services Administration, who will
7 lend us expertise from their agency's perspective. Ms. Pat
8 Kingsley, who is the branch chief with the Division of User
9 Programs and System Analysis, which deals with labeling and
10 human factors will provide us with FDA's expectations for
11 over-the-counter labeling and adequacy of directions for use
12 for in vitro diagnostic devices.

13 Your charge is to consider the presentations as
14 well as the information already provided to you in your
15 background package that you received, to deliberate the
16 issues of over-the-counter drugs of abuse testing in the
17 home setting. And two, to provide FDA with an opinion of
18 your expertise that can guide our staff while reviewing
19 these submissions.

20 No vote is necessary at this meeting. However, I
21 ask the Chair to clearly state any areas of consensus. We
22 at FDA also recognize that a non-consensus can be useful and
23 helpful information.

24 I should also echo and state that while we

1 understand the significance of the national and
2 international drug problem, this meeting is not a referendum
3 on the social issues surrounding drug abuse. It is a
4 meeting to zero in on the scientific criteria that needs to
5 be considered if and when FDA receives submissions on the
6 subject matter.

7 So we have a very full agenda and I ask the
8 participants, including the audience, as you have been, to
9 keep your remarks to the point so we can realize our meeting
10 objectives. I would ask everyone, especially the panel
11 members, to please keep an open mind. I will remind the
12 Panel Chair, Dr. Nipper, that there should be ample
13 opportunity throughout the deliberations for interested
14 audience to comment.

15 Lastly, I'd like to note that the press contact
16 for FDA is Ms. Sharon Snider over there, if you will raise
17 your hand, is here.

18 Thank you very much for your time.

19 DR. NIPPER: Thank you, Dr. Montgomery.

20 Are there any questions for Dr. Montgomery by the
21 panel?

22 [No response.]

23 DR. NIPPER: Hearing none, at this point it's my
24 pleasure to reintroduce to the panel Dr. Steven Gutman, who

1 is Director of DCLD, who is going to tell us more about
2 today's work. Dr. Gutman?

3 DR. GUTMAN: Good morning.

4 The goal of today's meeting is to begin a process
5 of input for FDA on review criteria for over-the-counter
6 laboratory test kits, as opposed to drug collection systems
7 for drugs of abuse testing. The Agency has a long history
8 of successful review of these types of tests in the
9 professional setting. Technological developments, and an
10 increased interest in expanding tools for use in the war
11 against drugs have allowed these products to be used in an
12 ever increasing number of ways and in non-traditional
13 testing environments.

14 The Agency, over the past several years, has been
15 developing new regulatory approaches and revisiting the
16 science, use and labeling of these projects, in an effort to
17 work with manufacturers and the professional community with
18 the aim of finding mechanisms to allow for the marketing of
19 these products in a safe and effective manner in expanded
20 settings.

21 [Slide.]

22 Over-the-counter laboratory tests have been
23 commercially marketed in the United States for more than 20
24 years. Following the passage of the Medical Device

1 Amendments of 1976, the first over-the-counter test, a urine
2 glucose test, was cleared by FDA in 1979.

3 Since then, the Agency has reviewed and cleared
4 over 300 in vitro diagnostic tests for over-the-counter use.
5 39 were cleared in 1996 alone.

6 [Slide.]

7 FDA's approach toward regulation of this type of
8 product was first outlined in a codified form in 1988, with
9 the publication of a guidance document entitled assessing
10 the safety and effectiveness of home use in vitro diagnostic
11 devices, draft points to consider regarding labeling and
12 pre-market submissions.

13 This document, which was created with input from
14 representatives of industry and professional groups, as well
15 as consumers, is designed to assist manufacturers of over-
16 the-counter in vitro diagnostic devices in complying with
17 existing regulations and pre-market clearance requirements.

18 [Slide.]

19 The document outlined, as was actually pointed out
20 in the public session, two key parameters of importance in
21 the FDA review of home use devices. One, can the lay user
22 obtain acceptable analytical results? And two, can the
23 product be labeled in a manner to assure that net beneficial
24 information is obtained from the use of the kit in the over-

1 the-counter setting?

2 [Slide.]

3 Documentation supporting the first point requires
4 field consumer studies designed to mimic real world use.
5 Data sets from consumers are required with demonstration of
6 key performance parameters, such as accuracy and precision,
7 in the hands of consumers.

8 [Slide.]

9 Documentation supporting the second point requires
10 a clinical evaluation of the proposed test and an intense,
11 some might say obsessive, review of proposed labeling.
12 FDA's review of the merit of an over-the-counter test takes
13 into account the impact of direct access to testing
14 information. A major issue in this evaluation is whether
15 information can be clearly communicated to lay users and
16 could be expected to lead to actions that promote public or
17 personal health and minimize harm.

18 [Slide.]

19 Guidance is available from NCCLS, which has
20 published a document on over-the-counter labeling. FDA has
21 also developed guidance on over-the-counter labeling. The
22 1988 points to consider document cited earlier includes a
23 fairly extensive set of recommendations on how to label OTC
24 products. The Agency has also published a booklet entitled

1 Write It Right, which provides manufacturers with
2 suggestions on development of user friendly instructions for
3 lay consumers.

4 [Slide.]

5 Although over 300 devices have been cleared for
6 over-the-counter use, they have included only eight
7 categories of tests: blood glucose, cholesterol, fecal
8 occult blood, fructosamine, pregnancy test, luteinizing
9 hormone tests, various dipstick urine analytes, and select
10 collection devices for tests performed in commercial
11 laboratories, notably filter paper strips for HIV testing
12 and for testing of glycosilated hemoglobin. And of special
13 interest today, specimen containers for drugs of abuse.

14 [Slide.]

15 In recent years, there has been increased interest
16 in extending testing for drugs of abuse testing to the home
17 setting. Two kinds of test systems are available for this
18 purpose. The first is a collection system consisting of a
19 cup or other container for collecting a specimen, directions
20 for use, packaging for storage or mailing, access to a
21 laboratory testing service using an appropriate test, and
22 finally access to test results and counseling.

23 Using this system, a consumer collects a specimen
24 from the body, mails it to the lab where the actual drug

1 test is performed, and then receives results from the
2 laboratory using a code system for confidentiality.

3 [Slide.]

4 Historically, FDA viewed this as a Class III
5 medical device requiring PMA. Critics have recently
6 vigorously argued that the Agency's categorization of these
7 test collection systems as Class III devices is
8 unnecessarily stringent and that there is benefit in making
9 these products available to consumers through a less
10 stringent process.

11 In light of these arguments, the Agency committed
12 itself to re-evaluating its policy to determine the
13 appropriate level of regulation for home drugs of abuse
14 collection systems. While developing a final policy for
15 this matter, on October 3rd, 1996 the Agency issued an
16 interim policy for the processing of home drug collection
17 kits.

18 This policy is available on the FDA CDRH home page
19 on the Internet through the World Wide Web. The Web site is
20 cited on the slide. It can also be obtained by request to
21 our Division of Small Manufacturer's Assistance.

22 [Slide.]

23 It indicates that using its enforcement
24 discretion, the Agency would not take regulatory action

1 against persons distributing home collection systems for
2 drugs of abuse tests so long as three criteria were met.
3 One, the laboratory conducting the test used an FDA cleared
4 test. Two, the test laboratory met standards set by SAMHSA
5 or equivalent standards for performing such testing. And
6 three, the product had accurate labeling.

7 [Slide.]

8 A final policy for regulating these collection
9 devices continues to be developed. Plans are to publish a
10 proposed rule in the Federal Register in the near future,
11 and to schedule a public meeting on this issue.

12 [Slide.]

13 Although not required under the interim policy, a
14 PMA has been approved for market by FDA on January 21, 1997.
15 That product is Dr. Brown's Home Drug Testing System, a home
16 urine collection system for drugs of abuse.

17 [Slide.]

18 That product was subject to a review of the
19 accuracy and reliability of the laboratory tests, sample
20 stability, laboratory credentials and procedures to ensure
21 accurate and reliable test results, and effectiveness of
22 labeling, along with availability of a health care
23 representative for conveying the meaning of test results and
24 their limitations to the consumers.

1 [Slide.]

2 A second and more direct mechanism for home
3 testing for drugs of abuse would be extension of existing
4 point-of-care technology into over-the-counter use. Over
5 the past several years, a number of companies have expressed
6 interest in marketing a variety of simple testing systems
7 for drugs of abuse directly to lay users. In light of the
8 considerable public interest in this product line and the
9 national commitment to the war on drugs, FDA is seeking
10 input today on this type of home testing.

11 FDA is seeking, as a first step, to get broad
12 input on appropriate studies to demonstrate the analytical
13 performance for this testing device in the hands of home
14 users and for determining appropriate forms of quality
15 control in this unusual analytical environment.

16 Second, the Agency is seeking input on appropriate
17 labeling and/or mechanisms to be used for ensuring that test
18 performance and the analytical and biological limitations
19 that exist in any test are appropriately communicated to lay
20 users.

21 [Slide.]

22 In particular, the controls in place in the SAMHSA
23 directed programs, which Dr. Bush will be discussing with
24 you shortly, and under the interim existing policy for home

1 collection systems which assure confirmatory testing and
2 promote test result counseling may not be as easy to address
3 in the setting of the home. Ideas on how to deal with these
4 issues, either in the labeling or in the design of these
5 tests is being sought.

6 [Slide.]

7 A draft guidance, providing a framework for review
8 of these products is on the Internet and provides a central
9 focus for today's discussions.

10 [Slide.]

11 FDA will be posing a series of questions to
12 stimulate discussion on this document. I intend very
13 quickly to run through all six questions so you will have an
14 overview of what's going to be asked, but would suggest that
15 this does not constitute the full range of the universe of
16 issues involved and should not be seen as a constraint on
17 your point of discussion.

18 The questions we are about to pose will be--and
19 the questions you will see, we cite the portion of the
20 guidance document for which the question seems to us to be
21 relevant. So question one, are the performance
22 recommendations outlined in the draft points to consider
23 adequate to characterize these tests? Should any additional
24 data sets be requested?

1 [Slide.]

2 Two, what studies are appropriate to ensure that
3 these tests product acceptable performance in the hands of
4 home users?

5 [Slide.]

6 Three, what recommendations can you make about
7 appropriate labeling for these devices for use by lay users?
8 In particular, what mechanisms should be used to communicate
9 test performance limitations to users?

10 [Slide.]

11 Four, what performance standards are appropriate
12 to establish safety and effectiveness?

13 [Slide.]

14 Five, what considerations should FDA use to
15 encourage or communicate the need for confirmatory testing
16 and for dealing with other recommendations commonly
17 associated with the SAMHSA regulatory paradigm?

18 [Slide.]

19 In closing, as Al indicated, we are not seeking a
20 final vote today. We are not seeking a final word today.
21 But we rather hope to obtain a variety of options and
22 opinions to help improve our guidance document and to help
23 direct us toward sound future scientific reviews.

24 To allow for further reflections on the document

1 at hand and on what we hope will be today's spirited
2 discussions, we seek input from members of this panel--you
3 get to change your mind on the plane--the manufacturing
4 community, professionals and consumers, over a 90-day post
5 panel period to suggest further improvements in the guidance
6 document and to help focus on the concerns reflected in our
7 questions and in our document.

8 Thank you.

9 DR. NIPPER: Thank you, Dr. Gutman.

10 Are there immediate comments or questions from the
11 panel for Dr. Gutman at this time?

12 The sixth question is how should the FDA address
13 the issue of quality control of these products in the home
14 environment, because Dr. Gutman's sixth slide got swallowed
15 by the computer, I think. So just to read that into the
16 record, I'll help you out there, Steve.

17 DR. GUTMAN: Thank you. The computer was
18 obviously not safe and effective.

19 DR. NIPPER: It's safe but it may be not
20 effective.

21 At this time, it's time to hear from SAMHSA and
22 Dr. Donna Bush has come to us to help us and guide us in our
23 deliberations. Dr. Bush, fire away.

24 DR. BUSH: Thank you, sir.

1 My name is Dr. Donna Bush. I am Chief of Drug
2 Testing in the Division of Workplace Programs in the Center
3 for Substance Abuse Prevention within the Substance Abuse
4 and Mental Health Services Administration. I would like to
5 identify myself as a Diplomate of the American Board of
6 Forensic Toxicology, and my agency, SAMHSA, as the lead
7 Federal agency for prevention and treatment of substance
8 abuse and mental disorders.

9 I hope that what I present to you today will
10 stimulate thought and discussion about home drugs of abuse
11 test kits. Please note that there is a handout that
12 contains each and every one of my slides. One page where an
13 errant slide slipped into that ineffective group, it was
14 safe but not effective. So we'll follow that with the
15 slides. So those of you with your backs to the screen can
16 follow along.

17 [Slide.]

18 I'd like to begin by reviewing the Federal Drug-
19 Free Workplace Program which was established in response to
20 President Reagan's Executive Order 12564 on September 15,
21 1986 and Public Law 100-71. From these, the mandatory
22 guidelines for Federal workplace drug testing programs were
23 developed to support the drug testing element of a
24 comprehensive drug free workplace program.

1 [Slide.]

2 These mandatory guidelines established the
3 National Laboratory Certification Program to certify drug
4 testing laboratories to test Federally mandated specimens.
5 They defined testing requirements and the two-tiered testing
6 system, an initial test followed by a confirmatory test if
7 the initial test is presumptively positive.

8 This two-tiered system, with its comprehensive
9 review of analytical data pertaining to the specimens
10 tested, ensures accurate and reliable drug testing. The
11 guidelines also provide the authority to protect the
12 interests of the Federal Government and those drug tested
13 under Federal authority.

14 [Slide.]

15 The National Laboratory Certification Program was
16 established to identify and certify qualified laboratories.
17 This is accomplished through rigorous performance testing,
18 comprehensive inspections of laboratory facilities and
19 standard operating procedures, and remediation of
20 deficiencies and testing errors.

21 Within this program lies the authority to suspend
22 and revoke certification of a laboratory to perform drug
23 testing on Federal and Federally regulated specimens.

24 [Slide.]

1 There are several different approaches for drug
2 testing which reflect different purposes to drug testing.
3 This is laboratory based forensic workplace urine drug
4 testing, laboratory based non-forensic urine drug testing,
5 non-instrument on-site testing done by hand-held devices,
6 home collection of a specimen for analysis in a laboratory,
7 and home drug test kits where the specimen is collected and
8 the testing is actually done at the home.

9 [Slide.]

10 There are several different purposes for drug
11 testing which can use these different approaches.
12 Laboratory based forensic workplace urine drug testing is
13 used when the mission is to deter drug abuse through a
14 forensically sound analysis of urine specimens to promote a
15 drug free workplace.

16 Laboratory based non-forensic urine drug testing
17 may be used for the deterrence of drug abuse or in
18 situations which are medical outcome based, such as in the
19 emergency department or drug abuse treatment situations.

20 Non-instrument on-site by hand-held device drug
21 testing may find uses in situations requiring immediate
22 results such as treatment situations or some criminal
23 justice testing settings.

24 [Slide.]

1 Home specimen collection for submission to and
2 analysis in a laboratory may be used for the detection of
3 drug use by lay users with the collection of the specimen in
4 a confidential setting such as the home. Home drug test
5 kits are proposed for the detection of drug use by lay users
6 in a confidential setting such as the home with immediate
7 results of the test made available. You will hear more
8 detail about these types of kits later on.

9 [Slide.]

10 Let's review the nature of these drug testing
11 systems. We'll start with laboratory based forensic
12 workplace urine drug testing. I want to review with you the
13 nature of this drug testing system. There is a specimen
14 collection under chain of custody in a secured selection
15 site by trained collectors. There is analysis in a secured
16 laboratory employing analytically and forensically sound
17 procedures.

18 The testing uses established cut-offs to determine
19 the presence or absence of drug. The initial or screening
20 test is immunoassay based, its purpose being to identify
21 negative from presumptive positive specimens. A
22 confirmatory test is performed on all immunoassay determined
23 presumptively positive specimens. This is done by today's
24 analytical gold standard, gas chromatography/mass

1 spectrometry, GC/MS.

2 [Slide.]

3 In HHS certified labs SAMHSA--formerly NIDA,
4 SAMHSA now since a corporate reorganization--in HHS
5 certified labs analysis is in accordance with the minimum
6 standards established by the mandatory guidelines and
7 enforced by the National Laboratory Certification Program.
8 The results of the laboratory tests are reported to and
9 interpreted by a Medical Review Officer, a medical doctor of
10 doctor of osteopathy who has had training in substance abuse
11 issues, who will interview the specimen donor in search of
12 an alternative medical explanation for the presence of a
13 drug or metabolite in the specimen.

14 [Slide.]

15 In laboratory based non-forensic urinary drug
16 testing, there may be specimen collection in a collection
17 site, analysis in an established laboratory, immunoassay
18 based initial or screening test to identify negatives and
19 presumptive positives, optional confirmation test on
20 immunoassay presumptive positives, and test results may be
21 reported directly to an employer.

22 [Slide.]

23 When non-instrument on-site testing using hand-
24 held devices is employed, the specimen may be collected at

1 the testing site, there is an immediate analysis of the
2 specimen on-site using test strip-type technology with
3 results determined by a color change, the lack of
4 appearance, or appearance of a line, or a change in color
5 intensity.

6 There may be optional follow-up confirmatory
7 testing at a remote laboratory on presumptive positives with
8 the on-site test results immediately available to an
9 employer.

10 [Slide.]

11 With home specimen collection with the specimen
12 then sent to and analyzed in a laboratory, the specimen is
13 collected in the home. Analysis of the specimen is
14 conducted in an established laboratory, and immunoassay
15 based initial or screening test to identify negatives and
16 presumptive positives is performed with optional
17 confirmatory testing on presumptive positives. And the test
18 results may be interpreted by a toxicologist or substance
19 abuse professional and reported to a parent or responsible
20 family member. You will hear more detail about the use of
21 these types of kits later on.

22 [Slide.]

23 With the concept of home drug test kits, the
24 specimen is collected in the home. The analysis of the

1 specimen is by test strip-type technology with results
2 determined by a change in color intensity, the appearance of
3 a line or lack of appearance of a line. The test results
4 are read and interpreted by a lay individual based on
5 written instructions on how to do so.

6 [Slide.]

7 Let's take a look at the safeguards for these
8 different drug testing systems. Let's return for a moment
9 to forensic workplace drug testing systems. Trained
10 specimen collectors are present to prevent contamination and
11 specimen mix-up. Controlled accessioning into an
12 established urine drug testing lab, initial testing by
13 immunoassay technology which meets the requirements of the
14 FDA and is validated in the laboratory setting with
15 calibrators and controls. Confirmation by valid GC/MS
16 procedures with authentic calibrators and controls. Quality
17 assurance/quality control analysis of initial and
18 confirmatory results for analytical aberrations.

19 [Slide.]

20 Certifying scientists review all analytical
21 results. The results are reported through a trained MRO for
22 interpretation of test results, the search for alternative
23 medical explanations for the presence of the drug.

24 Performance testing and site inspections of the laboratory

1 by an accrediting body--in this case, the National
2 Laboratory Certification Program--with error remediation as
3 part of the certification process and potential regulatory
4 action by the Government should a situation warrant it.

5 [Slide.]

6 The next slide, this slide depicts in big picture
7 format the distribution of immunoassay positive-GC/MS
8 negative results in six representative certified Department
9 of Defense--very similar certification program to HHS--and
10 HHS certified labs.

11 On the Y axis are the five drug classes and on the
12 X axis is the percent unconfirmed positives. Note that even
13 in these certified laboratories there is a range of zero to
14 26 percent of specimens which screen positive for
15 cannabinoids which do not confirm positive when tested by
16 GC/MS.

17 Zero to 18 percent of specimens screened positive
18 for cocaine do not confirm by GC/MS. 60 to 85 percent of
19 specimens screened positive for amphetamines fail to confirm
20 positive for amphetamines and/or methamphetamine by GC/MS.
21 35 to 80 percent of specimens screened positive for opiates
22 do not confirm positive for morphine and/or codeine by
23 GC/MS. And 10 to 46 percent of specimens screened positive
24 for phencyclidine fail to confirm by GC/MS.

1 This data clearly shows us that other substances
2 cross-react with the immunoassay tests used within the
3 laboratory system. The immunoassay screen, when used in the
4 laboratory setting determines those specimens which go on to
5 confirmation. It does not determine unequivocally which
6 specimens are drug positive. That is the whole concept of
7 immunoassay in this two test system.

8 [Slide.]

9 I'll take you a little deeper into this data.
10 This slide shows the individual experience of the six
11 Department of Defense and HHS labs showed in the last slide.
12 With immunoassay positives which failed to confirm, the labs
13 are A through D. They represent the six different labs.

14 You can see by looking at the confirmation rate
15 from each lab and each drug that some kits are more specific
16 for the analyte of interest while some have high cross-
17 reactivity indicated by the larger number of specimens that
18 do not confirm positive.

19 [Slide.]

20 I'll take you back to the big pictures. Just a
21 few minutes ago I showed you this slide. Then I took you in
22 for a closeup of the data from each of the six labs. Now
23 I'd like to take you back to the big picture and leave you
24 with this thought about laboratory immunoassay experiences.

1 In the laboratory, depending on the immunoassay
2 test kit that it uses, zero to 26 percent of the specimens
3 presumptively positive by immunoassay do not confirm
4 positive for cannabinoids. Zero to 18 percent of the
5 specimens presumptive positive by immunoassay for cocaine do
6 not confirm positive. And the three other drugs and drug
7 classes have much higher rates of unconfirmed immunoassay
8 positives.

9 I just want to remind you of the failure to
10 confirm rate repeated in this slide.

11 [Slide.]

12 Let's now take a step further and go to a study
13 titled evaluation of non-instrumented drug test devices.
14 This study was performed at the request of the
15 Administrative Office of the U.S. Courts and conducted under
16 a contract with Duo Research. This study was conducted
17 during October, 1996.

18 [Slide.]

19 In evaluating the devices, several operational
20 factors were noted. Ease of use will be a very important
21 one for the non-technically trained user. Some devices
22 required multiple steps and incubation. Most were quite
23 simple, requiring only the addition of a few drops of urine
24 to a well with a three to five minute development time. At

1 least three devices on the market, only one included in this
2 study, are collection cups in which the test is conducted
3 within the cup.

4 Reading endpoints was often equivocal, that is not
5 being able to clearly distinguish whether there was a line
6 present or not present. These variations are shown on later
7 slides by drug and operator and by device and operator for
8 the average of four drugs. Phencyclidine is the drug that
9 has been omitted from the five panel. There just was not
10 sufficient number in the clinical donor samples aggregated
11 for this study to be of significance.

12 Note that it would be a common assumption that
13 borderline readings would coincide with samples with
14 borderline concentrations of drug. This, however, was not
15 the case. Only 17 percent of the borderline markings by
16 operators fell within the plus or minus 20 percent of the
17 GC/MS concentrations, whereas 50 percent of the samples
18 tested were in that same range.

19 There were challenges in reading endpoints, as
20 well as operator differences. Prevalence itself has an
21 influence on how many people are impacted by inaccurate
22 results. The prevalence of drug positive specimens in this
23 study population was about 45 percent. This was not a
24 random population. These data could not be extrapolated to

1 a population of lower prevalence, such as the general
2 population as seen in the workplace.

3 [Slide.]

4 The study design was to evaluate as many non-
5 instrumented devices as were available at the time of the
6 study. 15 devices were purchased from 12 manufacturers or
7 distributors. FDA had cleared or the marketing company had
8 filed for FDA clearance these 15 devices.

9 Seven were multiple test devices with four or five
10 drugs per device. Eight were single test devices, which
11 included two pair from two different suppliers, one has a
12 test card and its matching dipstick.

13 The 16th device was an instrumented reference
14 method and enzyme testing system and ETS instrument using
15 Emit drugs of abuse for urine reagents.

16 The study included 100 samples for each of the
17 five drugs. 10 were laboratory prepared controls. 90 were
18 selected from specimens received by the laboratory
19 performing drug tests for Federal probation offices of the
20 U.S. Courts. Approximately 15 were negative, less than 25
21 percent below the cut-off. 30 between 25 percent below the
22 cut-off and the cut-off. 30 between 25 percent above the
23 cut-off and the cut-off. And 15 greater than 25 percent
24 above the cut-off.

1 The initial laboratory screening results were used
2 as a guide. Samples consisted of the screening aliquot
3 after a laboratory had tested them. The four to give
4 milliliters was more than sufficient to test 14 of the
5 devices. 14 of the devices were tested on the same day with
6 the same set of samples, approximately 25 samples per day
7 using the screening aliquots.

8 Because the Roche TesTcup required 30 milliliters
9 of sample, frozen specimens were selected using the same
10 criteria and were tested at a different time. Approximately
11 30 percent of those samples used in the other studies and in
12 this testing of the Roche TesTcup were from the pool of
13 specimens used with the 14 other devices.

14 [Slide.]

15 The tests were conducted by three medical
16 technologists, two with bachelor's degrees and one with a
17 master's degree. All were licensed in California. The
18 devices were distributed amongst the technicians operators
19 as evenly as possible, so each would have an equal
20 experience with each device.

21 The samples were screening aliquot tubes labeled
22 only with their original bar code number. The operators
23 knew which drug was the focus on any given day, but did not
24 know which concentration type any sample was. They also had

1 to record results for all drugs tested.

2 Most devices demonstrate positive results by the
3 absence of the appearance of a colored line. It was noted
4 that in some cases it was difficult to discern if a line was
5 visible or not. To evaluate the potential impact of such
6 equivocal readings, the operators were directed to mark the
7 results as borderline positive or borderline negative.

8 Results were recorded on individual scoring sheets
9 which were transferred on the same day to a computer data
10 base for subsequent analysis.

11 [Slide.]

12 As mentioned earlier, most devices produced a
13 colored line at the test zone for negatives and the lack of
14 appearance of a line for positives. One device is the
15 opposite. And one device requires comparing the test zones
16 to the color of the control zone. This slide also points
17 out the borderline situation with the devices.

18 [Slide.]

19 This slide is similar in concept and analysis of
20 the data to the one I took you back to twice before, with
21 similar laboratory experiences. Here we're looking at the
22 on-site testing device experiences.

23 This slide shows the range of the device with the
24 lowest immunoassay positive-GC/MS negative rate to the

1 device with the highest immunoassay positive-GC/MS negative
2 rate for the five drug classes. Surprisingly, the range of
3 immunoassay positive-GC/MS negatives was very similar for
4 amphetamines and cocaine, slightly less for PCP, then less
5 for cannabinoids.

6 One would expect a higher rate for amphetamines,
7 as it was assumed that there was a higher incidents of over-
8 the-counter drugs in these samples.

9 For these 15 devices tested, this indicates a
10 greater degree of cross-reactivity for other substances than
11 for immunoassay tests performed in the laboratory.

12 [Slide.]

13 This slide displays the range of immunoassay
14 negative-GC/MS positive results from the device with the
15 lowest, which was zero percent for all drug classes, to the
16 highest percent.

17 Looking at these results from the 15 tested
18 devices, there appears to be an unacceptable number of
19 specimens that failed to test positive when, in fact, they
20 contained confirmable quantities of drug.

21 [Slide.]

22 This is a composite slide for the four drugs--
23 again, as I told you, except for PCP--showing the true
24 positive, false negative, false positive and true negative

1 result for each device. This is your errata sheet. It will
2 be much clearer to you and it's also larger to see. Please
3 disregard that small frame that is in your handout.

4 This slide demonstrates the variability between
5 false negatives and false positives across devices. Now if
6 you data oriented people are like me, you'll note that there
7 are 18 bars on that slide when, in fact, I told you there
8 were 15 devices tested. Device A is Nirvana. That is the
9 most preferred device. It doesn't exist yet. That is where
10 there are zero percent false positives and zero percent
11 false negatives. So that's just the index to show you what
12 Nirvana is.

13 And column P and column R are the Emit test
14 reference method that was performed within the laboratory
15 setting while these devices were being evaluated. Remember,
16 14 were evaluated at one time. And then P is the control
17 for that. Then a particular device that required 30
18 milliliters of urine had to be tested at a later time. R is
19 the control for that, Emit laboratory based testing.

20 [Slide.]

21 This slide displays the percentages of borderline
22 results for each drug class and the total of all results.
23 It also shows the variation in the number of borderlines by
24 operator. Also, overall the accuracy of results recorded as

1 positive was 60 percent and for negative 89 percent,
2 paralleling somewhat the accuracy for borderline results
3 with borderline positive results having an accuracy of 38
4 percent and borderline negative results 77 percent.

5 In summary, this point supports the analysis of
6 the data counting all borderline results as negative.
7 Differences between operators were measured as to their
8 recording of borderline results and overall accuracy. There
9 were big differences in the distribution of borderline
10 readings, but the overall accuracy of the operators was not
11 significantly different, 63 percent, 54 percent, and 62
12 percent. Note this is overall accuracy, including all
13 samples, negatives and positives.

14 [Slide.]

15 This is a similar display but the average of the
16 four drugs, again except PCP, is displayed against the
17 percentage of borderline results. There are significant
18 differences indicating that some devices are superior in
19 their production of the negative line and are therefore
20 easier to read. Another factor can be in the manufacturing
21 procedure, which requires the spraying of precise bands of
22 material on discrete sections of the paper strip.

23 [Slide.]

24 There are some crucial decision questions that

1 arise from all of this data and information concerning home
2 drug testing kits. What are acceptable results for the lay
3 user? Results that will determine with reasonable certainty
4 that a positive test indicates drug use and a negative
5 represents no drug use.

6 [Slide.]

7 Can the lay user obtain acceptable analytical
8 results? To date, this has not been possible with
9 immunoassay alone. Also to be considered, uncontaminated,
10 unadulterated sample collection; avoid false negatives or
11 false positive results; variations in device performance;
12 sensitivity and specificity; avoid interfering and cross-
13 reacting substances. What do the results mean?
14 Specifically, interpretation of opiate and amphetamine
15 positive results in the context of alternative medical
16 explanations.

17 [Slide.]

18 Can the over-the-counter product be labeled in a
19 manner to assure that the lay user understands the meaning
20 of the test results and equally, or more importantly, the
21 limitations of the test result?

22 [Slide.]

23 What are the benefits of over-the-counter use of
24 on-site home drug test kits? Ease of use, confidential

1 setting for testing with accurate results and appropriate
2 knowledge. Lay users are able to make vital decisions about
3 drug use status. If reasonable confidence in test results,
4 decisions concerning future actions can be taken, such as
5 deterrence of drug use and intervention.

6 [Slide.]

7 What are the risks of over-the-counter use of on-
8 site home drug test kits? Test results may be
9 misinterpreted, particularly positive results. As
10 previously noted, in workplace drug testing situations, we
11 have found that confirmation is a crucial element given the
12 significant outcomes that may follow a positive drug test.
13 So what about confirmation and the home drug test kit? And
14 the concern that lay users may make decisions based on
15 technically inaccurate results.

16 I might also point out in closing that most
17 existing home test kits and on-site test kits do not measure
18 for some drugs commonly abused by young drug users, drugs
19 such as LSD and inhalants.

20 Thank you.

21 DR. NIPPER: Thank you, Dr. Bush.

22 We have about three or four minutes for questions,
23 if there are any of Dr. Bush from the panel. Donna, could
24 you stay at the podium for a second? We're going to limit

1 the questions, but you'll be available after lunch for
2 further questions?

3 DR. BUSH: Yes, sir.

4 DR. NIPPER: I thought I saw Dr. Kurt's hand up
5 first.

6 DR. KURT: Thank you for the very informative
7 information and rather shocking information about the rate
8 of false negatives and false positives. But I wanted to ask
9 you about something else that potentially could undermine
10 the Federal rules of drug testing that presently exist for
11 Federal employees, airline employees, et cetera.

12 The home test kits might not just be used by
13 parents and their children. These are potentially available
14 to say a union steward to test his union member before he
15 goes into an employee test, or by an airline pilot if he has
16 an accident so he can go home or something of that sort.
17 What would the potential of undermining Federal programs in
18 regards to making this available on an open label to other
19 than parents and their children?

20 DR. BUSH: Sir, that is of grave concern to me,
21 who oversees the program for Federal employees and all the
22 DOT regulated industry employees you mentioned, as well as
23 others. I don't know how to answer that. I mean, the kit
24 would be made available for home use, if that is the

1 decision made. Buyer beware or informed, as they are well-
2 informed on the Internet.

3 I honestly don't know how it might impact DOT
4 regulated testing and Federal employee regulated testing.
5 That would be something we would seriously need to consider
6 following any decisions made by this group and the Food and
7 Drug Administration.

8 DR. NIPPER: Dr. Gerson?

9 DR. GERSON: Likewise, I enjoyed your
10 presentation. Lots and lots of questions. I will be
11 uncharacteristically brief, however.

12 A little confusion on my part. I think it's
13 mainly presentation. Any one of your red and blue slides,
14 showing immunoassays that failed to confirm. That in
15 contrast to one of your other slides.

16 The implication is that at least one of the six
17 laboratories, either DOD or certified through your program,
18 claims to never have a marijuana or a cocaine that fails to
19 confirm. As a lab director myself, I find that hard to
20 believe.

21 Again, that may just be an artifact of the
22 presentation software and the way you did your bar graphs.
23 But is that what you meant to imply, that at least one lab
24 said it had 100 percent confirmation rates of marijuana and

1 cocaine?

2 DR. BUSH: They were the data that we collected
3 from those six labs, sir.

4 DR. BUSH: Okay, because then on a subsequent
5 slide, again I'm sure it's just a matter--you know, as one
6 who plays with presentation software itself, the bar graphs
7 are always a problem for me. It appears on some slide that
8 actually the range for all the drugs is zero to some large
9 number. Of course, the large number, I agree, is scary.

10 But I want to make sure that the implication is
11 that some of the labs claim they get 100 percent
12 confirmation on samples submitted. I find that surprising.

13 DR. BUSH: Do me the favor, over lunch let me call
14 and get the exact numbers?

15 DR. GERSON: Again, I'm not challenging the data.

16 DR. BUSH: I want to get you the information.

17 DR. GERSON: One other quick question. You made a
18 comment about needing immediate results and you mentioned
19 criminal justice. Not being involved in that to any great
20 depth myself, what's a criminal justice situation where you
21 need an immediate result? Again, as a physician, I sort of
22 liken that to the emergency room setting where you need a
23 result. It can't wait a couple of hours or even a day.

24 DR. BUSH: The criminal justice system is

1 embarking on review of these devices. Concern about
2 immediacy of testing within a particular situation, should
3 an individual be arrested again after they are on parole or
4 probation, there may be an immediate need for a judge to
5 know, or a hearing officer to know a result immediately.
6 And then maybe that specimen will go on to be further
7 tested. Maybe the decision maker will have enough
8 information based on knowing how accurate and reliable these
9 results are, to make the decision they need to make.

10 Is that kind of clear?

11 DR. GERSON: Yes, it's very clear. Thank you.

12 DR. NIPPER: Thank you, Dr. Bush. One more
13 question, Dr. Sohn?

14 DR. SOHN: On your EIA negative results and
15 GC/mass spec confirmed results, were you using--say, for
16 example, for the case of opiates or cocaine--a 300 nanogram
17 cut-off for screen and a 150 nanogram cut-off for
18 confirmation?

19 DR. BUSH: 300 and 300. 300 for screen and 300
20 for confirmation.

21 DR. SOHN: Let me ask you one other question. If
22 you had your druthers, in test design certain tests are
23 designed where you try to get the whole population, even
24 though you know that you may be getting some individuals who

1 are true negatives. This is the case, for example, with
2 syphilis screening. It's a case, pretty much, with HIV
3 screening.

4 With most of the drug screening that we do
5 nowadays, we really know that there are a certain number of
6 true positives that we are excluding, using a cut-off. If
7 you had your druthers for a home test, which of these two
8 paradigms would you select?

9 DR. NIPPER: Nobody ever said it would be easy,
10 Dr. Bush.

11 DR. BUSH: Thank you for reminding me of that.

12 It all goes back to application of a cut-off. Our
13 workplace cut-offs clearly are conservative. They are
14 applied in a workplace where individuals are given the
15 benefit of the doubt. These cut-offs have gone to the
16 Supreme Court 27 times along with their testing technology
17 and interpretation of the results, and have been upheld.
18 This is in a workplace setting.

19 These conservative cut-offs indeed may not be
20 appropriate in treatment arenas, in home test kit arenas.
21 And yet, I say to you, even looking at the device
22 performance with these conservative cut-offs, how can we
23 ensure the specificity and sensitivity to go lower
24 accurately and reliably?

1 That's a question to you, the panel, and nobody
2 ever said it would be easy.

3 [Laughter.]

4 DR. NIPPER: On that positive, optimistic note I'd
5 like to thank Dr. Bush for her enlightening presentation.
6 We have a final presentation from Patricia Kingsley, who is
7 chief of the Systems Analysis and Human Factors branch in
8 the Division of Device User Programs and Systems Analysis.
9 I'm afraid to get alphabetical on that.

10 Ms. Kingsley?

11 MS. KINGSLEY: Thank you very much. I appreciate
12 the opportunity to speak to you briefly this morning about
13 the challenges inherent in developing the labeling that
14 speaks to the issues that Dr. Bush just spoke about,. Over-
15 the-counter labeling for medical devices in general, and
16 specifically for drugs of abuse test kits, there are
17 significant challenges.

18 It's both an art and a science to put together
19 this kind of labeling. There's no one answer for every
20 particular situation. We can't really say that we could
21 develop a booklet, or a manual, or a guideline that would
22 serve for each and every case. It has to be done on a case
23 by case basis.

24 So I'd like to give you a few of the challenges

1 that I would ask you to consider. First of all, basically
2 with all over-the-counter devices drugs of abuse, when you
3 develop labeling for the lay user for these devices.

4 First of all, something that was mentioned earlier
5 today, the reading level or the readability, which is part
6 of the issue of comprehension. If we're targeting the
7 entire population of the United States we're talking about a
8 seventh grade level. That's a very difficult thing to do
9 when you have information that's full of medical, technical
10 terminology, medical jargon, things that are unfamiliar to
11 many consumers. The whole point of this is to make sure
12 that not only they can read it, that they can comprehend it.

13 There's also the issue of limiting the material
14 that should be presented in this kind of labeling. There
15 are reams of material very often for a particular device
16 that the professional user is given in addition to the
17 background information that he or she has to operate with.
18 We walk a fine line between the liability approach, and that
19 is to give them absolutely everything and then you run into
20 the problem possibly of sensory overload, or of shut-off of
21 the individual. I simply am not going to read 79 pages
22 before I do this test.

23 On the other side, the paternalistic approach that
24 we've all been up against in the past where the agency, the

1 manufacturer may choose to limit the material and say, I
2 know what's best for this individual.

3 So again, we walk a very fine line. Many
4 consumers will say to you, I want to know everything there
5 is about the device. But in fact, there is a limit. Who
6 decides what that limit is? How do we decide what that
7 limit is?

8 Beyond that, even if you limit the information
9 appropriately, there are a few things which each device that
10 you want to highlight for the user. How do we highlight
11 these things? There are approaches to highlighting. We
12 have to select the appropriate one for the particular
13 situation.

14 We also have to consider the need to either build
15 on or overcome a transference of knowledge. Consumers have
16 used devices and products before. They learned something
17 from doing this. In the case of a new device, if it looks
18 like the old one there is a transference of knowledge. The
19 labeling has to convey to them if there is something about
20 different about this device that they need to be aware of so
21 that they can overcome that transference, or perhaps build
22 on it. Sometimes that can be designed in; sometimes it has
23 to appear in the labeling.

24 Also the labeling has to anticipate problems that

1 the user might have in either interpreting the directions--
2 and I think that's been mentioned earlier today--or
3 interpreting the effects or the results of a device. The
4 preparer of the labeling has to build that into the
5 labeling, has to know the target population and anticipate
6 what those problems are.

7 These kind of issues would go across the board for
8 over-the-counter devices. There are some specific ones that
9 I would like to point out to you for drugs of abuse,
10 however.

11 Something that has been alluded to, some of the
12 devices give feedback to the user which is counterintuitive
13 or counter to what they have learned before. If you're used
14 to a device having some sort of visual readout, a color
15 associated with positive, and the actual readout of this
16 device is no response, no color, no marking, whatever it is,
17 that's counterintuitive. Somehow if that cannot be designed
18 out, the user has to be alerted to that fact appropriately
19 so that they pay attention to it and they understand it, so
20 that in fact they read the test right.

21 In addition, something that has been brought up
22 several times this morning, how do you convince a user to
23 take the next step for confirmatory testing, if that's an
24 important issue with this particular device? Confirmatory

1 testing has costs associated with it. Sometimes they're
2 financial; there may be a dollar value involved. They have
3 to fork out some more money. Sometimes they're
4 psychological; the few days has been brought up before.
5 Sometimes there may be additional costs associated with
6 them.

7 It's well documented in the literature that the
8 attention that individuals pay to hazard messages--and this
9 is a hazard message, can be taken as a hazard message--have
10 a great deal to do with the costs that are incurred to that
11 individual.

12 There's also the issue of accurately interpreting
13 the level of specificity and sensitivity. That's not a real
14 well-known concept to a lot of consumers, if we're talking
15 about people who are reading seventh, eighth, ninth grade
16 level. They don't use this kind of thing in their everyday
17 life.

18 The same thing for a control reaction, the
19 significance of using a control. Most of the things that
20 most of us do every day don't involve a control. Therefore,
21 how do we convey to them in the labeling the importance of
22 paying attention to this?

23 We do have some sources to assist us in overcoming
24 these challenges. Dr. Gutman referred to them earlier

1 today. He gave you background on how they were developed.
2 I'd like to point out to you what they do for us and what
3 they don't do for us.

4 The basis of a number of the principles that show
5 up in these documents come from the fields of risk
6 communication and human factors. There's been some
7 scientific research that's the basis for some of these
8 things. There's the science side to the science and art
9 that I was talking about earlier. For instance, warning
10 development, hazard messages. There's been research into
11 how to put those together so that users will actually be
12 alerted to them, will notice them, will read them, and will
13 comply with them.

14 So we have some foundation there for making
15 recommendations. But again, nothing works in every
16 situation.

17 Similarly, some of the format principles that we
18 use have some research behind them. Again, I would caution
19 you that they can't be used in every situation. The
20 documents that I referred to, and I think you've been given
21 a copy of Write It Right. This was developed generally
22 across the board for medical devices to be used in home
23 care. There are general principles in this document for
24 putting together user instructions for the lay user. The

1 document goes into planning, writing, and testing that kind
2 of labeling.

3 There are approaches in there for dealing with
4 some of the basic challenges that I talked about that go
5 across the board: for the readability issue, for
6 comprehension, for such things as the task analysis that is
7 necessary to determine what kind of problems that your user
8 may run into.

9 That document was developed as a model. A
10 labeling developer who uses it can follow the way it is set
11 up as well as the principles in it, and it gives other
12 sources as well for more in-depth research.

13 The draft points to consider document that Dr.
14 Gutman referred to focuses on regulatory compliance. It
15 does have important sections in it covering performance
16 labeling and testing. It is on the regulatory side.

17 The NCCLS document, GP-14(a) which was published
18 in June of 1996 entitled Labeling of Home Use In Vitro
19 Products Approved Guideline is a consensus document; a
20 voluntary guideline that recommends information for
21 inclusion in this kind of labeling pointing to the manner of
22 provision of this kind of information, the validation of the
23 information, and it also provides a number of examples.

24 It has extensive information on the testing of

1 that labeling that complements that that's in Write It
2 Right. It also has extensive appendices on writing
3 principles and on readability testing.

4 Those are the tools that are currently available
5 to us in FDA and for us to recommend to the manufacturers.
6 They go a long way to dealing with the basic challenges of
7 over-the-counter labeling, but they don't specifically
8 target the unique challenges presented to the user by the
9 kinds of challenges that I spoke about for the drugs of
10 abuse testing kits.

11 DR. NIPPER: Thank you very much. Are there a few
12 quick questions for Ms. Kingsley? Yes, Dr. Kurt?

13 DR. KURT: While I'm concerned about the seventh
14 grade reading level that you described, I'm concerned about
15 the people who do not read the labels at all. As Dr. Tong
16 and I know that have been involved in poison control and
17 drugs, probably there's a 30 percent or greater non-
18 compliance of reading labels. Could you comment on that?

19 MS. KINGSLEY: Absolutely. It's a separate issue
20 but it's a very important issue. Some of the
21 recommendations for overcoming that, which I am not sure
22 how--I don't think that there's much in the literature about
23 the testing of that--is getting the individual's attention.
24 A number of approaches have been used over time, but we also

1 know that they wear thin. You use color, you use certain
2 symbols, that kind of thing. Even you put at the top of the
3 page, make sure you read the whole labeling before you do
4 anything. A very challenging issue; extremely challenging
5 issue.

6 DR. NIPPER: I would assume that that issue
7 crosses all educational levels. I know a few people who
8 work in laboratories who read the directions as a last
9 resort.

10 MS. KINGSLEY: Absolutely. One of the things that
11 we do recommend, however, is as brief as possible because
12 that's one area that has been studied. That if you make it
13 as brief as possible, for instance, a one-pager with
14 appendices, there is an increased likelihood that
15 individuals will at least look at it.

16 DR. NIPPER: I believe Dr. Sohn had a question.

17 DR. SOHN: I agree with you. I think that most
18 people in this country feel that if all else fails, then you
19 read the instructions. Now my question basically is, do you
20 think it might be feasible, because we know that happens, to
21 encourage manufacturers to have fewer models so if there's a
22 carryover--if they know if model A works for me and I've
23 learned the instructions for test kit A, perhaps if they
24 were the same colors or were a similar format or something

1 where we could encourage carryover. Would that be something
2 that would be desirable?

3 MS. KINGSLEY: You mean to go along with the
4 transference of knowledge that once you learn one kit you
5 can use the same approach to the second kit? I'm not sure
6 that the manufacturers would agree that they'd want a one-
7 size-fits-all kind of thing. That would be one approach.

8 Another is to devise some sort of a scheme that
9 instantly alerts the reader to the differences. This goes
10 across all educational levels as well. I think about
11 something like blood glucose monitors or infusion pumps, you
12 get a new model that looks like the old one, you're going to
13 try your own way first.

14 DR. NIPPER: Our last question before lunch, Dr.
15 Manno?

16 DR. MANNO: I'm interested, you're directing or
17 targeting a seventh grade level of reading. I'm making an
18 assumption here that that's based on an average. Has there
19 been any work done to give us a handle on what percentage of
20 the population cannot even read?

21 MS. KINGSLEY: I've heard as high as 50 percent.
22 I think it's someplace a bit lower than that, but it's
23 amazingly high. There are a lot of people who can't read.
24 Other approaches to labeling a device, such as video,

1 pictograms, have been suggested to overcome that. That's
2 one of the reasons that we strongly recommend that labeling
3 be tested on a sample of the target population, a
4 representative sample of the target population, if at all
5 possible.

6 DR. NIPPER: Thank you very much, Ms. Kingsley.

7 Before we adjourn for lunch I'd like to mention to
8 the FDA staff and members of the panel that there's a place
9 to eat lunch downstairs where we can eat as a group in the
10 restaurant that's down off the lobby.

11 I would very much like to express on behalf of the
12 panel our appreciation to the members of the public who
13 spoke today and are helping us focus our attention to
14 various aspects, critical aspects of this issue. I also
15 want to thank Dr. Montgomery, Dr. Gutman, Dr. Bush, and Ms.
16 Kingsley for their assistance in helping guide our
17 deliberations.

18 We will adjourn now and reconvene at approximately
19 1:00 for open committee discussion. Our discussion at that
20 time will focus on the issues brought up to the panel this
21 morning. We will also attempt to ask the six questions
22 brought up by Dr. Gutman, and at that time if he decides
23 that it's important to hear from people who have spoken this
24 morning, we will recognize those people at that time.

1 Thank you very much and I'll see you again at
2 1:00.

3 [Whereupon, at 12:05 p.m., the open session was
4 recessed, to reconvene at 1:14 p.m., this same day.]

1 AFTERNOON SESSION

2 DR. NIPPER: I'd like the panel and public to come
3 to order, please. We're about to resume our meeting with
4 open committee discussion. If I could, I'd like to ask Dr.
5 Bush a question about her presentation before we begin.

6 Donna, on page 6 of your presentation, the one
7 where you reiterated the distribution of immunoassay
8 positive GC/MS negative results times two. That was the
9 slide that has percent unconfirmed positives, and it was the
10 slide that Dr. Gerson asked the question about with a little
11 bit of incredulity about a laboratory that had no
12 unconfirmed positives for marijuana and cocaine.

13 I wondered, in my experience in this area it's not
14 uncommon, although not extremely often, but we have
15 encountered a number of immunoassay positive specimens that
16 did not confirm but that was because the cutoffs for GC/MS
17 were set at a certain level and we felt that we could
18 quantitate those values, those drug samples with reasonable
19 scientific confidence. I'm wondering if you have any
20 guidance for the committee or the panel on the tit for tat
21 of GC/MS cutoffs versus the screening cutoffs?

22 We've seen marijuana or cannabinoids change
23 screening cutoffs, let the GC/MS cutoffs stay the same.
24 We've seen the opiates back and forth a little bit. Maybe

1 you'd help us a little bit with that. Are the GC/MS cutoffs
2 set reasonably appropriately for clinical work? Not
3 speaking with your SAMHSA hat on, but as a forensic
4 toxicologist, for example.

5 DR. BUSH: I can honestly tell you that within the
6 context of the cutoffs that have been set and are
7 established in the Federal guidelines, those mandatory
8 guidelines that I talked to you about concerning workplace
9 drug testing programs, the immunoassay cutoffs are set with
10 confirmatory cutoffs in mind, and vice versa.

11 So that there was a time in our life when our THC
12 immunoassay cutoff was 100 nannograms per mil. Yet the
13 confirmation cutoff, where we're looking specifically now
14 not at the myriad of metabolites that cross-react with this
15 immunoassay and have a similar chemical structure, but when
16 we go on to confirmation we pick one of those with the best
17 window of detection, which covers two dimensions, both the
18 amount of the metabolite excreted and the length of time
19 over which it is excreted.

20 So you want to confirm with the metabolite, when
21 you have a bunch of metabolites, many metabolites, you want
22 to pick the one to confirm which occurs in the largest
23 quantity for the longest period of time. Quite honestly,
24 that is how we approach and evaluate each and every one of

1 those cutoffs that have been established. And the
2 immunoassay kit manufacturers work with us concurrently to
3 help us achieve that marriage, if you will, between the two
4 cutoffs.

5 So we were able to go down to a cutoff, an
6 immunoassay cutoff, of 50 nannograms per milliliter in the
7 workplace and still leave the confirmation cutoff at 15
8 where we were very comfortable analytically because the
9 immunoassay kits got better and little bit more specific,
10 for better or for worse, for the analyte we were looking for
11 in the GC/mass spec analysis.

12 Now that's the long and the short of how the
13 cutoffs were set. How do they apply in a clinical setting?
14 By default many, many kits use these cutoffs, and they have
15 just achieved a level of usage in emergency rooms and other
16 places. Yet the metabolites, say for an analyte--now I'm
17 going off the beaten path here because I'll talk about
18 benzodiazopines for a minute. The new benzodiazopines, such
19 as triazolam, do not cross-react well nor are they in
20 sufficient quantity to react with the good old
21 benzodiazopine assay that was focused on oxazepam; the old
22 school benzodiazopines.

23 So clinically, I hear from my ER doc friends who
24 tell me that that's a problem. They can't rely on that in

1 that particular application. Yet I'm sure that clinical use
2 of the devices, should the drug be there at a concentration
3 sufficient, is going to react with that immunoassay test
4 kit. That's what the doc--I used to be a clinical
5 toxicologist in another life and the docs always used to
6 tell me, we want to know, is it there; is it there a little
7 or a hell of a lot? Those were the answers they were
8 looking for.

9 So I'm not sure how a workplace cutoff should be
10 driven in the clinical arena.

11 DR. NIPPER: By clinical arena I'm including the
12 home arena as well because I'm including home testing as a
13 clinical type. It's not, obviously, a workplace so
14 therefore it's--what I should say by clinical is non-
15 workplace environment.

16 I'm sure that Dr. Bush's presentation may have
17 engendered other concerns, maybe some over lunch after
18 reflection. While she's up at the podium, does anybody else
19 on the panel have a question or want elaboration on anything
20 that she said? Dr. Everett?

21 DR. EVERETT: On page 6, there is this chart at
22 the top. Can you review that again for me quickly here? It
23 wasn't obvious what the purpose of this particular chart
24 was.

1 DR. NIPPER: Should we try to project that slide
2 so the audience can see it?

3 DR. BUSH: Sure. While we're waiting for the
4 projection, we can look at it on our handouts here. Let me
5 go back to this. I'm going to revisit my written notes and
6 just say it again and then go on from there.

7 [Slide.]

8 This slide is the distribution--it's titled, the
9 distribution of immunoassay positive, GC/MS negative results
10 within the laboratory settings. There were six laboratories
11 that provided information to us. They were laboratories
12 certified under the Department of Defense military workplace
13 drug testing program, and the HHS drug testing program. So
14 there's six certified laboratories who are using the liquid
15 reagent A, reagent B, kind of immunoassay test to be used
16 with a drop of the donor's specimen to obtain results in a
17 very controlled laboratory setting.

18 So what I'm trying to show that even in a
19 laboratory setting we have our challenges with cross-
20 reacting substances. Even though you have many samples,
21 specimens testing positive for, say cannabinoids, depending
22 on which one of those six labs you talk to, between zero and
23 18 percent of their specimens now that they screened--excuse
24 me, zero and 26 percent of the specimens which screened

1 positive for cannabinoids and go on for an additional
2 confirmatory test, they do not confirm.

3 So somewhere between zero and 26 percent of the
4 specimens tested in these labs have a cross-reacting
5 analyte. Now that's in a very controlled laboratory setting
6 where data hounds thrive. You have an initial value that is
7 determined as the baseline for that specimen. You add your
8 reagents. You have a rate of activity with the reagents.
9 And then you read an endpoint.

10 So something is in there, in that specimen other
11 than the drug in zero to 26 percent of the cases that is not
12 the drug. Essentially we're talking about an immunoassay
13 false positive.

14 DR. EVERETT: Now were you able to translate this
15 into sensitivity and specificity?

16 DR. BUSH: Yes, and this follows actually what Dr.
17 Gerson, his question. I immediately went and got my data
18 hound to read for me some of the numbers. The kits each
19 differ in their sensitivity and specificity for the drugs
20 they are testing. This is true for any immunoassay kit. I
21 could just give as an example, the six labs that we chose to
22 make this point, that there is a range of cross-reactivity
23 extant, existent even in the laboratory testing population.
24 That even varies with the manufacturer of that laboratory

1 implemented immunoassay kit.

2 There are many different types. There's the
3 competitive enzyme immunoassay kit. There's a kinetic
4 mobilization type of assay kit. There are competitors
5 within some of these industries, and for example, that
6 range--I presented that as a range and I'd like to give you
7 those numbers because that leads us, this discussion of
8 slide 16 leads us to the next slide, slide 17 where you see
9 the individual experience of those laboratories.

10 What I'm trying to show is that different kits
11 using different technology detail, as their basis, an
12 immunoassay. For the marijuana kits, I want to give you
13 these numbers. One lab has a 99 percent confirmation rate
14 using one particular type of technology, one particular kit.
15 Another has a 100 percent confirmation rate. In other
16 words, all of those that screened immunoassay positive in
17 fact confirmed positive for that metabolite. There's
18 another kit that has a 93 percent confirmation rate, another
19 one 98 percent. The fifth one 76 percent, and the sixth one
20 99 percent.

21 So that comes back to the specificity and
22 sensitivity issue.

23 DR. EVERETT: Any numbers on the specificity?

24 DR. BUSH: No, sir. What is interesting for us,

1 in our drug testing laboratories we do not further test
2 specimens that test immunoassay negative and take them on to
3 GC/mass spec to see if there's anything there. That is
4 totally contrary to our rule.

5 However, our receipt of this data has stimulated a
6 thought that maybe we ought to look at that, too. So we
7 just were in receipt ourselves of this data last week and
8 the wheels are grinding. I hope to have some of that
9 information to you in the future.

10 DR. EVERETT: So at this time you don't confirm
11 negative test results?

12 DR. BUSH: That's correct. The immunoassay
13 negative result, by virtue of it being below the cutoff, is
14 sufficient and it is the necessary criteria for that
15 specimen result to be reported as negative.

16 DR. EVERETT: Thank you.

17 DR. BUSH: Now we're talking about confirmed here.
18 When I keep talking about confirmed, keep in mind that these
19 are confirmed at or above our HHS cutoff. We did not go
20 down to the limit of detection on GC/MS methodologies.
21 We're looking at the cutoff, that marriage of the cutoffs.

22 DR. NIPPER: That was the purpose of my question.
23 You can call it an immunoassay false positive when the GC/MS
24 is finding drug there but it's below the cutoff that's

1 specified by the regulations.

2 DR. BUSH: That is absolutely correct, yes, sir.

3 DR. NIPPER: Dr. Kurt?

4 DR. KURT: This means that you're saying that if
5 this kind of immunoassay were used on, say teenagers by
6 parents, that there would be a large percentage of them that
7 would be falsely accused of having drugs aboard that really
8 would not be confirmed. This is why immunoassay alone--not
9 necessarily by a thin layer of chromatography, which is one
10 of the test methods that's been proposed in some of the home
11 test kits.

12 DR. BUSH: Yes, immunoassay has its limitations.
13 But so does thin layer chromatography. You may make that in
14 an analogous comparison with the appearance or disappearance
15 of a color on certain devices.

16 DR. KURT: Yes, but if I were a consumer say from
17 the National Association of Teenagers, I think that using
18 this method would lead to a large number of people who would
19 be falsely accused, if you were using the immunoassay alone.

20 DR. BUSH: Now let's go to another slide, the one
21 similar to this slide, 25.

22 [Slide.]

23 DR. BUSH: Let's go to slide 25 for a minute
24 because this is the one that is analogous now to where we

1 just were within the laboratory. Now we're looking at the
2 same kind of information for all devices by drug. So
3 looking at the same analogous slide now but with those urine
4 specimens--remember, a large percentage, 50 percent of them
5 were around the confirmation cutoff. They were selected
6 purposefully as part of the study design to test the
7 accuracy and reliability of these devices around the cutoff.
8 Yet we have immunoassay positive test results which in fact
9 confirm GC/MS negative for all devices.

10 Now that, again, is around the chosen cutoff that
11 is stated by the device manufacturers, which happens to be
12 consistent with workplace drug testing cutoffs. Are we
13 confused enough yet?

14 DR. NIPPER: I'm fine. Anybody else on the panel
15 confused? Dr. Kurt, you relinquished the microphone?

16 Dr. Sohn?

17 DR. SOHN: When you say GC/mass spec negative,
18 you're not using a limit of detectability?

19 DR. BUSH: That's correct, they're using the
20 cutoff that is stated on the kit.

21 DR. SOHN: So that there will be a population
22 which would be IA positive but GC detectable, if you will,
23 which is--for example, if this was sent to a second
24 laboratory for testing, the SAMHSA guidelines are to use

1 your limit of detectability. Lab 1 said that I'm positive
2 for cocaine or cocaine metabolite. I now go to Lab 2 and
3 say, I can't be positive for cocaine; send it to Lab 2. Lab
4 2 would be using a much more lower limit, generally very
5 close to their limits of detectability.

6 DR. BUSH: That is correct. They would use that
7 limit of detection, that's correct.

8 DR. SOHN: Now would you accept that as the limit
9 for the GC/mass spec decisions whether these are negative or
10 positive? I hear what you're saying in terms of using the
11 cutoff, and what would appear maybe is that some of these
12 kits are promising less than they're capable of doing. In
13 other words, they're using a cutoff which may reflect on the
14 standardization of the kit by the kit manufacturer, but the
15 kit appears to be more sensitive at the cutoff.

16 It's looking at a concentration and seeing a
17 concentration of drug and gets a signal which is equivalent
18 of the signal of a cutoff quantity of that drug even though
19 what has been presented to it might be 50 percent or 75
20 percent or 60 percent of the cutoff.

21 DR. BUSH: That's correct. Essentially, if you
22 want to talk about it, maybe it's the degree of variability,
23 the tightness around that cutoff. We all know that when you
24 establish a cutoff there's going to be a bell-shaped curve

1 of occurrence of this normal distribution around that curve.
2 We try to minimize that as much as possible in any
3 laboratory situation, testing situation.

4 Whereas, you may indeed have a very wide bell-
5 shaped curve where, if here is the cutoff and this is the
6 lower part minus two standard deviations or 20 percent,
7 whatever number you choose, may be detecting visually the
8 presence of that drug even though it is below the cutoff.
9 That's correct.

10 DR. NIPPER: Dr. Sohn, I don't want to put words
11 in Dr. Bush's mouth, but the way I'm interpreting this data
12 is that there are two possible reasons for it. As an
13 analytical chemist, when I see data like this I think that
14 there's either been a slippage in the calibration. In other
15 words, the calibrator of whatever was used to determine
16 whether the immunoassay device was responding is hitting the
17 cutoff. So it may be missing the cutoff because the
18 calibration was set either too high or too low.

19 The other was, just as Dr. Bush said, there may be
20 imprecision in the signal around the cutoff so that in one
21 lot the bell-shaped curve is wide, in other lots the bell-
22 shaped curve is narrow. I'm not sure which it is, and I
23 don't think we can tell from this data.

24 Dr. Manno had her hand up.

1 DR. MANNO: I think I agree with Dr. Bush in basic
2 concept of what she's delivering, but I think there's a
3 point that we're all missing. When she presents the data
4 from the SAMHSA laboratories, I'm not as concerned about the
5 cannabinoids, for example, or the cocaine. Where I'm more
6 concerned is down around the amphetamines and the opiates
7 because the other slide that she had up here had a large
8 number of unconfirmed.

9 What bothers me is that we're looking at this home
10 drug testing less as a regulatory thing, as Dr. Bush looks
11 at, but we're looking at it more as a medical device, if you
12 will. The problem that comes in, if you use totally the
13 SAMHSA guidelines, while they're a good place to start, when
14 you look at amphetamines, you only confirm for amphetamine
15 and methamphetamine. There are any number of products that
16 are out there that the kids are getting a hold of, the
17 phenylpropanolamines and the other stimulants, that you
18 never confirm. That can account for a great deal of cross-
19 reactivity.

20 And it varies by manufacturer. We've had this in
21 our own hospital recently. This same thing with the
22 opiates. There are some opiates that will nicely cross-
23 react with the enzyme assays, but you're only looking there
24 for morphine and codeine. If you happen to have someone on

1 hydrocodone, you don't look for it.

2 So I think there has to be some bringing together
3 in these classes where there are a lot of pharmacologic
4 classes of drugs that are chemically or structurally
5 related, that we have very good information on cross-
6 reactivity and have something that we can assure reliability
7 based on that.

8 DR. NIPPER: Did I see Dr. Habig's hand up?

9 DR. HABIG: Yes. Dr. Bush, you talked about the
10 likelihood of the problems with the false positives probably
11 being cross-reactivity things. While I think that's a major
12 contributor--it may be the major contributor--immunoassays
13 are not so simple as sodium and a flame photometer that us
14 analytical chemists understand pretty well.

15 So that it might not only be cross-reactivity, but
16 things that enhance activity, confirmation, a lot of
17 different aspects. So there might not be in fact another
18 substance there but just the substance you're really looking
19 at reacting a little differently, or with a bit more vigor,
20 creating what looks like a more positive result. Would that
21 be correct?

22 DR. BUSH: I'm not sure that we've ever down that
23 road to examine that in our laboratory situations to
24 determine that.

1 DR. HABIG: I guess I'm just concerned that if we
2 blanket assume that all of these issues are simply cross-
3 reactivity, it's over-simplifying it.

4 DR. BUSH: That may very well be, sir.

5 DR. NIPPER: Are you asking how gold is the gold
6 standard? Is that your intent?

7 DR. HABIG: No, it's just that the screening tests
8 have more variability to them than simply cross-reactivity.

9 DR. NIPPER: Dr. Rej?

10 DR. REJ: A couple points. I think maybe some of
11 Dr. Sohn's concerns and maybe even some of Dr. Habig's might
12 be addressed on your next slide.

13 [Slide.]

14 Because in addition to this, this case which is
15 cross-reactivity and the apparent false positives, and if I
16 read this right that there's one of these devices that's
17 under-reporting by 90 percent actual positives for
18 cannabinoids. So it's not merely one of interference, or it
19 could be perhaps negative interference. There's some
20 inhibition of the enzyme assay.

21 But I think that these two slides I find
22 particularly interesting, and if these data hold up and are
23 confirmed, I think argue very strenuously on the need for
24 confirmation of all immunoassays, certainly the positive

1 results.

2 However, I have a serious question about the
3 indeterminate or borderline results, because if you go two
4 more slides or three ahead for us--

5 [Slide.]

6 --that there's one of the devices that has a 25
7 percent--25 percent of the results, if I read that right,
8 for device M were borderline. So they were neither positive
9 or negative by the device.

10 Now I may have missed it in your presentation, but
11 you said that the operators were asked to call it borderline
12 positive or borderline negative; is that--

13 DR. BUSH: That's correct.

14 DR. REJ: Where did those go into the previous
15 data? Were they counted or were they thrown out? I think
16 that's very important because if you go back two slides--

17 [Slide.]

18 So we want to avoid red and green, if I read this
19 slide correctly. The perfect device is device A. What
20 percentage of the red and green data are from the so-called
21 borderline or indeterminate? In other words, if we were to
22 just throw those out would we get more like the imaginary
23 device A?

24 DR. BUSH: I was reviewing my notes and I believe

1 that those specimens, those borderline specimens were
2 included in the negatives.

3 DR. REJ: So borderline result was declared a
4 negative result?

5 DR. BUSH: Yes.

6 DR. REJ: So that might help explain the slide
7 just before this, which is the high error rate.

8 [Slide.]

9 The high negative error rate for the immunoassay
10 device. But had you thrown all of those to be positives,
11 then it would have influenced the previous slide rather than
12 this one.

13 But I think that's very important then that these-
14 -one, I find it interesting data that a large percentage of
15 the results could not in fact be reliably read, which to me
16 argues against at least some of these devices. When you get
17 25 percent are neither positive or negative by the device,
18 there's something in the system for the operator--and these
19 are trained operators--to look for a color change or
20 whatever change it is. So that I think argues against the
21 effectiveness of certainly that device.

22 Then how that impacts on the decision-making I
23 think is important. I think that it would be interesting to
24 me at least, and perhaps for the whole panel, if we could

1 have a little more details on where those borderline results
2 went in this analysis.

3 Are these data being published?

4 DR. BUSH: I can get much more complete discussion
5 of these data from Dr. Willette who presented this in much
6 more detail at a recent meeting, September 9th and 10th, of
7 our Drug Testing Advisory Board.

8 DR. REJ: I found your presentation very
9 informative and a lot of good data there, but I think this
10 question about the borderline, especially since the
11 borderline results were very high in some of the devices.
12 In some of the devices they were very low so you could--this
13 graph and its companion graph are very informative because
14 there we only got really positives or negatives, and the
15 number of borderlines were relatively low.

16 But when we're getting up to 25 percent
17 borderlines, then I think it's very important in the
18 performance of at least some of the devices.

19 DR. BUSH: I think what's interesting to again
20 revisit is that the specimens that were borderline and their
21 visual, their ability to be read, were not borderline in the
22 concentrations.

23 DR. REJ: Right, you've made that point clear and
24 that also is important. But the fact that--it really is in

1 the detection system or the eye of the person who's reading
2 this, or in the design of the product.

3 DR. BUSH: If the board wishes, I can easily get a
4 copy of more detailed speaker notes with more slides and
5 provide it to you through the executive secretary. That's
6 an offer.

7 DR. NIPPER: I think that might be very helpful.
8 It certainly would be very educational.

9 Dr. Sohn, you had a comment. Then after that I'm
10 going to ask if anybody else on the panel who hasn't spoken
11 would like to ask a question.

12 DR. SOHN: Donna, most laboratories using the
13 immunoassays will tweak their assays so that the curve
14 represents the concentration on the X axis and signal on the
15 Y axis can vary greatly. For example, I had two specimens
16 tested forensically on the same individuals on the same day
17 two days ago where we could not distinguish on the enzyme
18 immunoassay between a concentration of 150 and 400
19 nanograms per mil of THC by GC/mass spec.

20 I'm sorry, by GC/mass spec the concentrations were
21 respectively 150 and 400 nanograms per mil. On the enzyme
22 immunoassay there was virtually no difference between the
23 two because that was on a flat portion of the sigmoid curve.

24 Likewise, a curve may or should be a nice--have a

1 slope of 45 degrees, and very frequently they don't have a
2 slope of 45 degrees. And if a manufacturer had tweaked his
3 product so that the curve or the slope of the linear portion
4 is almost 90 degrees, a very little change is going to give
5 you a huge change in signal. I don't know whether a
6 comparable process is what has happened here.

7 One of the things I would wonder using these
8 devices, whether someone has taken a series of
9 concentrations for each device and seen what--you're not
10 getting a signal, but whether it's positive or negative, and
11 whether it would be possible to construct a comparable
12 curve. Because we may see that the slope of that curve
13 differs for each device.

14 I have two other comments. One is, have you had
15 an opportunity--

16 DR. NIPPER: Can you make them brief, please?

17 DR. SOHN: Sure. Have you had an opportunity to
18 go by--you had 100 specimens or 90 specimens. Have you had
19 an opportunity to do each lab specimen versus specimen
20 rather than as the totality?

21 Secondly, have you had an opportunity to run these
22 same specimens? I wasn't sure whether--I thought you did--
23 by enzyme immunoassay, by the standard classical enzyme
24 immunoassay of fluorescence polarization immunoassay, and

1 again by specimen?

2 DR. BUSH: Each specimen--I think I'm going to try
3 the second part of your question first. Each one of the 90
4 test specimens was tested by classical enzyme immunoassay
5 and a result obtained. Then that specimen was run on the
6 devices under evaluation.

7 DR. NIPPER: Wasn't that column P and R in your--

8 DR. BUSH: P, and then there was another test that
9 had to be done another time, so on another day another
10 control had to be run. But indeed, an immunoassay, an
11 enzyme immunoassay Emit test was run and that data is part
12 of the bars on that 18 bar chart.

13 DR. SOHN: How do they compare by specimen? In
14 other words, if you looked at each specimen individually,
15 how did the devices compare with the, if you will, classic
16 current methods?

17 DR. BUSH: Remember that these are visual
18 endpoints, and there was an N of three individuals reading
19 them. As I understand it, the way this study was set up--
20 what we're presenting to you is the summary data. But each
21 manufacturer of the kit was provided that information
22 specifically concerning their test kit as part of the
23 product of this contract work.

24 So I don't have that, nor do I have the identity

1 of each and every one of those kit manufacturers. So I
2 guess my point is, I can't answer your question. The
3 manufacturers have that data, but I don't.

4 DR. NIPPER: Let's go around the room and see if
5 there's anybody who hasn't had a chance to talk or ask a
6 question who would like to do so.

7 I'd like to thank you, Dr. Bush, for coming back
8 to the podium and helping us additionally. And your offer
9 to provide the additional material that you have is most
10 appreciated. I'm going to ask if there are members of the
11 public who would like to either comment briefly or ask a
12 question. If that's the case, Dr. Bush, you might be more
13 comfortable in the audience or you could join us at the
14 table there and maybe we could all hear from people in the
15 public who would like to comment briefly or ask a question.

16 DR. BUSH: Thank you, I'll take the audience.

17 DR. NIPPER: We may call you back to the podium.

18 Thanks.

19 There was a hand in the back. I didn't recognize
20 who it was. Maybe I need to get my glasses changed. Maybe
21 it was Dr. Bogema?

22 DR. BOGEMA: Yes.

23 DR. NIPPER: Please come to the podium and state
24 your name and your financial involvement, again for the

1 record.

2 DR. BOGEMA: My name is Stuart Bogema. I am here
3 at the request of Roche Diagnostics, a manufacturer of an
4 on-site drug test kit. I've been in both the laboratory
5 field drug testing as well as doing research actively for
6 the last 10 years on on-site drug testing products.

7 There were three points that I wanted to get
8 across during my presentation this morning. First is, from
9 my experience at looking at different devices, there is
10 variation certainly from one device to another in their
11 performance. I'll get into that more in just a minute with
12 the slides.

13 Second, that there are devices that have been
14 developed in the recent past that are comparable to the
15 laboratory initial screening immunoassays. Again, I'll get
16 to the slides to show that here in a minute also.

17 The third thing that I emphasized this morning was
18 that, in my opinion, confirmation testing is necessary. I
19 think that we all can see, from both the laboratory testing
20 and the on-site device testing that confirmation testing is
21 necessary because of cross-reactants and other reasons for
22 false positive screening tests.

23 If I could have the slide put on--I think it was
24 probably like number 26. Can we turn those back on?

1 [Slide.]

2 Yes, this is the one. I think that this slide is
3 where you see that each one of those letters, except for the
4 controls and the A bar graph which is the optimum
5 performance, is a different on-site device, and how it
6 reacts to specimens and really shows, in my understanding,
7 the number of let's say false negatives and false positives
8 that the device has around the cutoff. That slide, to me,
9 is a good way to see how much variation there is indeed from
10 one device to another.

11 You have some, if you look at C and D, you look at
12 K, that are very similar in their response to these samples
13 as the reference test, the Emit test. You can just see that
14 in general by the amount of green and red color above and
15 below the 50 percent. So there are devices in this study
16 that showed comparability to the Emit testing, which is one
17 of the points that I wanted to make this morning.

18 Obviously, not all of the devices do. Again,
19 that's because there is a lot of variation in the
20 performance of different devices.

21 Now if we go to the slide before this, I believe
22 it's number 25.

23 [Slide.]

24 DR. BOGEMA: Donna showed two slides, one for the

1 laboratory reagents and this one is for the on-site devices.
2 Now what you've got in this slide is you have the spread of
3 range of percent unconfirmed positives for all the different
4 devices. So again this shows how much variation there is
5 from one device to another.

6 But on the left-hand side is, for that particular
7 drug, the best performing device in that it had the lowest
8 unconfirmed positive. And on the right-hand side, at the
9 other end of the range are the devices that showed the
10 highest unconfirmed positives, that had more false
11 positives.

12 But if you concentrate on the left-hand side, that
13 shows that there are devices that had relatively small and
14 very comparable percentages of unconfirmed positives to the
15 laboratory. So if we go back to the laboratory slide--

16 [Slide.]

17 Here for PCP, amphetamine, cocaine and
18 cannabinoids, you had devices that had percentages of
19 unconfirmed positives close to zero; in the range of zero to
20 10 percent. If you look at the slide for the--I think if we
21 go to probably number 16 I think is what--

22 [Slide.]

23 If you go back and you look at the percent
24 unconfirmed positives at those six labs, you have for

1 cannabinoids and cocaine, you had labs that were very close
2 to zero with unconfirmed positives, but you had some that
3 were in the 20 percent. You actually for the on-site test
4 have devices that had significantly lower percentages of
5 unconfirmed positives for amphetamine than any of the labs
6 did in this study.

7 So again I just want to make the point about
8 comparability, the potential that there are devices that can
9 compare to lab screening.

10 And the last thing I want to say is that because
11 there is this variation in devices, I commend what the
12 Division of Clinical Laboratory Devices is trying to do by
13 setting up specifications, criteria for these devices in
14 their analytical performance characteristics, and then going
15 further and actually telling the industry what the
16 requirements will be.

17 DR. NIPPER: Dr. Bogema, don't leave, because Dr.
18 Gerson raised his hand and then I think Dr. Rej raised his.

19 DR. GERSON: Actually Dr. Rej beat me to it so
20 I'll defer and let him go first, in case we were going to
21 say the same thing.

22 DR. REJ: Perhaps not. What you say may be true
23 but it's really only part of the story, because even though
24 we have a zero false positive with some of the devices, it

1 seems from that other graph those that have zero false
2 positives tend to have a very, very high false negative
3 rate.

4 DR. BOGEMA: It's really hard to--

5 DR. REJ: That may not be comparable to what
6 you're looking as the best performance for one device in
7 terms of false positives, another device for false
8 negatives. What it may be is that one has set a higher
9 threshold. Actually, if you go ahead a couple slides to the
10 first one you showed.

11 DR. BOGEMA: I think it was 26.

12 DR. REJ: It was the 18-bar graph of true
13 positives, true negatives.

14 [Slide.]

15 In broad terms, the amount of red and green on the
16 slide is roughly constant. It's just a trade-off. Device
17 G, for example, is very good in the true negatives, I
18 believe, which is the bottom; is that correct?

19 DR. NIPPER: Yes.

20 DR. REJ: Or those are the positives; the
21 positives, very good. But in terms of the negatives, it's
22 very, very bad. It's missing certainly more than 50 percent
23 in that case.

24 DR. BOGEMA: I agree.

1 DR. REJ: So it's really not--you can look at the
2 red plus green as total error, and the trade-off above and
3 below that line as due to the cutoff or some tweaking of the
4 device.

5 DR. BOGEMA: Yes, and my point is, you look at R,
6 which is the reference Emit testing which is the most common
7 immunoassay used for drug testing in laboratories, that some
8 of them comparable.

9 DR. REJ: Since the technology is almost the same,
10 that's not surprising, is it?

11 DR. BOGEMA: That's correct, yes.

12 DR. NIPPER: Dr. Gerson?

13 DR. GERSON: My comments were actually going along
14 the same lines but let me try and state it a different way.
15 Actually Drs. Everett and Sohn about 30 minutes ago got into
16 this same topic. The one statement that Dr. Bogema made
17 that sort of makes me react is, just in casual conversation
18 you defined good performance as no false positives.

19 Well, we're really talking about sensitivity and
20 specificity. When I teach statistics I try not to use the
21 terms good and bad, although people like to do that. If
22 you're going to use the words good and bad with statistical
23 terms then it's less bad to use the terms efficiency or
24 predictive value. As most of us around this room know, you

1 need more data, more individual statistics to be able to
2 come up with the sensitivity, the specificity of so-called
3 efficiency.

4 In the normal operation of a SAMHSA laboratory,
5 the way they're supposed to do things, that data is not
6 available. That is, going back and re-testing the
7 negatives. That's not the way they're supposed to do
8 things. Now a study could be designed, and in fact I think
9 that I've seen data out of that agency in the distant past
10 where they did go back and re-test specimens that had been
11 negative at lower cutoffs. If there's anyone here who has
12 that data or remembers that data, it might be useful for us
13 to see it.

14 The temptation is for some device to get to the
15 market, have no false positives, have that be presented as
16 being inherently good, and have a whole lot of false
17 negatives. Then we get back to the comment that Dr. Kurt
18 made a long time ago of, is the product delivering what they
19 think they're buying?

20 So I think we need to be very careful when we get
21 into sensitivity, specificity, predictive value, the
22 cutoffs, how does the population for which this is intended
23 resemble the workplace population where we have the best
24 data so far? It gets to be a little complex and I think we

1 need to be careful not to over-simplify.

2 DR. BOGEMA: I used the terms good and bad--until
3 we really have criteria for defining what good and bad, they
4 don't really mean a lot. That's why I commend the division
5 for moving in that direction, not only to set the criteria
6 but hopefully to say what's acceptable and what's not
7 acceptable.

8 DR. NIPPER: The goals for testing in various
9 settings define what good and bad are. If you go back to
10 Galen and Gambino's initial work in which you decide whether
11 you would like a high specificity test, a high sensitivity
12 test, a test with really good predictive value, or a highly
13 efficient test, each one of those is a value judgment which
14 applies to the setting in which the setting is run.

15 I would venture to say that in the workplace
16 testing area where one assumes that there's a very low
17 prevalence situation, that you go for the testing
18 environment and the testing cutoffs that give you the
19 highest predictive value of a positive result.

20 On the other hand, in a lay testing environment
21 which is not workplace, I'm not sure what value judgment you
22 would like to place on the situation. I don't know whether
23 you want the best efficiency. But I worry about any
24 situation which would cause us to deviate substantially from

1 a tried and true procedure where there is a gold standard
2 available. That's my personal view of what good and bad
3 mean.

4 I think that we are not at a position yet in this
5 meeting to determine what that means and I think there are
6 going to be lots of different views of that.

7 Dr. Habig? Then I think I'd like to move to
8 another speaker, if you don't mind.

9 DR. HABIG: I just wanted to comment that this
10 particular slide might leave us with an impression that
11 things are not so good, when in fact lumping four
12 statistically parameters into the same bar graph; that is,
13 four different drugs on the same graph, is a bit misleading.

14 It will be good to see Dr. Willette's more
15 complete data where I assume the individual slides that
16 probably build this slide would be available, because it's a
17 big unfair to take four tests and run the whole range
18 because it looks like then everything is--I'm actually
19 presuming that things are not that bad on any individual
20 test. We don't know till we see the results.

21 DR. NIPPER: Right. We've had some other hands in
22 the air. I think that you're going to find out how terrible
23 I am with names. Is it Thad Morris?

24 MR. MORRIS: Yes. I'd like to comment on the

1 presentation as well and also utilize some of the graphics
2 that we've all had a chance to see.

3 DR. NIPPER: Mr. Morris, before you go into that,
4 just launch into your financial involvement and then we'll
5 let you go.

6 MR. MORRIS: I'm the president and chief executive
7 officer of Worldwide Medical Corporation. My company
8 develops, manufactures, and markets rapid diagnostic
9 products, specifically in the area of drugs of abuse.

10 If the goal of the FDA, or the decision of the FDA
11 is to say, yes, we think a product of this nature has a
12 benefit to society, and in making those kinds of
13 determinations I would think that we would want to have a
14 product that was as close to or better than what we were
15 already using in the screening environments.

16 While I agree with your comments on having four
17 and five different products grouped together, but if we
18 wanted to say for just a moment that we wanted a product
19 that's already been through the FDA, that's already been
20 used in the emergency rooms and so on, we'd want to compare
21 it to the immunoassays.

22 If you look at these graphs, without looking at
23 any specific company-wise, if you look at the graph on the
24 right as being the gold standard of immunoassay and you look

1 at the graph on the left as being perfect of all worlds, if
2 you had products that fell within those ranges of both the
3 red and green bars all the way across you could draw an
4 imaginary line across there and determine that there were a
5 number of those products in those bars that approach that.
6 So that's one of my comments.

7 The second comment I have--and the data was really
8 well presented as an overview of this particular study. But
9 one of the things that I think that bears mentioning is that
10 this study was carried out as a way to help the court
11 systems determine if there was a value of on-site tests that
12 would allow the court systems to make their decisions,
13 whatever they had to be, at a cost effective and timely
14 basis, which on-site testing provides. Because as part of
15 that study in the prologue, it was said that this court
16 system in itself and the 50-some-odd districts sends out
17 700,000 urine tests annually.

18 And the last part, in fact the very last part of
19 the comments of the study were that we recognize the
20 differences in the statistical data may not be that good
21 from a statistical point of view. However, realizing that a
22 preponderance of the samples that were, not collected but
23 constructed for the study, were at or near the cutoff
24 levels, which also affects your statistical variability.

1 My final comment on that is that at the end of all
2 this study, the U.S. Federal court systems determined that
3 this in fact was an acceptable method to use in their
4 particular environment. I think that bears stating that may
5 have been omitted from the study.

6 Very last part is, this is a study, and it was
7 brought up from the panel that this has not been a published
8 paper, it's not been a peer-reviewed article, it's not been
9 subjected to all the things of the clinical construction of
10 the study and the samples used and so on. I think we should
11 bear that in mind as well.

12 I thank you for the opportunity.

13 DR. NIPPER: You're welcome. Does the panel have
14 any questions for Mr. Morris? Thank you very much.

15 Is it Mr. Evans?

16 MR. EVANS: Yes, Dave Evans, executive director of
17 National On-Site Testing Association. We are a group of the
18 consumers and manufacturers and distributors of on-site
19 tests. I also forgot to mention, I am an attorney in
20 private practice and I represent drug and alcohol test
21 manufacturers, laboratories, third-party administrators,
22 MROs, and alcohol and drug treatment programs.

23 We really applaud this study because I think it
24 shows something that we've been saying for a long time, that

1 on-site tests are comparable. At least some of the on-site
2 tests, hopefully all the ones that NOTA represents are
3 comparable to the laboratory immunoassay screening tests.

4 An issue came up earlier, a question was addressed
5 to Donna Bush about whether or not these tests would upset
6 the current Federal programs. We think they would not
7 because people are required to do things, if they're
8 regulated by the Federal Government to have to do drug
9 testing, they have to do it the Federal way. They can't use
10 something that's not approved by the Federal Government.

11 They can do additional testing other than what's
12 required by the Federal Government. So they could use an
13 on-site test in addition to what the Federal Government
14 requires. But again, that would not upset the Federal
15 program, and Federal sanctions could not be applied against
16 the employee for anything other than a federally-approved
17 test.

18 We feel that we can meet all of the Federal
19 standards and we will in the future. HHS has given us a
20 list of standards that we must comply with. We will be
21 submitting our response in writing, and based on talking to
22 all of our members we feel we can jump over each and every
23 hoop that HHS has put up in front of us. We will make that
24 information available to you. We should have it out within

1 a couple of weeks and we'll send that to you also, so you
2 can see how we are. We feel we can slip right into the
3 existing Federal program.

4 Laboratories are using on-site tests, so we have a
5 number of laboratories that are NOTA members that are using
6 on-site tests in a variety of situations. Again, the issue
7 here is not so much how the test might be used, but a lot of
8 people are using it in a variety of ways.

9 As far as the false negatives go, we also would
10 like to see data on laboratories with false negatives and
11 see how many of them are coming up with false negatives.
12 Before on-site testing is judged by that standard, we think
13 labs ought to be judged by that standard also.

14 We have some evidence that some labs are taking
15 the reagents from the manufacturer and diluting the
16 reagents, which would cause a false negative. And of
17 course, nobody is going to complain if their drug test comes
18 up negative. You're certainly not going to get a complaint
19 from an employee, so that's probably why you haven't heard a
20 whole lot about it.

21 DR. NIPPER: I'd like to interrupt you on that.
22 As a person who directs a laboratory, I think that it's
23 important to remember that there are quality control
24 specimens and blind proficiency in both in-house and outside

1 proficiency samples that are run in reputable laboratories.
2 These are plus or minus 20 percent usually of the cutoff.
3 And if reagent dilution or any kind of tweaking, as Dr. Sohn
4 called it, were to affect the number of false negatives,
5 these would appear in the blind proficiency samples.

6 That doesn't mean laboratories are perfect. It
7 just means that there--I want to reassure you that quality
8 control that is run in laboratories is designed to pick up
9 that kind of defect. There are systems in place and there
10 is data out there that will show you what's going on.

11 MR. EVANS: I understand that. But I'm saying,
12 this is the practice that we understand is occurring at
13 least in some laboratories and I have documentation of that
14 from the labs themselves.

15 The other issue is, sticking with a system that's
16 tried and true. We agree with that. We think that on-site
17 testing can fit into the Federal scheme.

18 By the way, every court so far--and I'm familiar
19 with the court cases. I've written a two-volume book on the
20 legal aspects of drug testing, and I keep up to date with
21 it. Every court case so far that has considered on-site
22 testing has said that it was okay. I'm not aware of a
23 single negative legal precedent with on-site testing so far.
24 Now it may be out there and I haven't heard about it, and I

1 probably would have.

2 I can give you some Federal cases that have looked
3 at on-site testing and have approved it. Again, not under
4 the Federal employment guidelines. These are cases
5 involving criminal justice situations.

6 The only other thing that I'll ask is that if you
7 put a standard on the on-site testing industry, to not make
8 it a stricter standard than you're applying to any other
9 test device or laboratory. We just ask that you take a look
10 at that and not apply more strict standards.

11 Thanks very much.

12 DR. NIPPER: Thank you, Mr. Evans. Wait for a
13 second, there may be a question for you. I don't see any
14 hands raised. Thank you very much.

15 There is one other hand I see in the back. I
16 think we're going to--you'll have to help me with your name
17 and your affiliation.

18 DR. TAYLOR: Dr. Howard Taylor.

19 DR. NIPPER: I apologize, Dr. Taylor.

20 DR. TAYLOR: With Sensor Technologies Corporation.
21 We do laboratory-based testing.

22 As part of my talk earlier I did include all of
23 Dr. Willette's slides, so you should have that before you,
24 in which he did break it out by drug. There were a

1 significant number of false positives by drug. And to
2 answer this question about the slide of all four drugs being
3 together, I think that will help with that.

4 Also, I would like to return to Dr. Kurt's
5 question, which I'm not sure was exactly answered in which
6 he asked, if I'm a member of the Teenagers Association, or
7 whatever, would I be falsely accused of a test result, by
8 using one of these devices? I'm not sure I heard Dr. Bush's
9 answer, and I would like to call her back and have her
10 answer that. I guess specifically to answer the question in
11 two parts.

12 Certainly, the presence of analyte may be below
13 the cutoff--that is the analyte present--and above the LOD.
14 But is there or would there be a case in which the analyte
15 is not present at all--in other words, a true false positive
16 where there's no analyte present? And would that be the
17 case with these devices? I'd ask that question again of Dr.
18 Bush.

19 DR. BUSH: As for the detail of Dr. Willette's
20 study and whether or not a specimen containing absolutely,
21 positively no drug at all detectable by GC/MS, how did that
22 fare through the study of 14 or 16, 15 devices, I don't know
23 the answer to that. That will need to be posed to Dr.
24 Willette directly. So I'm not sure how the person from your

1 group, your National Association of Teenagers, or whatever,
2 would feel about that. I don't know the answer. I can't
3 help you there.

4 DR. TAYLOR: Thank you, that's all I had to say.

5 DR. NIPPER: Thank you. Are there any questions
6 from the panel for this person? Thank you, Dr. Taylor.

7 We are approaching the time set aside for a break
8 and I would like to call a 15-minute break and reconvene at
9 2:35 for questions to the panel and consideration of the
10 document points to consider.

11 [Recess.]

12 DR. NIPPER: When the panel is re-seated and ready
13 to go to work again, which I hope will be within a minute,
14 we're going to try to review the questions to the panel.
15 We're going to put up question number one first. Then what
16 I'd like to do is go around the room. We'll try to be fair
17 in putting people on the hot seat. I don't think it's right
18 to put Dr. Habig on the hot seat every time, although most
19 of the time is not too bad, I guess.

20 [Laughter.]

21 [Slide.]

22 The first question is, are the performance
23 recommendations outlined in the draft points to consider
24 adequate to characterize these tests? Should any additional

1 data sets be requested? If I remember correctly, that
2 refers to Section I.A. under analytical performance
3 characteristics, page 2, 3, 4, 5, all the way down to the
4 top half of page 6. So this is a fairly all-encompassing
5 group of performance recommendations, including recovery,
6 analytical sensitivity, analytical specificity, precision,
7 accuracy by comparison studies, stability data, and last but
8 certainly not least, specimen collection, handling, and
9 storage, including specimen integrity considerations.

10 So at this point I'm going to start with our
11 favorite engineer, Ms. Rosenthal.

12 MS. ROSENTHAL: Thank you. Actually I thought
13 when I read this at home that this was going to be pretty
14 simple. But then after looking at Dr. Bush's slides with
15 the false positives and false negatives and cutoffs, and
16 slide number 26 which looked like an Agam painting, I
17 realized that this is really a very complex situation.

18 I felt in reading the points to consider, I
19 questioned whether 30 to 40 percent--recommends confirmation
20 of 30 to 40 percent of the negative results as well as all
21 positive results. I question, especially now after seeing
22 how these devices look--I don't mean look, how the regime
23 tests--I wonder if that's enough, if everybody is
24 comfortable with that. That's six, accuracy by comparison

1 studies.

2 Then I also, another thing that crossed my mind is
3 when you talk about cutoff sensitivity--not sensitivity,
4 cutoff concentration, is there a way that we can test to be
5 sure that this is actually urine we're testing?

6 DR. NIPPER: That would deal with the adulteration
7 issues, specimen integrity and so forth in part 8.

8 MS. ROSENTHAL: That's my comment. Those are my
9 questions.

10 DR. NIPPER: Thank you very much. Dr. Sohn,
11 you're next unless you choose to pass.

12 DR. SOHN: No, I don't choose to pass. However, I
13 do feel these are pretty much most of the standard FDA
14 questions, which I think are tried and true and I think
15 cover most of the--not most, virtually every area of
16 importance in testing. I do think that what was brought up
17 in terms of adulteration--I shouldn't say adulteration--
18 dilution of the urine may be important in the sense that one
19 can drink enough liquids or imbibe enough liquids to change
20 the concentration of the excreted urine which may,
21 particularly near the cutoff, render a specimen containing
22 drug negative.

23 DR. NIPPER: So are you proposing that there
24 should be a dipstick type specific gravity on there as a

1 quality control issue?

2 DR. SOHN: Either specific gravity or there may be
3 a quick creatinine test that could be done on a dipstick or
4 on that type of level. So that I would be concerned about
5 that. Of course, we could not distinguish between water
6 added to the specimen or water taken internally. But I do
7 think that some measure, if possible, of dilution would be
8 important.

9 DR. NIPPER: How about pH? If you put vinegar in
10 there or something?

11 DR. SOHN: Again, you'd have to see how that
12 affects the test itself. Some of the enzyme systems that
13 are used may or may not be involved. I think we just have
14 to look at it and see.

15 DR. NIPPER: Thank you. Dr. Goldsmith?

16 DR. GOLDSMITH: I think most of the performance
17 recommendations as outlined are just fine. As Dr. Sohn
18 said, it's very much consistent with what's being done now
19 within the laboratory in terms of how you evaluate these
20 assays.

21 I would just point out a few things which were
22 certainly stressed before in the presentation regarding
23 workplace testing and how important it is to define the
24 cutoffs, or how important cutoffs are. I would just want to

1 point out that I think that has to be applied here in this
2 document as well or stressed in some way.

3 Because we talked mostly today about the
4 application of this point of care drugs of abuse test with
5 parents using it for their children. But I can see a whole
6 spectrum of applications, particularly in the pre-employment
7 arena, where people before they go for their pre-employment
8 test would want to test themselves to make sure that it's
9 negative, et cetera. So that that cutoff, I think, is
10 extremely important and needs to be broad enough for a whole
11 range of populations.

12 I only have one other comment, and that is
13 something that was also brought up earlier. I'm not sure if
14 it really addresses this particular question, but it is in
15 the guidelines about seventh grade reading level. I would
16 just stress that seventh grade I think should be used very
17 liberally because any of us who have either written consent
18 forms or have reviewed them for IRBs know that it is
19 extremely difficult sometimes to write them so that it is
20 understood by all. Seventh grade may even be, when it comes
21 to medical jargon, a little high. So I would just point
22 that out, when you review the recommendations.

23 DR. NIPPER: Dr. Rej?

24 DR. REJ: We certainly covered many performance

1 characteristics of devices. I have one question though
2 about the comparison studies. Is it typical for an FDA
3 document not to put in what is an acceptable comparison
4 rate? Looking at the famous slide 26 or 27, whatever it
5 was, that was a comparison with another established
6 procedure, and in fact the current gold standard procedure.
7 And some of the devices had error rates, either false
8 positive or false negative, approaching 70 or 80 percent.

9 I was just curious whether that--that seems to be
10 curiously absent, or is it something that comparison is in
11 the eye of the beholder?

12 DR. GUTMAN: It's a cross between the two. The
13 equivalency standard or lack of standard that we follow is
14 challenging, and we have a dazzling array of analytes
15 pouring through the chemistry branch each year. When you go
16 to the literature to look for performance standards that
17 have either been published or established by standards
18 organizations, as you probably know from reading and
19 dreaming about the literature, there is an astounding
20 paucity of knowing exactly what's right. And when you get
21 chemists or clinicians together, they will all argue about
22 what's right.

23 So it is a little bit of seat-of-the-pants. We
24 have experienced reviewers and managers, medical officers

1 who struggle with it. And we know the extremes. We know
2 when it's really good and we know when it's really terrible,
3 we'll try to either unable to determine or NSC a product.
4 Where we get into trouble is, how good is good enough?
5 Although we don't have--this isn't planned to be a standard-
6 setting session, if anybody has an opinion on targets, we
7 would certainly be willing to listen.

8 DR. REJ: Because I think that's very important,
9 in particular for systems that might have an unacceptable or
10 a higher than desired false positive rate without a
11 necessity for confirmation of a presumptive positive. I
12 think in this particular case, it may be more important than
13 some other cases. And certainly when you're going to
14 quantitative testing then there's a wide spectrum of
15 analytical performance.

16 But in this case I think it's a little bit simpler
17 because you have a gold standard that's yes or no, and you
18 have a test kit that's yes or no. That comparison I think
19 can be a little bit more facile. And if the type of study
20 that we saw presented by Dr. Bush is representative of other
21 studies with a different design, then I think the FDA might
22 need to consider what is the lowest case that they would
23 accept.

24 DR. GUTMAN: You'll see that actually is a

1 question that's going to come up. Again, we don't usually
2 have standards so we would--

3 DR. REJ: I would recommend that there be some
4 minimum standard for comparison with the gold standard
5 assay. I think that comparison of negatives, a 40 percent
6 comparison with a GC/mass spec. I would recommend that all
7 negatives be compared at least to a laboratory-based
8 immunoassay procedure, all negatives be compared to that.
9 If those are positive, then those certainly go on to GC/mass
10 spec.

11 Apart from misdefining analytical sensitivity, I
12 think you have--what you mean is the minimum detectable
13 concentration. That's not sensitivity, although they're
14 related.

15 DR. NIPPER: Dr. Lewis, we're on question 1.

16 DR. LEWIS: And is 1-something-8 part of that
17 consideration, the specimen collection, handling, and
18 storage?

19 DR. NIPPER: Yes, all the way down to B.

20 DR. LEWIS: It may seem a frivolous concern on my
21 part, however when it comes to specimen integrity, and with
22 all the best intentions of a parent in providing a proper
23 specimen, from personal experience I know youngsters to be
24 extremely ingenious as to how they might, if they were

1 suspicious of being subjected to drug testing of one sort or
2 another, find all means of providing samples that are not
3 even their own samples. We know this happens in the adult
4 generation and I'm sure kids can figure out even better ways
5 to possibly even provide a sample that's anything but their
6 own.

7 So I say, with the best intentions on the part of
8 parents, children could probably have drug-free urine
9 available to them or ways of defeating that part of the
10 system, and the parent with due concern for the child's
11 privacy or what have you might not never suspect that what's
12 being submitted is nothing at all as to what they imagine it
13 to be. So that's a concern of mine.

14 DR. NIPPER: Thank you. Dr. Everett?

15 DR. EVERETT: I agree with the guidelines here.
16 But in addition to that, the data sets that I would like to
17 see would deal largely with looking at how the test kits
18 perform under a variety of conditions that may mimic what
19 happens after the kit is manufactured and by the time it
20 reaches the consumer.

21 In my particular case, the problem has been with
22 pregnancy tests where we've had patients who walked around
23 with the pregnancy test in their pocket for a day and then
24 they go home and do the test, and then the test is positive.

1 And then they come in and we check and now the test is
2 negative. We've gotten a variety of results with pregnancy
3 tests just based on what happens on the storage conditions
4 with the test kit.

5 So even with this test kit, the kind of data again
6 that I would like to see would be that which deals with how
7 the kit changes in its performance under a variety of
8 conditions, particularly those conditions leading till after
9 the time the kit is manufactured until the time it reaches
10 the consumer.

11 DR. NIPPER: Thank you. Dr. Boughman?

12 DR. BOUGHMAN: I've been reminding myself that at
13 this stage of the process we are being asked to provide
14 advice to the FDA for the points to consider. Then at some
15 future time members of this panel or others in fact might be
16 looking at the data presented for any one of these kits.

17 And to remember that we are now looking at the
18 bigger picture and asking about standards for the kits
19 themselves, if you will, and reminding ourselves that I
20 think the very interesting data presented by Dr. Bush out of
21 Dr. Willette's study did exactly what it was supposed to do.
22 That was to be provocative, and it has certainly provoked us
23 to think of many things that many of us might not have
24 otherwise addressed directly.

1 With regard to several of the comments that have
2 been made and in the context of question number 1, there has
3 not been an emphasis sufficient, at least I think, to say
4 that any kit that would be presented should have been tested
5 on the target population. In fact, we would want to see
6 complete data on samples collected from teens or pre-teens,
7 knowing that most kids make their decision to use or not use
8 drugs by the fifth or sixth grade. So we would want to see
9 data from the population for which the kits might be used.

10 We in fact should be able at the original 510(k)
11 or pre-market application stage, have a very good idea of
12 what several different types of contaminants or potential
13 contaminants might do. And three or four things that I've
14 listed here for myself are, somebody with a bladder
15 infection, for example. Would that affect anything one way
16 or another? The presence or absence of menstrual blood?
17 There are several other kinds of things that I think have
18 not been specifically addressed, but in fact were I to be
19 looking at a 510(k) I might want to ask those questions.

20 The main thing I think I learned from the
21 presentations this morning was that at the time of
22 examination of an individual device or kit, we as a panel
23 would want to see the complete data; false positives, false
24 negatives against the gold standard, the GC/MS. Not against

1 intermediate kinds of things. So that the evaluation of
2 concentrations and cutoff points could be evaluated for each
3 drug being tested. So that I think we are in fact urged on
4 by these data to in fact ask for very complete analyses to
5 be done.

6 Two more quick comments here, specific
7 recommendations. Additional data sets, I think in fact when
8 we are looking at performance indicators and performance
9 recommendations we need to also see on the part of the
10 manufacturer some consumer response in the process of
11 collection of those data. I'm not sure whether that
12 addresses question number 1 or other places, but I would
13 like to see some of that if I were ever to review one of
14 these kits, per se.

15 Secondly, I would urge the FDA to in fact address
16 in a standard-setting meeting some of the issues. There was
17 a challenge from the public today that the numbers, the
18 kinds of statistical analyses would be asked for. That
19 group in fact could address issues very specifically of
20 cutoff concentrations and so on. But having been a part of
21 a standard-setting conference for other devices or groups of
22 devices, I would urge the FDA to consider such a meeting.

23 DR. NIPPER: Thank you. Dr. Harrington-Falls?

24 DR. HARRINGTON-FALLS: To briefly add two points

1 to the first question. In terms of performance I would be
2 interested what type of marketing might be considered for
3 alcohol, which is probably the number one used drug in this
4 age group. And secondly, maybe having a temperature
5 correlation on the specimen bottle so that adulteration of
6 the specimen could be minimized.

7 DR. NIPPER: Thank you. Dr. Kurt?

8 DR. KURT: I think there needs to be a great deal
9 more attention to the definitions in addition to the
10 sensitivity, specificity, accuracy, et cetera, which would
11 define, one, what are the test reagents? Is it indeed an
12 Emit system, or is it a TLC system, because that kind of
13 system analyzes differently. And what is being tested for?

14 Such as Dr. Harrington-Falls pointed out alcohol,
15 the testing for that has different implications, not only
16 from the standpoint of the type of the test, but also
17 perhaps regulatory implications from that as well. That
18 would include not just alcohol but other hydrocarbons that a
19 teenager might be inhaling that someone might be looking
20 for.

21 Another factor to consider I think is the medium
22 that's being tested, the biologic substance. If a person
23 has a test kit available for testing for urine, it should be
24 specified that it's for urine and not necessarily spun-down

1 plasma, et cetera, so that that's used for that purpose
2 alone. Until we have the information from the specific
3 field trials of this available with the sensitivity,
4 specificity available I would be hesitant to necessarily
5 pass on this.

6 DR. NIPPER: Dr. Manno?

7 DR. MANNO: I just would like to support
8 everything that's been said so far, but I would like to
9 touch on a few of those points. I have great concern about
10 whether we are directing our interest to licit or illicit
11 drugs, and that comes in, depending on your definitions,
12 with the inclusion of alcohol. I think that is a highly
13 prevalently used drug of abuse in the teenage and the young
14 people population. I think it would give us a better handle
15 as parents to handle those situations early on.

16 The other thing is that I'd like to echo the
17 concerns on specimen adulteration. I'm most concerned about
18 the pH to take into account the addition of such things as
19 lye or bleach or something that would negate a test. I am
20 concerned with specific gravity for the dilutional--those
21 should be easily engineered around.

22 One point that has not come up on specimen
23 integrity would be the question of whether or not the kit
24 should include a suitable collection container. This is

1 important from two standpoints. One being a positive--and
2 if the panel should decide or the agency should decide to
3 include confirmation as part of the system, the decision
4 whether to send the sample that had been previously tested,
5 is of concern in terms of lower response later for
6 adsorption to the container. So there should be some
7 concerns there.

8 There is also possible contamination if we don't
9 include a container in the matter. Anybody's jelly jar or
10 pickle jar or mustard container could in term influence
11 results because it's been either not properly prepared or
12 has been improperly prepared and altered the character of
13 the sample. So I think those are things that we need to add
14 to that list.

15 DR. NIPPER: Thank you, Dr. Manno. Dr. Gerson?

16 DR. GERSON: If we follow the instructions to back
17 out the emotional and the social issues then we're back to
18 basics. All studies should be on the population for which
19 it's intended. That is just as everything we've ever done
20 that I've ever been involved in. One of the things we look
21 for is, how does the study population resemble the
22 population for which the sponsor intends to use?

23 In this document we talk about the SAMHSA drugs.
24 I question why only those. I mean, those are very

1 important, but in other populations you may want a different
2 menu, an expanded menu.

3 Cutoffs, if you believe in them, are politically
4 not medically derived. I've always been an advocate of, do
5 your best work. In other words, LOD and LOQ are misused
6 terms, so I'm talking about the lowest number that you can
7 reproducibly report out of your system.

8 In terms of for purposes of the study and
9 submitting to FDA, I would at least raise the question that
10 not only should all positives be confirmed by GC/mass spec,
11 but maybe all negatives for the purpose of the study. Now
12 again, that gets into how big is the study, what are the
13 questions? So that's clearly something just to think about.

14 As part of a study protocol, I would enhance the
15 portion where it talks about the robustness of the specimen.
16 I would like to see some emphasis on stressing those
17 specimens, time, temperature, sort of anticipating all the
18 things that people might do even though it's not the way the
19 specimen is supposed to be handled.

20 I am an advocate of built-in adulteration check if
21 it's at all practical. I'm also an advocate of a built-in
22 control. I mean a real control, not a process control.

23 Also based on what I've heard today, I strongly
24 recommend that there's got to be confirmation, somehow.

1 This is a position which I arrived at based on what I've
2 heard today. In the labeling, in the instructions somehow
3 to convey to the user something that most of us know, that
4 confirmation is not repeating it by buying another of the
5 same or different kit.

6 Just sort of a little perspective and then I'm
7 done. Something that occurs to me that may or may not be
8 important is, it sounds that unlike other devices, here
9 we're talking about a device which may be used by one person
10 for testing someone else's specimen, not his or her own, for
11 health care purposes--testing someone else's. In addition
12 to which, there's probably a punitive implication. Based on
13 that I think it's not exactly correct to compare this to
14 other OTC or home use products.

15 Thank you.

16 DR. NIPPER: Thank you, Dr. Gerson. Dr. Tong?

17 DR. TONG: Thank you, Dr. Nipper. I might begin
18 by saying that my experience is not with devices but with
19 medicines, and in our advisory group, the Non-Prescription
20 Drug Advisory Group, we consider medicines for non-
21 prescription status. In doing that, we have criteria for
22 what we call OTC-ness. We consider the OTC-ness of a
23 product. So my learning gradient today has been very steep
24 with the subject that we've covered, and I appreciate all

1 the presentations. I truly have learned a great deal.

2 So I've tried to apply some of those OTC-ness
3 criteria specifically to answer the question. I agree with
4 Dr. Boughman and Dr. Everett and their comments about
5 applying the product to its actual use situation, because
6 amongst the OTC-ness criteria that we address when we're
7 talking about non-prescription drugs is the actual use
8 circumstance of that particular product.

9 I think the other situation with OTC-ness amongst
10 the--it's not a very long list, but I think the other
11 question that we always have is the risk for error,
12 misinterpretation, or problems related to addition of
13 putting a product on an OTC status.

14 Again, we generally talk about individual
15 products. Sponsors come to our committee and present a
16 product. Today's discussion on a category I think fits
17 again what Dr. Boughman was talking about, that we need to
18 develop some criteria for a category, because apparently
19 this is something that is just beginning for this particular
20 group.

21 So I think there are several other so-called
22 criteria that I guess when we answer the other questions
23 that I can bring up. But I think the critical things--and I
24 agree with all the comments that have been brought up. I

1 found when I prepared for this meeting the so-called
2 performance characteristics is pretty specific in general,
3 but not in the specific context as the conversation today
4 has gone.

5 So I think my only contribution to this might be
6 at this point is emphasize the necessity to study the actual
7 conditions of use, and when we come around again we can talk
8 about labeling, because I also was very moved and compelled
9 by Ms. Kingsley discussion about labeling and making sure
10 that the use is appropriate in the conditions.

11 DR. NIPPER: Thank you, Dr. Tong. Dr. Habig?

12 DR. HABIG: I actually have a number of specific
13 comments that I've written on this sheet of paper that I'll
14 turn into the executive secretary which I won't bore you
15 with the details.

16 I have two specific issues in paragraphs 5.a. and
17 the introductory paragraph at 6, where I'd like FDA to
18 remember that technology changes and improves. If you, like
19 in the beginning of 6, talk about GC/MS as the accepted
20 standard, that's true today for the metabolites and drugs
21 we're looking at today, but might not be adequate in the
22 future. So I will suggest wording that broadens that to
23 allow for things other than GC/MS should something other
24 than GC/MS become an accepted standard for some new drug or

1 metabolite. Because when we write these kind of documents
2 they tend to be around for a long time and it would not be
3 good, I think, to get locked in.

4 The only other comment I had is at the bottom of
5 page 5 and top of page 6, the comparison discrepancies. I
6 think that's really important as a submission for the
7 510(k). But I think it's absolutely wrong to try to include
8 that in lay user labeling. They won't understand it. I
9 think it would confuse and be very difficult, and I would
10 ask that you consider a different way to approach the issue
11 that you're really trying to get at. But to have a
12 description to lay users about discrepant results and two-
13 by-two boxes and things would, I think, not work.

14 Thank you.

15 DR. NIPPER: Thank you very much.

16 Moving on to question 2, what studies are
17 appropriate to ensure that these tests produce acceptable
18 performance in the hands of home users?

19 [Slide.]

20 I've asked Dr. Boughman to start this one, to be
21 more fair to Ms. Rosenthal and Dr. Habig.

22 DR. BOUGHMAN: I think this is the question
23 wherein we transcend from the factors themselves to the use
24 in the lay public, and in fact raise many of the human

1 factors issues that Ms. Kingsley did in fact address very
2 well this morning.

3 If or when these products come along for
4 examination by reviewers, I think at that point there are
5 going to have to be some very serious examination of some of
6 the comments that were made earlier that would be very
7 appropriate during the--to test the accuracy of the kit
8 itself, but the use in the lay public. The concept of a
9 control or the background testing, for example, that was
10 mentioned, the pH, the specific gravity and so on. To
11 expect lay users to perform such a series of tests prior to
12 the actual positive/negative test itself I think will need
13 some specific examination.

14 The other point that I would make here, and save
15 some other comments for the question specifically on
16 labeling. There have been several comments today about--and
17 several terms used: positive, presumptive positive,
18 indeterminate. I'm not sure whether some of those phrases
19 might be in the vocabulary tests of seventh graders. But in
20 fact, in general populations I can imagine that phrases such
21 as presumptive positive or indeterminate would not meet the
22 criteria for use by such a broad population as would be
23 expected to be using these kits.

24 So I think there are some real challenges here.

1 Even if the kit itself in the hands of a professional would
2 meet all of the appropriate criteria, I think the transfer
3 to the lay user will create some real challenges.

4 DR. NIPPER: Thank you. Dr. Everett?

5 DR. EVERETT: I guess for me the issue still is
6 what happens when the test gets in the hand of the user. In
7 this case the user is either the person who's having the
8 test performed on them or the person who's actually
9 performing the test. In this particular case I would like
10 to see some data stratifying the people who at least are
11 having the test done on them into male and female.

12 Particularly with kits, we run into a problem when
13 we talk about having a patient prepare to take the sample.
14 That is, with females when we do urine tests, particularly,
15 we have a wipe that we use to clean them prior to giving the
16 urine test because it increases the rate of false positive
17 if we don't try to clean up that environment and remove some
18 of the possible contaminants that will cause a cross-
19 reaction of the test.

20 So I would like to see data clarifying that
21 particular issue. When we do the test, particularly on
22 females, whether they're close to their time of menses as
23 opposed to doing them when they're not close to menses so we
24 don't have blood mixing into the sample itself.

1 The other issue is, when we talk about the user we
2 don't define the age of the user which kind of clarifies
3 what level of education they have. What we're talking about
4 in teenagers who are using the test to check themselves
5 before they get home knowing that mom is going to do the
6 same test when I get there, so I'll know to avoid it.

7 But in essence, we had some data on how well
8 adults versus I guess teenagers using the test, and how well
9 they could actually carry out those instructions. So that
10 we don't get confusing information again and then falsely
11 being blamed for something they really are not responsible
12 for. So I'd just like to see some of that data stratified
13 in that sense.

14 DR. NIPPER: Thank you, Dr. Everett. Woody?

15 DR. LEWIS: As far as acceptable performance and
16 how one could evaluate this in advance of release, something
17 struck me earlier when it was mentioned by the gentlemen who
18 were involved with poison control centers, that there are
19 I'm sure many examples that you could relay and probably a
20 very large database, because the poison control centers
21 keep, I believe, pretty accurate records of the kind of
22 responses that they make to people either calling in or
23 trying to get information.

24 In many cases, I suspect it's because of improper

1 usage of some product which they or their children have
2 gotten hold of and, therefore, have led to these disastrous
3 results that they're calling a poison control center about.

4 I just wonder if that kind of information in some
5 way is translatable to what happens with the performance of
6 a good and proper kit by individuals who, for whatever
7 reasons, end up with poor performance. Does that ring any
8 bells with Dr. Kurt or Dr. Tong and the fact that there is
9 that kind of information in poison control centers about the
10 adverse consequences of properly designed devices but
11 improper performance on the part of individuals when it
12 comes to poisons?

13 DR. KURT: Poison center calls, there's
14 approximately one call out of the 200 that our poison center
15 in Dallas receives per day not about that but they say, I
16 have a friend who's going to go in and have some testing
17 performed, and how long is the marijuana or cocaine going to
18 be in the urine. They want to know specifically, will it be
19 there after a day or how many days and that type of thing.
20 So they're not asking about a friend, they're asking really
21 about themselves. About one call a day on that.

22 DR. NIPPER: Dr. Tong?

23 DR. TONG: There is a national system of
24 collecting poison data, and the database in 1996 was over

1 2.2 million exposures to something potentially harmful or
2 poisonous. It would be interesting to go and see the
3 numbers of cases involving a home or on-site test kit.
4 Because my feeling is that that number is going to increase,
5 just like any new product that's put on the market.

6 That's an interesting point because if the
7 product, the kit contains any material that may be
8 potentially harmful, a reagent or whatever, you can bet that
9 the poison centers will be getting calls from parents whose
10 young children may have gotten into it, or some other way
11 come in contact with it. So I think in regards to poison
12 centers, I think there is a possibility in terms of the role
13 that they can play in this.

14 DR. LEWIS: Don't misunderstand me, I wasn't
15 thinking of the poisonous nature of the material in these
16 kits, but simply as a source of information such as this
17 database that you mentioned as to products that people do
18 misuse unintentionally and then end up calling the poison
19 center. That gives you a kind of a rough feel for how often
20 are people likely to misuse the over-the-counter product, in
21 this case the drug testing kit. That was my thought there.

22 DR. TONG: In the conversations with non-
23 prescription drugs, this comes up often in terms of what is
24 the industry's responsibility. Simply putting an 800 number

1 where you can call to get information isn't sufficient. You
2 have to have people at the other end who can answer
3 questions.

4 So again, on the product itself, it may need some
5 additional information than simply where it's made and who
6 made it, because I'm sure individuals are going to be
7 calling for the kind of things we're talking about,
8 interpretation. I had it in my pocket for two days and now
9 I'm looking at it. Is it positive or negative? What does
10 it mean? And you'll need individuals who can respond to
11 that.

12 DR. NIPPER: Thank you. Dr. Rej?

13 DR. REJ: I think someplace in Section B, since we
14 had seen from some preliminary evidence the large number of
15 so-called indeterminate or borderline reactions, somewhere
16 in the design there has to be something of what one does
17 with those data, since they seem to be reasonably prevalent,
18 at least with some of the devices, and whether they're
19 somehow excluded or there should be some guidance to the
20 sponsor so that they're handled in the same way. Of course,
21 that will be addressed later, but that should be also in the
22 labeling if these indeterminates are there.

23 I think that some aspects regarding the visual
24 acuity skills needed--can somebody who's colorblind be

1 expected to read the results of this test? Actually, I
2 think to do a study that these tests reproduce acceptable
3 performance in the hands of the home users may actually be
4 very hard to duplicate in a controlled study because the
5 actual users of these tests are likely to be parents who
6 have strong emotional and family ties to the individual
7 who's being tested.

8 I suspect that if this test were to be done at
9 home, it would not be under the most tranquil family
10 situations, and I think that would be hard to duplicate in a
11 field trial unless it was done on real parents with real
12 kids with their own urine.

13 DR. NIPPER: Thank you. Dr. Goldsmith?

14 DR. GOLDSMITH: I would agree with Dr. Rej's
15 comments about borderline values. I think that definitely
16 specimens that are in this borderline range ought to be
17 included in any of the studies that are done. In addition,
18 I very much agree with Dr. Everett's comments that the
19 emphasis of the studies have to be on the end user and on an
20 appropriate user group.

21 DR. NIPPER: Thank you, Dr. Goldsmith. Dr. Sohn?

22 DR. SOHN: In line with what Dr. Lewis said
23 earlier, I'd like to see that the temperature strip on the
24 container can be read by the lay person who is reading the

1 kit to prevent substitution of a sample. Dr. Rej mentioned
2 color and color-blindness. I think equally important is the
3 lighting and can this kit be read, can the results be read
4 under different lighting intensities?

5 Many of these substances, most of the drugs that
6 we deal with are pretty robust substances so I don't think
7 that some of the problems in terms of when the sample was
8 collected until it was put in the device are important, but
9 they should be looked into. However, I think it is
10 important to verify that the time that the substance, the
11 urine is brought--if we're dealing with urine, is brought in
12 contact with the test kit should--there may be varying
13 intervals between the time that this occurs and the sample
14 is read.

15 Also, I believe that stability is important. Mom
16 looks at the sample and says, it's positive, and Dad comes
17 home three hours later. Is the result going to be the same?
18 If that result is not stable one gets into a variety of
19 problems there.

20 I would like to see cutoffs being the same because
21 there may be two kits in the house and what happens, the
22 kids--we test the kid again, and look, he's negative. Where
23 do you get--so I think we a compatibility of cutoffs, at
24 least we would know that if a second kit were used that it

1 would work. So I think that's--

2 DR. NIPPER: Do you mean a second kit of a
3 different brand?

4 DR. SOHN: Of a different brand, yes, sir. I mean
5 I hope that there's a--let me put it this way. I think we
6 deal regularly with the concept of interlaboratory
7 variability. I think this thing is important because people
8 may buy two kits, two kits from two different manufacturers.
9 And they say, let's check it with this kit. I think that
10 standardizing cutoffs, for better or for worse, may be
11 important in this situation.

12 Also, I'd like to see a container, I'd like to
13 see, if it's urine, that it be placed in a container which
14 has--and this technology is available--a cap which seals so
15 that it cannot be readily opened, and it could be sent on to
16 a laboratory for confirmation.

17 DR. NIPPER: Ms. Rosenthal?

18 MS. ROSENTHAL: Thank you. I think we have a real
19 human problem here. I agree with Dr. Gerson who said that
20 this is not a person testing themselves as we have with
21 glucose testing and with pregnancy tests. What we have here
22 is essentially a hostile takeover. We have a parent trying
23 to test a child who probably doesn't want to be tested.

24 And we don't have a regime like the laboratory-

1 based forensic protocol where a specimen is collected and
2 monitored, and collected by somebody who's trained. We have
3 urine being collected by an anxious parent, and probably the
4 urine of a child who has already spoken to Dr. Kurt and
5 stayed out of the house for three days and come home and now
6 his urine may look fine. If that parent gets a negative,
7 they think their child is fine. They don't understand that
8 this is a screening test, not a test that is actually a
9 diagnostic test.

10 We saw slides today that generated several hours
11 of discussion among panel members who really are educated in
12 this, and I'm wondering who we're expected to convey all of
13 this at a seventh grade level to a population that knows
14 nothing about screening versus diagnosis. I wonder if there
15 is a point at which we say, the test may be good for what it
16 does, but it may not be good in the hands of the public.

17 DR. NIPPER: Thank you. Crossing the barrier
18 there, I'd like to call on Dr. Habig to answer question 2,
19 please.

20 DR. HABIG: I think really my only concern here is
21 about--I feel positively about the consumer survey. I think
22 that is a critical aspect for assessing before a product
23 goes on the market that it is going to do, or many of the
24 aspects of what it's going to do will be appropriate.

1 I think I would recommend--this is a little out of
2 character for me--that the FDA create a somewhat common
3 questionnaire, or provide some essential requirement type
4 questions because if there's 14 test kit companies providing
5 questionnaires it would be really hard I think for the
6 agency to interpret how effective the labeling or the design
7 of the devices are. I'm not sure that a proscribed
8 questionnaire is the answer, but perhaps some particular
9 questions or some guidance specifically about questionnaires
10 would be useful.

11 DR. NIPPER: Thank you, Dr. Habig. Dr. Tong,
12 question number 2?

13 DR. TONG: I can't help but go back to the OTC
14 experience, because I know we're very often frustrated at
15 performance in the sense of getting our consumers to take
16 the medicines as the label instructs. In fact there was a
17 recent study out of Emory University that showed that half
18 the time, despite the fact that the label is there,
19 readability, font size, print size, half the time the
20 caregiver still gave the medicine in error, most of the time
21 under-dosing.

22 So the concern is, can we improve performance?
23 Can we look ahead and say, there may be some needs to
24 enhance the performance of the user of these particular

1 products.

2 In the pharmacy medicine situation we talk about
3 the learned intermediary, the nurse, the pharmacist, the
4 physician reminding patients about the proper use of non-
5 prescription type medicines. In this particular situation,
6 I'm not sure--you know, do teachers get involved? Are there
7 learned intermediaries in this environment where a parent
8 and a child is dealing with a question of abuse or misuse?

9 But that's something I think that's worth thinking
10 about or asking people who are in the business, how can the
11 performance be enhanced, assuming that the performance isn't
12 going to be at the level that we all want it to be.

13 DR. NIPPER: Thank you. Dr. Gerson?

14 DR. GERSON: Sticking to the theme of getting back
15 to basics, one of the questions is about achieving
16 acceptable analytical results. I don't think that we've
17 defined what is acceptable. Until we do that we can't move
18 forward.

19 It sounds to me like we're dealing with a
20 population that believes--to use terminology that we're used
21 to, that believes it is 100 percent sensitivity, 100 percent
22 specificity, 100 percent efficiency, 100 percent predictive
23 value of a positive test as well as of a negative test. And
24 those of us who deal with these things know that that just

1 doesn't happen.

2 It sounds like what this population would want is,
3 a positive test means I or my kid is using drugs, with 100
4 percent reliability, and a negative test means, I don't have
5 a problem. I think FDA needs to address that.

6 You also go on to say, understanding concepts of
7 sensitivity, specificity--if you want to keep that wording
8 in then I would run the whole thing, predictive value of
9 positive test, predictive value of negative test, and
10 efficiency. Lay it all out, have the sponsor address those.

11 Reacting to a comment that Dr. Everett made, if in
12 fact there is--and I don't pretend to know if this is
13 correct or not. If in fact there is a relationship between
14 age and education level, ability to read, follow
15 instructions and all that, and in view of the fact that FDA
16 has gotten into the business recently of having ages to
17 purchase certain products--and I don't mean this to be
18 flippant--should there be some consideration of how old you
19 have to be to buy such a product, if in fact there is a risk
20 that it won't be used appropriately?

21 Then finally, I find it most interesting, the
22 comment made by the consumer representative about whether
23 this is ready for the public or the public is ready for it.

24 DR. NIPPER: Thank you. Dr. Manno?

1 DR. MANNO: I'm having a little problem here
2 getting my thoughts lined up. But at any rate, I think
3 that--

4 DR. NIPPER: Do you think that we should drug test
5 you to see if you're on some mind-altering material here?

6 DR. MANNO: It's probably this cough drop that I
7 have, given to me by one of the FDA people.

8 [Laughter.]

9 DR. MANNO: At any rate, some of the points that
10 have come up about having a time that is acceptable for
11 testing from time of collection to test, I think is
12 important to include in our evaluation. I think that's very
13 important. It takes in, again, the pharmacology of the
14 drugs as well as just the shelf life, if you will, whatever
15 the environmental conditions are.

16 I think I would be interested in seeing
17 information about at all ages that this would be directed
18 at. This is assuming that a parent can squeeze a specimen
19 out of a kid. I have been there as a parent. It took me
20 three years, and I'm an experienced laboratorian. It took
21 me three years to get the appropriate specimen to get
22 tested, mainly because I was testing teenagers who flatly
23 refused to give. And there wasn't a thing I could do if I
24 didn't have a positive.

1 So the families that I've heard today mention they
2 had the rapport. We thought we had the rapport too, but
3 they were educated kids and knew what to do, which reflects
4 Dr. Rej's comments about the educated kid can get around an
5 awful lot.

6 DR. NIPPER: Or what not to do.

7 DR. MANNO: That's right.

8 DR. NIPPER: Dr. Kurt?

9 DR. KURT: As a parent of three children myself
10 plus, on the other hand, being a professional in dealing
11 with thousands of calls from parents in the past through the
12 poison center, I think that the social issues pointed out by
13 Ellen Rosenthal, plus the professional circumstances where
14 misunderstanding on the part of anxious parents occurs in a
15 situation like this, creates a situation where the only
16 comfortable way that I feel that a home test kit could be
17 offered of this sort would be to have an empty urine
18 container to send in to a proper laboratory.

19 Now under the circumstances, if that does not
20 indeed occur, I think that the population that is tested
21 should not necessarily be parents and children of Ph.D.s or
22 M.D.s, but it should be a population that's comparable to
23 the seventh grade level, and not necessarily lexic enough to
24 read a newspaper ad to come in and obtain the test. I think

1 one way of possibly approaching that, if it can be done,
2 would be go to school counselors and find out what parents
3 have called in to school counselors and make the test kit
4 available to the parents through a school counselor.

5 Then I think that other questions should be asked
6 concerning confirmation, such as would you send in the urine
7 for a confirmation if it were free, if it cost \$25, \$50, or
8 if the result would come back in a week? Or would you want
9 to be told that your original result was wrong and you'd
10 have to make amends with your child on decisions that you've
11 made already, if the original test was wrong?

12 DR. NIPPER: How about if you get a rebate for
13 confirmation of the original test?

14 DR. KURT: A survey of that sort to be conducted
15 among the parents to find out what really would be followed
16 up from the standpoint of the parents.

17 DR. NIPPER: Thank you. Dr. Harrington-Falls?

18 DR. HARRINGTON-FALLS: Just to summarize, I agree
19 that studying the group that we're intending the use in is
20 going to be very helpful. Regarding the various tests that
21 might be marketed, I think our media and discussion will
22 kick in. I have faith that the system will kick in to
23 educate the public as to what potentially the test--what
24 benefits the test can have, and the limitations of the test.

1 I think that a good media presentation comparing
2 three or four of these tests and saying, this one worked
3 very well and confirmed the results that were found, and
4 this one we found was not reliable would, in and of itself,
5 take care of a number of questions.

6 Once again, I'd be curious to see, as Ms.
7 Rosenthal had mentioned, how well we could get the kids to
8 give the samples since they were not testing themselves,
9 they were being tested by a parent.

10 DR. NIPPER: Thank you. I have a couple of
11 comments about question 2, and I hope you'll forgive me for
12 injecting the chair's opinion at this point.

13 I think that in dealing with question 2, I think
14 you have to separate the hands of the home user from the
15 person who gives the specimen. For example, I think it
16 would be highly appropriate to test specimens from kids
17 without necessarily injecting the lay parents' performance
18 of the test kit into the system. You take specimens that
19 are from children whose parents--who have been brought into
20 the system. You test those on the kid.

21 You then turn around and give the kit to parents
22 and give them a urine to test and see how well they do it
23 when it's not on their own kid. You try to divorce--that's
24 a bad word--try to remove the psychological tension and

1 trauma from this particular issue.

2 I hope that I can also inject another basic, in
3 addition to those that Dr. Gerson has so aptly injected.
4 That is that I would like to know if--and I would like to
5 know this from reasonable studies, if there is a medically
6 allowable error rate that is acceptable to the public and to
7 health care professionals from this type of device.

8 We are used to or trying to adjust our testing
9 expectations in clinical laboratories to tolerate a
10 certainly medically allowable error. I cannot remove myself
11 from the notion that these are clinical tests because they
12 deal with the health of the tested person, if not just
13 mental health, and the health of the family relationship,
14 and the mental health of the parent. I would like to know
15 what error rate we are willing as a nation to tolerate in
16 order to have these devices on the market.

17 So I'll leave that one lying on the doorstep, and
18 I would like to move along to question 3 about labeling and
19 communication of test performance limitations to users.

20 I think Dr. Harrington-Falls is not only next up
21 but she's an appropriate choice because she deals with the
22 patient care public and communicates, I'm sure, some test
23 performance limitations to users in other settings. Maybe
24 she'll comment on question 3.

1 [Slide.]

2 DR. HARRINGTON-FALLS: Regarding this question, I
3 think as long as whoever the test kits are marketed to
4 understands it's a screening test, not necessarily a
5 diagnostic test, although that is what they're going to
6 believe. But just a chance to open the communication, get
7 some type of information to continue the communication
8 process I think will be extremely helpful, with the
9 screening, identify the positives, and then allow treatment.
10 So I think that's going to be very helpful.

11 I would use the example of HIV testing. When we
12 decided that we had a test available for the HIV virus we
13 didn't just give out the test, but it was coupled with
14 counseling beforehand as to methods of transmission, and
15 prevention measures, and what would the test potentially
16 screen for, that there was going to be a follow-up test and
17 so forth. So I think that would be a very comparable
18 example as to what we can look for here.

19 What I would like to see in terms of labeling for
20 these devices by lay users is, again, the ability to have a
21 resource 800 number that the user can call for further
22 information on positive or negative results. The Roche
23 representative in his presentation did include some pictures
24 that I thought were very helpful that we could use in our

1 non-literate lay user.

2 Then once again, I was just awakened today
3 listening to the parents in particular talking about their
4 concern, their love for their children, their concern for
5 the well-being of their children, that the medical
6 profession and the social resources that we have, we really
7 have to wake up and address this issue much better, because
8 we need to really take more action and be much more
9 proactive in dealing with this problem.

10 DR. NIPPER: Thank you. Dr. Kurt, could you
11 address question 3, please?

12 DR. KURT: Yes, I certainly agree wholeheartedly
13 with the 800 number to call, not only from the standpoint of
14 interpreting the test but for at least brief professional
15 advice, and also a confirmatory laboratory available.

16 I also am concerned about the legal implications
17 of perhaps a person being tested and then losing a job or
18 being dropped out of school. So I think that there should
19 be a disclaimer of some sort, which of course I'm sure that
20 the manufacturer wants to protect himself or herself as
21 well; a disclaimer saying that this kind of test, because
22 it's a screening test, cannot necessarily be used in any
23 kind of a regulatory or legal basis.

24 DR. NIPPER: Dr. Manno?

1 DR. MANNO: I really would like to support the
2 previous two comments. I am concerned about the level of
3 reading comprehension. That keeps coming back to my mind.
4 I think it's primarily through the experience in my own
5 institution which has had many years as a charity hospital,
6 and we have had to revamp so many of our simple instructions
7 of why give a vaccination--something as simple as that--in
8 order to reach our, in this case, patient population. But
9 those are the same people that we're addressing here.
10 They're the citizens of the country. I can't stress enough
11 that we need to look into that very definitely.

12 DR. NIPPER: Dr. Gerson, how would you communicate
13 test performance limitations to users?

14 DR. GERSON: The mechanism should be, keep it
15 simple. I'll just make four comments that I feel are the
16 most important. Just make it very explicit, positive
17 doesn't mean drug use. There are false positives. Negative
18 does not mean lack of drug use. You must get a
19 confirmation. Then there should be a referral source for
20 help or consultation.

21 DR. NIPPER: Thank you. Dr. Tong?

22 DR. TONG: I think the development of a label for
23 an over-the-counter product really requires a great deal of
24 skill or experience or sophistication. It's not a simple

1 thing just to make something look attractive. A label can
2 actually contribute to enhancing performance, getting people
3 to do it correctly or to follow the instructions.

4 So my suggestion would be to involve people who
5 are experts in labeling. As we've heard this morning, write
6 it right, do it right. So I would say there are people and
7 resources for developing labeling for consumers and the
8 public, and to begin addressing that and begin working on
9 that.

10 DR. NIPPER: Dr. Habig?

11 DR. HABIG: I also agree that it needs to be kept
12 simple. Something that Dr. Harrington-Falls said that
13 encouraged me to say that it shouldn't maybe just be labeled
14 as a test for drugs of abuse, but it could be labeled as a
15 tool for communication of drug abuse issues, or resolution
16 of drugs of abuse confrontations or something. So people
17 understand it's not the single thing upon which decisions
18 are made.

19 We're kind of talking about Section 2, and near
20 the bottom of page 7 we need to, I think based on Dr.
21 Willette's data, challenge the assumption that HHS testing
22 has a universally accepted level of performance. It may be
23 universally accepted, but I think one would strike the word
24 high, if it were in there, and that is the assumption I

1 believe. When we see that data a little more carefully, I'm
2 not sure we'll agree with that assumption.

3 So I think that that issue needs to be addressed.
4 That's not addressing labeling specifically, but it's in
5 Section 2 called labeling. Thank you.

6 DR. NIPPER: Ms. Rosenthal?

7 MS. ROSENTHAL: I agree, keep it very simple. I
8 think even of greater importance than what the instructions
9 are is the order that they are given in. I think the very
10 first thing has to be in some way to convey to the user that
11 it isn't a diagnostic test.

12 I just want to go--I'll get that later. That's
13 all.

14 DR. NIPPER: Thank you. Dr. Sohn?

15 DR. SOHN: I agree with everything, but I would
16 add that the labeling should clearly indicate those
17 substances that the kit sees with their common names, as
18 well as those substances which the kit does not see, again
19 with their common names. I wonder whether this kit probably
20 should be bilingual, the labeling should be bilingual. In
21 other words, a companion, particularly in Spanish.

22 DR. NIPPER: Thank you. Dr. Goldsmith?

23 DR. GOLDSMITH: If there are other words to use
24 other than positive and negative, because there is so much

1 iffy-ness around that. Indeterminate is probably too
2 difficult a word, I agree. But to try and come up with some
3 language perhaps other than positive and negative would be
4 helpful.

5 Pictures, multiple languages, I agree; I had that
6 down. And to keep it as short as possible for labeling.

7 DR. NIPPER: Thank you. Dr. Rej?

8 DR. REJ: Much of what I was going to say has been
9 said by other panel members. I think that an appropriate
10 answer though to point 3 is really what the answer to point
11 5 is regarding confirmatory testing. I think the labeling
12 can be a little bit simpler and somewhat more relaxed if
13 confirmatory testing is really part and parcel of the
14 package.

15 I quite agree that--again I'll betray my bias in
16 this particular situation in saying that a false positive is
17 probably more dangerous than a false negative, but I fully
18 appreciate what parents would not want to get false negative
19 results. But I think having a result that says, requires
20 confirmation, rather than positive, because I think positive
21 is really too highly charged.

22 It may reflect on the quality of my lecturing, but
23 my public health students really don't quite grasp the idea
24 of a screening test without more than one or two exposures

1 to it. So I think for the lay public, I think the idea of a
2 screening test is really a hard concept to get because, I
3 think it was Dr. Gerson who said, the bias of the person
4 buying it is 100 percent sensitivity, 100 percent
5 specificity. That's really hard to overcome, and certainly
6 saying negative and positive reinforce that concept.

7 I agree that the drugs that it can detect with
8 their street name, and those that it can't, is very
9 important. Maybe something about drug disposition, half-
10 life, that after a certain time certain drugs, even if
11 they're used, can't be detected. In fact all of those
12 enhance any OTC-ness of such a product.

13 DR. NIPPER: Dr. Lewis?

14 DR. LEWIS: I really don't have anything to add,
15 but as I listen to all of the other comments I think that if
16 we did everything that's been recommended we would end up
17 with that 79-page document that accompanies the kit.
18 Somebody earlier this morning said, you want to keep it
19 simple. But all that's been said, how simple can you make
20 it?

21 DR. NIPPER: Thank you. Dr. Everett?

22 DR. EVERETT: With the label it's important to
23 keep it simple. However, in medicine there's some
24 safeguards we have to take. That is, this is probably one

1 of the first kits that will use large amount of body fluid,
2 and as I look through the documents there's mention of
3 educating the public on universal precautions.

4 Whereas, if you worked in a doctor's office or you
5 worked in a hospital, you would know everything about
6 universal precautions because they're plastered everywhere.
7 Because the first time somebody gets HIV and they don't know
8 where they got it from, they go back to their employer and
9 look for sources of contamination. And the first time the
10 girlfriend get infected, only to discover she was doing this
11 test on somebody else who's already infected, they're going
12 to sue somebody.

13 So in this particular case somehow, either in the
14 kit insert, package insert, or on the label itself there has
15 to be some mention of how to protect yourself from body
16 fluids, particularly when they may be contaminated with HIV
17 or hepatitis B or some other infectious agent. This is not
18 always obvious when you look at a person. And even though
19 in this particular case we tend to think of the biological
20 parent performing the test on their own kid, it will be
21 other people performing the test on people who they are
22 somewhat casually associated with.

23 Trying to educate the public has to be
24 incorporated either into the test itself--and of course it

1 should be--or if there's some mass media blitz to explain
2 the limitations of this particular test, that kind of
3 information needs to be included.

4 The last thing I'd like to indicate is that there
5 should be some simple labeling or diagrams or pictures
6 instead of words to explain the limitations of this
7 particular test as well.

8 DR. NIPPER: Thank you, Dr. Everett. I think we
9 tend to assume that this is parent testing child or guardian
10 testing a minor. But I think that a realistic individual on
11 this panel will continue to stick the pin in his leg to
12 remind himself that once these things are on the market,
13 Katie, bar the door, everybody is going to be testing
14 anybody they can make pee in a bottle.

15 Dr. Boughman?

16 DR. BOUGHMAN: In fact I would like to address
17 that population for just a moment. Having spent a routine
18 Saturday night in a Baltimore City police cruiser--I've done
19 that recently--and another night in a homeless shelter in
20 Baltimore, knowing that there have been over 20,000 drugs of
21 abuse uses in the city of Baltimore since we've sitting here
22 this morning, knowing the huge problem that we have out
23 there, it worries me that we seem to be approaching this
24 from, for lack of a better phrase I'll say a PTA mentality

1 where we have been talking about the labeling that a caring
2 set of parents would look at in this process, when in fact
3 the question that's going to be asked by many people who
4 would use such a test is, did the kid use?

5 The question really is, use what? If we have
6 numerous tests out there testing for different substances
7 and different combinations of substances, we have compounded
8 this problem.

9 I don't know the street names, but one of the
10 groups that I can imagine very easily using this kind of
11 test would in fact be a middle level dealer who is testing
12 their transporters or their deliverers, and in fact they
13 don't want to know about whether these kids have used
14 cannabis or opium, they want to know whether they have used
15 blues or glories or pops. And I have no idea whether those
16 are street names or not. I just made all those up, just
17 picked those words out of thin air.

18 But the point is that to have a listing on the
19 insert to talk about cannabinoids or opiates and have any
20 expectation for people to understand what those actually
21 mean I think is extremely unrealistic, and I have a real
22 concern about that correlation.

23 DR. NIPPER: Thank you. At this time we should
24 move on fairly rapidly to question number 4.

1 [Slide.]

2 I'm going to start with our industry
3 representative on this one about what performance standards
4 are appropriate to establish safety and effectiveness of
5 these devices? You're on the plank, Bob. Take a step.

6 DR. HABIG: I don't have a definitive answer to
7 performance standards. Because of the analogy with some of
8 these tests that are already available for use in the
9 laboratory I don't think--no, I'm be more positive--I don't
10 agree with the assumption that a pre-market approval
11 actually is the approach to answer the question about safety
12 and effectiveness. I think the major concern about that is
13 confirmatory testing, and one can sort of order confirmatory
14 testing without having a PMA application.

15 My advice is simply, let's not over-regulate how
16 to put tests on the market that are useful by leaning on the
17 words safety and effectiveness. Let's put tests on the
18 market if that's a good idea with the least amount of
19 regulatory requirement that assures that the tests are used
20 as intended.

21 DR. NIPPER: Thank you. Dr. Tong?

22 DR. TONG: I've given some thought on this and I
23 really don't have anything to add to a lot of what's already
24 been said. So I'll pass to Dr. Gerson.

1 DR. NIPPER: Thank you. Dr. Gerson?

2 DR. GERSON: I think first we need to define the
3 population, define what questions are going to be asked.
4 Then you can do something very simple like go to your
5 receiver operator curves. Then you can define performance
6 standards that are going to give you the performance you're
7 looking for.

8 My response is, I don't think we are at the point
9 where we can define what the performance standards should
10 be.

11 DR. NIPPER: Thank you. For those of you who
12 couldn't hear, Dr. Gerson said, I don't think we're at the
13 point where we can define what the performance standards
14 should be.

15 Dr. Manno?

16 DR. MANNO: I'm not sure that I understand the
17 definition of safety with this device in terms of how we
18 usually think of safety with over-the-counter drugs or with
19 the prescription drugs. So I'm not quite certain at this
20 point how to address that. However, I do echo the concerns
21 of Dr. Everett on the infectious nature, let's say potential
22 infectious nature of specimens. And I think we've pretty
23 well covered the effectiveness at this point.

24 DR. NIPPER: Dr. Gutman?

1 DR. GUTMAN: I can clarify this question a little
2 bit. When we think about an in vitro diagnostic--and I
3 don't suggest that infectious problems from handling these
4 materials may not be problems. Actually, the safety of an
5 in vitro diagnostic in many ways is connected to its
6 effectiveness because it's the impact of false positives and
7 false negatives, and the way information may be misused.

8 And performance standards, whether this is a
9 510(k) or a PMA is really not as clever as what our chair
10 has come up with, which is allowable medical error. That
11 would be what I would seeking, whether it was a PMA or a
12 510(k). Dr. Gerson may have the extant answer, which is
13 there's no answer at this point. But if anybody did have an
14 answer or a way to help us align that answer, I don't know
15 that the first company that comes through with a product
16 like this will be satisfied with an answer that there's no
17 answer.

18 DR. NIPPER: Thank you. Dr. Kurt?

19 DR. KURT: The first performance standard that I'm
20 concerned about is from slide 26 which shows a considerable
21 variability from the available test kits for professional
22 laboratories now where the proportion of false positives to
23 false negatives varies a great deal. So I think that there
24 should be some comparability among existing tests for the

1 relative false positive or false negative and how they fall,
2 because it would be better in general to have a false
3 negative test than too many false positive tests. That
4 relative range should be comparable.

5 Then I think you have to really ask the question,
6 do you want this test performed as it is now in a laboratory
7 where a professional laboratory person is doing it or by an
8 amateur? Similarly, as you are flying home this evening, do
9 you want an airline pilot to fly your 727 or a person who
10 doesn't have a pilot's license?

11 DR. NIPPER: That's certainly graphic.

12 Dr. Harrington-Falls?

13 DR. HARRINGTON-FALLS: Since we're relating safety
14 and effectiveness to the false positives and false negatives
15 I would just say that as long as the instructions can be
16 easily followed and the person understands in perspective
17 what the result says. If it's just screening, needs
18 confirmation, or if it's, this is positive, that means the
19 person definitely used this. As long as they're aware of
20 those two things I would be satisfied.

21 DR. NIPPER: Thank you. I would like to make a
22 comment about allowable medical error and reasonable
23 standards. I think that at the last meeting of this panel
24 which dealt with home use glucose test, test materials, saw

1 a graphic illustration and heard allegations of problems
2 that occurred when a device for measuring glucose that did
3 not have the same accuracy and precision as a central
4 laboratory device was allowed to be in the hands of
5 consumers, for the best of all possible reasons, and that
6 was improvement in glucose control.

7 There are great benefits to that particular
8 medical application of a home use device, and there are
9 potential great benefits of the application of home use drug
10 test kits. I draw the parallel because I think it's
11 important when we decide what performance standards should
12 be established that we not go down the road of relaxing
13 performance standards for a home use device over that
14 required in a central laboratory.

15 I think that if we have a chance to have devices
16 out in the field that perform at a higher standard than
17 those laboratory screening devices that require
18 confirmation, we should move in that regard.

19 Dr. Boughman?

20 DR. BOUGHMAN: I would just like to add one
21 comment and that has to do with the data that we heard about
22 today that had a great deal of difficulty with borderline
23 readings among professionals. I think that if we're talking
24 about effective use and interpretation of home use kits, if

1 we have not only the variability but a great deal of
2 difficulty at the edges and in interpretation among the
3 professionals that we need to be very careful about the same
4 situation magnified many-fold in the lay public.

5 DR. NIPPER: Thank you. Dr. Everett?

6 DR. EVERETT: What I would say is for performance
7 standards, again I agree we're not really ready to determine
8 what those are. At some point those performance standards
9 should be determined based on the sensitivity and
10 specificity in both the ideal situation, which is with the
11 laboratories, and then of course, compared to what those
12 numbers are in the home or real world situation. And
13 hopefully we can pick some point between those two extremes
14 so that the public will be safe from the analytical or
15 biostatistical analysis of those numbers, and then setting
16 the performance standards.

17 The other thing is, of course, when we get away
18 from numbers we deal with people and not so much numbers.
19 And that safety, perhaps could be just including a pair of
20 gloves in each kits and informing patients or people in the
21 real world to use them when they're going to do this
22 particular test. That may add a little, maybe 50 cents or
23 15 cents to each kit, but in essence it would protect a lot
24 of people.

1 DR. NIPPER: Thank you, Dr. Everett. Dr. Lewis?

2 DR. LEWIS: Pass.

3 DR. NIPPER: Dr. Rej?

4 DR. REJ: I quite agree with the chairman's point
5 that we shouldn't relax standards just because they're
6 designed for over-the-counter use. In fact, they should
7 probably be more stringent because one is unsure of exactly
8 how they will be used. I think that the performance--I
9 raised that issue in my answer to question number 1.

10 It would be difficult to say an exact performance
11 standard, but certainly no less than that of the laboratory
12 immunoassay system. But those are all confirmed, and I
13 think it's going to be very hard to say that performance at
14 that level is adequate, because those tests go on to another
15 level. Again, that is also raised by the next question
16 about whether you're going to require confirmatory tests. I
17 think that the performance standard could be a little bit
18 different depending upon whether you're going to require
19 confirmatory tests.

20 I think the end result should be certainly no less
21 than what's currently available from the laboratory.

22 DR. NIPPER: Thank you. Dr. Goldsmith?

23 DR. GOLDSMITH: I agree with that. I think we
24 should not have relaxed standards outside of the laboratory

1 setting. But exactly what those standards are, I agree with
2 Dr. Gerson, I don't think we can really define that at this
3 point.

4 DR. NIPPER: Dr. Sohn?

5 DR. SOHN: I strongly support what Dr. Rej and Dr.
6 Nipper has said in terms of not relaxing standards. I'm
7 aware of Dr. Gutman's statement regarding safety. However,
8 just using the word safety I think we should remember that
9 OSHA does not consider urine as a biologic fluid that goes
10 under the blood-borne infection standards.

11 At the present time, DOT requires that a certain
12 number of samples be tested as blind sample containing a
13 variety of analytes. I do wonder seriously whether at this
14 stage of development we cannot have a standard challenge
15 panel to be given to kit manufacturers. Namely, have a grid
16 which contains drugs say at various levels. Level 1 may be
17 a negative sample, level 2 may be 25 percent below the
18 cutoff, level 3, 25 percent above the cutoff. Where we have
19 this grid where we can say, present or have a contract to
20 develop a 100-sample test challenge kit to be used by
21 manufacturers to evaluate drug testing kits.

22 I have taken urine-containing drugs, have had it
23 microfiltered, encapsulated, in vials, and they've lasted
24 like forever, for many years. I think we are at a state of

1 development where we can do this and instead of having, say
2 100 drug users in a program tested, I think we should be
3 able to at this stage have a common panel that every kit
4 manufacturer would use to have that kit challenged, where
5 the kit would have a variety of substances in addition to
6 whatever substances are used to evaluate cross-reactivity,
7 to evaluate sensitivity and the like.

8 DR. NIPPER: Thank you. Ms. Rosenthal?

9 MS. ROSENTHAL: I agree with Dr. Nipper that we
10 shouldn't relax standards. That's it.

11 DR. NIPPER: Thank you. Dr. Habig?

12 DR. HABIG: I think we've come full circle, but I
13 now have a comment on the relaxing standards issue. That's
14 a pretty neat position to take, but I want to draw an
15 analogy that might shed a little different light on that.
16 When glucose and the laboratory standards were developed,
17 you know people talk about 1 and 2 percent, and when glucose
18 meters for the self-monitoring of blood glucose--a different
19 indication for use than diagnosis of, say diabetes, were put
20 on the market. The indications were different and in fact
21 the standards are different.

22 So the analogy here is that laboratory, SAMHSA
23 laboratories that do diagnosis, if you will, of people who
24 may be using drugs have a certain set of standards, and an

1 over-the-counter screening test, not diagnostic, for the use
2 of drugs might have different performance standards. I'm
3 not advocating that they should, I'm just putting on the
4 table that if one uses that glucose analogy I'm not sure
5 it's so clear that equal or even better standards are
6 required.

7 DR. NIPPER: I'm glad you said that. And the
8 reason I brought it up, Dr. Habig, was that in the back of
9 my mind was the pre-SAMHSA drug testing days in which there
10 were unconfirmed immunoassays and unconfirmed thin layer
11 chromatography devices, unconfirmed gas chromatography
12 methods, lack of national standards, lack of proficiency
13 testing, and the drug testing situation in this country
14 needed improvement. How's that for being euphemistic?

15 What SAMHSA and CAP, and some other organizations
16 that I'm probably leaving out, have tried to do is shut the
17 barn door. The horse is still out there in terms of
18 unconfirmed immunoassays still being used widely for all
19 sorts of purposes. The question before us in question 5,
20 which I'm going to encourage you to move toward in a minute
21 is, what do we do to improve the situation so that the
22 unconfirmed immunoassays that are still out there looking
23 for markets can be improved to the point where the SAMHSA,
24 GC/MS situation, where it would parallel that?

1 Because I would put to you that the indications
2 for use of a SAMHSA test and a home use drug test are very
3 similar, and deserve the same accuracy. I would put that to
4 you as a question. I think that, unlike the glucose thing
5 which may be, or it used to be different. Now it may not
6 be, but I'd say they're pretty--the SAMHSA test and the home
7 use test in use are pretty close in terms of indications of
8 use and a need for accuracy.

9 [Slide.]

10 So tell me what you're going to do about
11 confirmation, and tell me why I'm wrong.

12 DR. HABIG: I sure don't want to act as though
13 this position is one for lowering standards or having
14 unconfirmed tests. But the indications for use for a SAMHSA
15 test result in the keeping or losing of a job, the keeping
16 or losing of insurance, much more dramatic things than a
17 parent confirming or not confirming use in a child of drug
18 use.

19 DR. NIPPER: Those are consequences. Those are
20 not indications for use. Indications for use would be, do
21 we suspect drug use? Do we have an indication for doing the
22 test because of behavioral characteristics? Or do we
23 randomly check this person because of need and, fill in the
24 blank, for either public safety or whatever need the family

1 would determine? Those are the indications for use to me.

2 DR. HABIG: There may be someone here with a
3 better handle on the differences between intended use, which
4 is to, in this case I think, determine presence or not
5 presence of a drug, and indications for use which normally
6 have to do with patient populations. Here we're really not
7 talking exactly about patients in either of these cases. So
8 it seems to me a little fuzzy.

9 Yes, the outcome, that is what you do with the
10 answer might not be an indication for use, but it's the
11 reason for the test. I would want standards that require
12 confirmation before a decision is made to terminate someone
13 from employment, or to not hire them, or other dramatic
14 issues that are different from what happens when a parent
15 finds out in a screening test that there's a--I forget Bob
16 Rej's terminology--a requires confirmation result. I find
17 that dramatically different.

18 I just think we ought to be careful of assuming
19 that we have to have equal or more stringent standards just
20 because of, say the likelihood that these tests would not
21 require confirmation. I certainly think confirmation is
22 important, and perhaps may be important enough to be
23 required in order to have the test cleared for marketing.

24 DR. NIPPER: How would you require it? How would

1 you require it of a test that doesn't include the
2 confirmation as a part of the test?

3 DR. HABIG: I don't have the answer to that.

4 DR. NIPPER: Thank you. Dr. Tong, question number
5 5?

6 DR. TONG: Dr. Nipper, I don't have the answer to
7 that question either, so I'm going to pass and hear the
8 conversation from the panel.

9 DR. NIPPER: Dr. Gerson?

10 DR. GERSON: It occurs to me, listening to all
11 this, that the dilemma in which we find ourselves at this
12 late hour is that we're talking about a screening test or a
13 family of screening tests, but we're talking about an
14 application which is diagnostic. And you can't have it both
15 ways. I'm trying not to use the word oxymoron, but that's
16 where we're at.

17 So my advice to you--and I say very few things
18 worth writing down, but here's probably one of them--is have
19 the sponsor, manufacturer be very explicit. Is this
20 application a screening application or is it a diagnostic
21 application? If it's diagnostic, it's got to be as good as
22 the best out there.

23 Now be default today, although I don't know what
24 Dr. Bush's intention was, her program has become the

1 reference, the gold standard today. I'm going to quote a
2 number but I don't pretend to speak for her agency and I
3 invite Dr. Bush to correct me. I think the data I've seen
4 is that their testing done their way has reliability in
5 excess of 99 percent.

6 DR. BUSH: Absolutely.

7 DR. GERSON: So that if you want a standard, and
8 someone is coming and saying, we've got a diagnostic test,
9 then you've got to say, FDA, fine, we don't care how you got
10 there, but show that you're at least 99.99 percent, or
11 whatever that number is, because that's what's out there.

12 If it's screening, then it's screening. And my
13 view as a physician, as a lab medicine type, is when we
14 design a screening test we want the false positives. False
15 positives is a desirable attribute of a screening test. It
16 allows you to eliminate the ones that are truly the ones you
17 don't need to worry about, and then focus your best
18 resources on the ones that might be positive. That's a
19 wonderful cholesterol screening test. That's a wonderful
20 glucose screening test, whatever.

21 Now we're back to, there's got to be confirmation.
22 Somehow you've got to require it. In the interest of time
23 I'll stop right there.

24 DR. NIPPER: Thank you. Not for stopping, but

1 thank you for your comments.

2 Dr. Manno, do you have comments now?

3 DR. MANNO: I think Dr. Gerson has made a very
4 good point. One thing that has come to my mind in the past
5 few minutes, that if you're going to limit this purely as a
6 screening test without a confirmation, one alternative would
7 be, if this test indicates additional testing, see your
8 physician or your mental health counselor. That may be a
9 way to get it into the confirmation process.

10 But unfortunately, that might not get the urine
11 that was tested and they may slip through the cracks. That
12 would be one--the very best answer, of course, would be to
13 include confirmation in some way. But I don't know how you
14 could require it. That's something that needs work on.

15 DR. NIPPER: Thank you. Dr. Kurt?

16 DR. KURT: I think confirmation should be strongly
17 encouraged to get as near 100 percent compliance as
18 possible, and even think of putting some type of coupon on
19 your confirmatory thing such as, those who do come out with
20 a negative confirmatory test are entitled to get life
21 insurance or automobile insurance for their child at a lower
22 rate. And a positive test would get into the treatment
23 program at such-and-such a discount.

24 [Laughter.]

1 DR. KURT: Something to encourage people to do the
2 confirmation test.

3 On the other hand, with the regulatory, the SAMHSA
4 regulatory paradigm I see all sorts of potential quasi-
5 abuses, such as say the high school coach who's testing his
6 players and that has to be a prerequisite of staying on the
7 team. He's not going to consult regulatory people, and yet
8 the student could then sue the school system and the
9 manufacturer, the person in a school where drug abuse
10 questions occur, and other situations that could occur if
11 you go into a credit agency because you want a home
12 improvement loan. Are they going to ask you for a urine
13 sample?

14 I sure hope that the manufacturers of these buy
15 sufficient insurance since the workplace testing has been
16 tested some 27 times in the Supreme Court, which has upheld
17 it with a confirmatory test, I wonder how many times it's
18 going to be upheld without a confirmatory test. I hope you
19 buy a lot of insurance.

20 DR. NIPPER: Dr. Harrington-Falls?

21 DR. HARRINGTON-FALLS: I think everybody has
22 pretty much said that encouraging a confirmation is very
23 helpful.

24 DR. NIPPER: Thank you. Dr. Boughman?

1 DR. BOUGHMAN: The process of requiring a
2 confirmatory test reminds me of some of the comments that we
3 heard this morning wherein we do have groups, we have
4 manufacturers out there who in fact are promoting the
5 confidential collection of samples and appropriate
6 laboratory testing that can be confirmed once the sample is
7 sent away. So in some respects we are already at that
8 interface.

9 The oxymoron that Dr. Gerson was talking about to
10 me is not quite an oxymoron. But we don't have a system, at
11 least that I'm aware of right now, where the screening test
12 is actually performed before the individual is inside the
13 system, if you will. It is already the professional that is
14 doing the screening test and looking for the sensitivity in
15 such a way that false positives are okay, because we the
16 system know we are going to follow up.

17 What is happening here is a crossing of boundaries
18 from OTC to inside the system where the screening is in the
19 hands of non-professionals and the follow-up on confirmation
20 would be in the hands of professionals. Therein lies the
21 problem and the gap in the information.

22 DR. GERSON: Not to make this a private dialogue,
23 but what I envisioned, for instance, what is the consequence
24 of checking your own cholesterol and getting a false

1 positive? The consequence is, you go to see a doctor. The
2 consequence here I think--I'm speculating--is a whole lot
3 more serious. That was my concern.

4 DR. NIPPER: Dr. Everett?

5 DR. EVERETT: I agree with everything I've heard.
6 I'd just say, FDA should spell out those conditions for
7 confirmatory testing in such a way that the people who are
8 using the kit, at least once it gets that far, understand at
9 least some of the reasons as to why the confirmatory testing
10 actually needs to be done, so that it's not too confusing.
11 Because right now it still seems kind of confusing to me to
12 try to separate what I would do for confirmatory testing as
13 a physician versus what the average layperson would do when
14 they read the instructions and decide what they should do
15 about confirmatory testing.

16 Then of course, there's a third person, the
17 manufacturer, who may be liable if they don't put in some
18 statement of a disclaimer. So with all these people
19 involved, FDA in essence should recommend at least some of
20 the reasons that are clear as to why confirmatory testing
21 should be done.

22 DR. NIPPER: Thank you. Dr. Lewis?

23 DR. LEWIS: In one sense, I'm in agreement with
24 everything that's been said. At the same time, I have a

1 very basic problem with the whole notion of encouraging,
2 communicating the need for confirmatory testing. Based upon
3 my own experience, which has been doing drug testing or
4 being responsible for those who do drug testing in a variety
5 of settings over many years.

6 And the only setting in which the unconfirmed
7 presumptive positive was considered an acceptable
8 alternative was in the clinical setting where for the
9 emergency room docs who were satisfied to know that, yes, it
10 was positive for opiates or whatever the screening test
11 might have been used for. In the hands of that end user,
12 the ER doctor, we're talking about somebody highly educated,
13 very capable of understanding the implications of this
14 presumptive positive.

15 In all other settings, and all of those that have
16 been discussed here today where confirmatory testing is de
17 rigueur, as they say, here now we're talking about something
18 that goes 180 degrees from that. That's the basic problem
19 that I have.

20 I don't have any answers for it, but it just seems
21 to me that we're sitting here talking about something that
22 is just so counter to everything that I've been taught,
23 everything that I have practiced in the area of drug
24 testing, for a variety of different settings and

1 environments.

2 So I really am struggling with this whole idea of
3 how do you now provide for the end user, who we know isn't
4 that highly trained professional, and say to an irate parent
5 who now has a positive, don't tell me about presumptive.
6 Don't tell me about it's only a screen. I've already spent
7 this amount of money and I'm not going to pay for this
8 confirmatory, so-called--I guess I'm getting a little too
9 rambunctious here.

10 In any case, that's the problem that I have with
11 the whole issue of just screening versus the included
12 confirmatory.

13 DR. NIPPER: Dr. Lewis, I always knew you were too
14 quiet and reserved. Dr. Rej?

15 DR. REJ: Without a confirmatory test, this is
16 clearly a screening procedure. I don't think screening
17 procedures, especially for detecting illicit drugs, meets
18 the OTC-ness criteria. I don't know how you could build in
19 requiring confirmatory testing. But labeling that would
20 say, a confirmatory test is needed, build that into the cost
21 of the product and send a urine that's a needs-confirmation
22 for a laboratory analysis for confirmation of it. There
23 would be no additional charge.

24 That might encourage compliance with that, and the

1 labeling that says that it's not positive, it needs
2 confirmatory testing.

3 DR. NIPPER: Thank you. Dr. Goldsmith?

4 DR. GOLDSMITH: I really have nothing to add other
5 than the fact that obviously confirmatory testing has to be
6 done. How that is effected, I'm not sure either.

7 DR. NIPPER: Dr. Sohn?

8 DR. SOHN: This requires massive consumer
9 education similar to what many of the pharmaceutical
10 manufacturers will do in sending literature by mail to
11 interested individuals who feel a need for the product,
12 whether it's Rogaine, and so on.

13 DR. NIPPER: Thank you. Ms. Rosenthal, when you
14 start answering question 5, just keep right on going to
15 question 6, please.

16 [Slide.]

17 MS. ROSENTHAL: I think that confirmatory implies
18 that you have an answer, and I think that would be specific
19 to a test. For instance, in glucose monitoring, when you
20 have an answer, every time you test your answer you don't
21 have it confirmed. I think in a test like this you will
22 need confirmation.

23 I'm not sure we need--is it necessary for the
24 person who does the test to have an answer? Might they

1 instead just get a line, a color, and have to call an 800
2 number to find out what that means? Maybe they don't need
3 to have the answer right then, or they don't need it in
4 front of them.

5 I had another thought before when we talking about
6 studies, how to structure studies. It occurred to me that
7 maybe when we're studying this product we might not want to
8 give the user an answer, fill in the square, yes, no, color,
9 et cetera. Educate them and maybe let them describe what
10 they see. That might give us some information,
11 incidentally, in testing of how well the public can read
12 these results, how well they could read a screening device
13 as opposed to a diagnostic device. I just was throwing that
14 in there.

15 For quality control, I think the most important
16 thing would be follow-up. That, of course, goes right back
17 to confirmatory testing.

18 DR. NIPPER: Thank you. Dr. Sohn, do you have
19 thoughts on quality control?

20 DR. SOHN: I think we've said it already.

21 DR. NIPPER: Thank you. Dr. Goldsmith?

22 DR. GOLDSMITH: I thought this was referring to
23 quality control within the device. Obviously there are
24 models out there with over-the-counter devices now, so

1 something similar to that where you would have internal
2 quality control which the user then would know whether or
3 not the device is working correctly or not.

4 DR. NIPPER: Thank you. Dr. Rej?

5 DR. REJ: Some system of quality control to know
6 that the product is working is required. In an OTC setting,
7 something built into the product rather than a positive and
8 a negative control in the traditional laboratory sense
9 probably makes a better option.

10 DR. NIPPER: Thank you. Dr. Lewis?

11 DR. LEWIS: I have nothing further to contribute.

12 DR. NIPPER: Dr. Everett?

13 DR. EVERETT: The only thing I can say is that it
14 should involve the end user in the sense of providing
15 information to determine how well the product is working and
16 whether it's working or not. In some cases I know we
17 already use the manufacturer, but the problem becomes
18 whether or not the manufacturer's data is correct or whether
19 it's been altered so that they can continue to sell the
20 product.

21 Then quite frequently, when we do survey people
22 who are actually using these types of devices, the results
23 are usually quite different than what the manufacturer
24 reports. So I would strongly recommend that that end user

1 somehow gets surveyed to evaluate how well the product is
2 actually working.

3 DR. NIPPER: Thank you. Dr. Boughman?

4 DR. BOUGHMAN: Post-market surveillance, it would
5 seem to me, is a critical component in this, should these go
6 forward. I have no other specific comments on quality
7 control, but an issue that has--I'm not sure which question
8 it actually fits into--has to do with the role of the
9 pharmacist and/in individual in the pharmaceutical
10 situation.

11 I'm getting the feeling that the Pharm.D.
12 curriculum is going to be extended to six or seven years
13 sooner rather than later as these kinds of things become
14 available and the pharmacist is expected to be the back-up
15 for the 800 numbers, all of those 800 numbers that were
16 thrown away with the box in the test kit.

17 DR. NIPPER: Thank you. Dr. Harrington-Falls, do
18 you have comments about quality control of these products?

19 DR. HARRINGTON-FALLS: The fewer pieces, the
20 better.

21 DR. NIPPER: Thank you. Dr. Kurt?

22 DR. KURT: As soon as the teenagers are
23 represented by the American Civil Liberties Union I think
24 there will be a lot of quality control.

1 DR. NIPPER: Thank you. Dr. Manno?

2 DR. MANNO: I think any quality control should be
3 built into the device and be simply something that's a color
4 change unto itself to show that the device still has
5 integrity. Something very simple, and I think that can be
6 done.

7 DR. NIPPER: Thank you. Dr. Gerson?

8 DR. GERSON: Built in, passive, real quality
9 control, not a process control.

10 DR. NIPPER: Thank you. Dr. Tong?

11 DR. TONG: I'd echo the encouragement that studies
12 be carried out in the environment, because I think we can
13 learn a lot in terms of seeing how post-market surveillance
14 and quality control can be managed. We are talking about a
15 different device.

16 I think there are a lot more than just pharmacists
17 who could be learned intermediaries here. I know school
18 nurses are losing their positions, but there are a lot of
19 individuals that interact with parents that have to deal
20 with an anxious, turmoil, home situation where drugs are
21 abused. We just need to let that learned public be
22 involved, to know more, and to give advice and help in those
23 circumstances.

24 DR. NIPPER: Dr. Habig?

1 DR. HABIG: I think that built-in quality control
2 seems to make the most sense, but I would encourage the FDA
3 to simply allow the people who build, the sponsors who
4 present these kits to present quality control possibilities
5 and allow them to demonstrate that the quality control
6 system is effective. Built-in sounds like a good idea, but
7 I don't know that it's the only idea.

8 DR. NIPPER: Thank you. I have two brief
9 comments. I think that the manufacturer that builds a
10 screening kit that is as good as GC/MS will beat the socks
11 off the rest of the market. I think that's the challenge
12 for the manufacturer. That obviates the need for
13 confirmation. If we can do some of the things that we've
14 done in this country up until now and some of the things we
15 heard about this morning as well as we've done--as well as
16 they appear to have been done, I don't think that's too tall
17 an order.

18 Quality control, in my opinion, should include
19 quality control in the sample as well as the test. So I
20 would like to see built-in quality control also test for
21 common methods to defeat the integrity of the specimen, if
22 that's possible.

23 At this point we are a half-hour over our limit.
24 I did that because I thought that Dr. Bush's provocative

1 presentation deserved some comment from the floor. I was
2 asked to provide that time and we did it. I appreciate the
3 audience staying with us.

4 I'd like to ask the members of the panel if they
5 have any final comments? I won't go around the room, but if
6 you do--Dr. Manno?

7 DR. MANNO: In due respect to the input from Dr.
8 Bush and some of the comments I've heard here today on a
9 very confusing issue at times with the statistics, I think
10 that this is a logical time--I would like to end with a
11 positive. We are where the SAMHSA program was when it
12 started. They asked many of the same questions. And I
13 think we're at a natural progression.

14 The end result of the DOD programs and the SAMHSA
15 programs has been effective reduction of drug use, and
16 that's the name of the game, respective of whether you're
17 dealing with individuals or groups. So I think we're in a
18 natural place.

19 DR. NIPPER: Thank you very much. Dr. Rej?

20 DR. REJ: A quick question that maybe somebody on
21 the panel or in the audience can address. It's somewhere
22 between a social issue and a laboratory issue. I think of
23 it as an analysis issue. I think of it as an analysis issue
24 because it has to do with turnaround time. I'm just

1 curious, if there are available from--there's an FDA
2 approved device for collection of this type of sample with
3 results with confirmation. What is the average turnaround
4 time if one were to make use of that? Does anybody know?
5 Approximately days, weeks, months?

6 MS. HUNT: Depending on what mailer is utilized in
7 the test it could be anywhere from five to eight days after.
8 The test that we at Parents Alert use is an overnight and
9 it's three-day turnaround.

10 DR. REJ: So something in that time frame. What I
11 suspect is true, and Dr. Manno confirmed, was that the
12 hardest thing is going to be getting the sample. I'm just
13 wondering what the instantaneous or near instantaneous
14 result will provide over and above a turnaround time of a
15 week or two, if it takes three years to get a sample? Just
16 a comment and observation.

17 DR. NIPPER: Any other members of the panel that
18 have a comment? Dr. Sohn?

19 DR. SOHN: I'd still like to say that a negative
20 test is not drug-free, and I urge that the manufacturers
21 look at more of adding additional analytes, as has been
22 brought up by the panel, so that we can at least get a
23 better picture, if we do bring this into public commerce, of
24 what may be present in the urine of a child.

1 DR. NIPPER: I believe Dr. Gutman wishes to--

2 DR. GUTMAN: Yes, I have a final question. I
3 apologize. It's late in the day but no one brought this up
4 in the spontaneous discussion and I can't let you leave the
5 room without at least seeing if I can elicit a response to
6 this.

7 You may have noticed that there were two versions
8 of the guidance document; that we sent one out and put it on
9 the Internet. And we made some fairly minor corrections and
10 then re-posted it and sent it out, and I hope--maybe some of
11 you didn't get around to looking at the first and only
12 looked at the second, or maybe some of you looked at both,
13 and would note that they're really quite parallel in most of
14 their requirements.

15 But there was some new stuff on the second
16 guidance document and it particularly appeared in something
17 that may be an acquired taste, or arcane in terms of your
18 interest at the end, that had to do with the regulatory
19 route and whether the product would be a 510(k) or a PMA,
20 and which posed the beguiling question, gee, if the product,
21 whether it's called screening or diagnostic or whatever it's
22 finally called ends up with a claim of negative versus maybe
23 as opposed to negative versus presumptive positive, would
24 that make a difference or should that make a difference in

1 terms of the regulatory route?

2 I'm not asking you to say whether you think that
3 should make a change, but I'm asking whether anybody has a
4 reaction to the difference between calling something
5 negative versus maybe, versus negative versus positive, or
6 presumptive positive or something else. And you're allowed
7 not to comment and just go home.

8 DR. NIPPER: Who would like to answer the question
9 first?

10 DR. KURT: That would make a difference to me.
11 But I would be concerned about other tests coming on the
12 market that are not necessarily comparable that skate
13 through on a 510(k) when they really would require a PMA
14 because the reagent system would be not comparable.

15 DR. NIPPER: Does anybody else wish to add to
16 that?

17 I have a comment about it. My answer to that
18 would depend on how frequently a pilot study of people using
19 this test would get confirmation for screening positives.
20 If a pilot study, a well-done pilot study in an appropriate
21 population were to prove that one out of 1,000 people got
22 their screening positives confirmed, I would have a real
23 problem with allowing this kind of stuff to continue on the
24 market.

1 On the other hand, if the screenings were
2 confirmed most of the time--and that means two-thirds or so
3 or more--then you've got a possibility of educating the rest
4 of those people to do it right, then I'm more than willing
5 to let 510(k)s go do it. My problem is the lack of
6 confirmation. To me, that's the tip of whether you keep
7 these devices off the market until we can get them making
8 better quality devices or whether you allow them on the
9 market because you know that the public will confirm.

10 Dr. Rej?

11 DR. REJ: I'd like to agree that they could be
12 considered a less stringent route if it were possibly no,
13 and maybe you need to do another laboratory test. But I
14 think once they go out on the market, the actual use and by
15 word of mouth people will say, you know, these are really
16 pretty accurate; you don't need to do the screening, and
17 don't believe that maybe; what it really means is positive,
18 may also come out. So you have to think that into it too,
19 if they are allowed for unrestricted over-the-counter use.

20 DR. NIPPER: Any other comments? At this point I
21 would like to thank everyone for their leather-bottomed
22 approach to our long day. I'd like to thank the
23 contributors, both from the public, from the invited
24 speakers, from the panel and the FDA staff, for a masterful

1 job of organization of the meeting. I appreciate in
2 particular Sharon Lappalainen's outstanding job, and I
3 appreciate Dr. Gutman being here to help us with our
4 deliberations. And I hope that we've made it all worthwhile
5 by protecting the public good.

6 At this point, unless I hear other business, I'd
7 like to declare the panel adjourned.

8 [Whereupon, at 4:37 p.m., the open session was
9 adjourned.]

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