U.S. FOOD AND DRUG ADMINISTRATION

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RADIOLOGICAL DEVICES PANEL

OF THE

MEDICAL DEVICES ADVISORY COMMITTEE

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OPEN SESSION

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TUESDAY,
MAY 23, 2006

The above-entitled matter convened at 10:15 a.m. at the Holiday Inn Gaithersburg, Two Montgomery Village Avenue, Gaithersburg, Maryland, Elizabeth A. Krupinski, Ph.D., Acting Chair, presiding.

PRESENT:

ELIZABETH A. KRUPINSKI, Ph.D.	Acting Chair
JOHN D. BOURLAND, Ph.D.	Member
JUDY M. DESTOUET, M.D.	Temp. Voting Member
SCOT E. GOLDBERG, D.O., M.B.A.	Temp. Voting Member
JACQUELIN HOLLAND, R.N.C., C.R.N.P.	Consumer Rep.
BHARAT B. MITTAL, M.D.	Member
DEBORAH J. MOORE, B.S.	Industry Rep.
E. JAMES POTCHEN, M.D., J.D.	Temp. Voting Member
XIAO-HUA ZHOU, Ph.D.	Member
NANCY G. WERSTO	Executive Secretary
NANCY BROGDON	

FDA PRESENTER:

ROBERT A. PHILLIPS, Ph.D.
Chief, Radiological Devices Branch, ODE

SOUSAN S. ALTAIE, Ph.D.
Scientific Policy Advisor, Office of In Vitro Diagnostic Device Evaluation and Safety

THOMAS P. GROSS, M.D., M.P.H.
Director, Division of Postmarket Surveillance, Office of Surveillance and Biometrics

SOPHIE PAQUERAULT
Office of Science and Engineering Laboratories, Office of Device Evaluation

ROBERT J. JENNINGS
Office of Science and Engineering Laboratories, Division of Imaging and Applied Mathematics

RICHARD KACZMAREK
Office of Communication Education and Radiation Programs, Division of Mammography Quality and Radiation Programs

PUBLIC SPEAKERS:

COLLEEN HITTLE-DENSMORE
The Anson Group, LLC, for Giotto USA

ANDREW VANDERGRIFT
Fujifilm Medical Systems USA, Inc.

EUNICE LIN
Konica Minolta Medical Imaging

JOHN M. SANDRIK, Ph.D.
GE Healthcare

SAMI TOHKA, Ph.D.
PLANMED OY

ROBIN WINSOR
Imaging Dynamics

CAROL RYERSON
Eastman Kodak

ETTA D. PISANO, M.D.
University of North Carolina, Chapel Hill, North Carolina

MARGARITA ZULEY, M.D.
American College of Radiology

JOHN GOBLE
Sectra

ROBERT UZENOFF
Fujifilm Medical Systems USA, Inc.

A-G-E-N-D-A

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

10:17 a.m.

DR. KRUPINSKI: Good morning. I would like to call this meeting of the Radiological Devices Panel to order. I also want to request that everyone in attendance at this meeting sign in the attendance sheet that is available outside the door. The agenda for this meeting is also available outside the door.

I would like to announce the remaining tentatively scheduled meetings of this panel for 2006, September 12th and November 7th. Please remember these are tentative dates. You may monitor the panel website for any updated information.

I note for the record that the voting members present constitute a quorum as required by 21 CFR Part 14. At this meeting the panel will be making a recommendation to the Food and Drug Administration on an FDA initiated reclassification proposal to reclassify full field digital mammography systems. This proposed device identification does not include for consideration devices such as Computer Aided Detection Devices, CADs, or tomosynthesis.

Before we begin this meeting I would like to ask our distinguished panel members who have generously given their time to help the FDA in the matter being discussed today and other FDA staff seated at this table to introduce yourself. Please state your name, your area of expertise, your position, your institution, and your status on the panel, voting member deputized voting member, consumer representative, or industry representative.

I am Elizabeth Krupinski from the University of Arizona, Department of Radiology. I'm an experimental psychologist. I do medical image perception research, observer performance, and evaluation in the Department of Radiology there and a lot of telemedicine work as well.

DR. DESTOUET: I'm Judy Destouet, Chief of Mammography for Advanced Radiology in Baltimore. I'm in private practice. My practice performs over 130,000 mammograms a year as well as all aspects of breast imaging and I'm a temporary voting member.

DR. MITTAL: I'm Bharat Mittal. I'm Chairman of Radiation Oncology at Northwestern

University in Chicago. My area of expertise includes all aspects of radiation oncology.

DR. BOURLAND: I'm Dan Bourland, Associate Professor and head of physics research and education at Wake Forest University. I am a voting member here. My area of expertise is medical physics, principally in radiation oncology and imaging for radiation oncology.

MS. BROGDON: Good morning. I'm not a member of the panel. I'm Nancy Brogdon. I'm the Division Director for FDA's Division of Reproductive, Abdominal and Radiological Devices.

MS. MOORE: I'm Deborah Moore. I'm the Vice President of Regulatory and Clinical Quality for Windward Medical Systems. I previously was with Proxima Therapeutics with a focus on radiation delivery systems and oncology.

MS. HOLLAND: I'm Jacquelin Holland and I'm an advanced practice nurse for approximately 35 years working in the area of cancer screening and community education. I am with the James Cancer Hospital at Ohio State University Medical Center. The

name of my department is the Diversity Enhancement Program trying to concentrate on helping the community understand cancer and clinical trials. I am a nonvoting Consumer Representative.

DR. POTCHEN: I'm Jim Potchen. I'm Professor and Chairman of Radiology at Michigan State University. I have been involved in these panels for some time off and on, more off than on. I teach a variety of things, management, decision making. My major area of expertise has been decision making in medicine, law, and business, and observer performance in evaluation of diagnostic modalities and technology transfer is the area that I have had a major interest in.

DR. GOLDBERG: I'm Scot Goldberg, diagnostic radiologist. I work at the Women's Imaging Center of Delaware in Newark, Delaware. I specialize in breast imaging. I'm a voting member.

DR. ZHOU: I'm Andrew Zhou. I'm a Professor in the Department of Biostatistics at the University of Washington. My research area is to develop the statistical message for evaluating

diagnostic tests, particularly dealing with some of the biases associated with the design in the study of the diagnostic test. I'm a voting member.

MS. WERSTO: Good morning. My name is Nancy Wersto, and I'm the Executive Secretary for the Radiological Devices Advisory Panel.

DR. KRUPINSKI: Okay. Thank you. Ms. Wersto would like to make some introductory remarks.

MS. WERSTO: Good morning, everyone again. Before I turn the meeting over to Dr. Krupinski I'm required to read two statements into the record, the conflict of interest statement and the temporary voting authority for our added members. FDA conflict of interest disclosure statement for general matters, Radiological Devices Panel of the Medical Devices Advisory Committee, May 23, 2006.

The Food and Drug Administration, FDA, is convening today's meeting of the Radiological Devices Panel of the Medical Devices Advisory Committee under the authority of the Federal Advisory Committee Act of 1972. With the exception of the industry representative all members and consultants of the

panel are Special Government Employees (SGEs) or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this panel's compliance with federal ethics and conflict of interest laws covered by but not limited to those found at 18 USC Section 208 are being provided to participants in today's meeting and to the public.

FDA has determined that members and consultants of this panel are incompliance with federal ethics and conflict of interest laws. Under 18 USC Section 208 Congress has authorized FDA to grant waivers to Special Government employees who have financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Members and consultants of this panel who are Special Government Employees at today's meeting have been screened for potential financial conflicts

of interest of their own as well as those imputed to them including those of their employer, spouse, or minor child related to the discussions of today's meeting.

These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment. Today's agenda involves a discussion regarding the reclassification of full-field digital mammography systems, or FFDMs.

These systems would be classified as Class 2 special controls. Currently full-field digital mammography systems are Class 3, or PMA devices. Based on the agenda for today's meeting and all financial interest reported by the panel members and consultants, a conflict of interest waiver has been issued in accordance with 18 USC Section 208(b)(3) to E. James Potchen, M.D., J.D.

A copy of the written conflict of interest waiver statement may be obtained by submitting a written request to the agency's Freedom of Information Office, Room 212A-30 of the Parklawn Building. A copy

of this statement is also available on the web at www.fda.gov/ohrms/dockets/default.htm.

Deborah Moore is serving as the Industry Representative acting on behalf of all related industry and is employed by Windward Medical, Inc. This conflict of interest statement will be available for review at the registration table during this meeting and will be including as part of the official transcript.

We would like to remind members and consultants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement and their exclusion will be noted for the record. FDA encourages all other participants to advise the panel of any financial relationships that they may have with any firms at issue. Thank you.

Now for the temporary voting authority statement. Pursuant to the authority granted under the Medical Devices Advisory Committee Charter dated

October 27, 1990, and as amended August 18, 1999, I appoint the following individuals as voting members of the Radiological Devices Panel for this meeting on May 23, 2006. Judy M. Destouet, Scot E. Goldberg, E. James Potchen.

For the record these individuals are Special Government Employees and are consultants to this panel under the Medical Devices Advisory Committee. They have undergone the customary conflict of interest review and have reviewed the material to be considered at this meeting.

In addition, I appoint Elizabeth A. Krupinski, Ph.D., as Acting Chairperson for this meeting. This memorandum was signed by Daniel G. Schultz, M.D., Director, Center for Devices and Radiological Health on May 2, 2006.

If anyone has anything to discuss concerning these matters, please advise me now so that we may leave the room for discussion. Okay. Dr. Brogdon has a few remarks regarding panel members who have recently rotated off our panel.

MS. BROGDON: On behalf of the Food and

Drug Administration, the Division of Reproductive, Abdominal and Radiological Devices, and the Radiological devices Advisory Panel, I would like to acknowledge Dr. Prabhakar Tripuraneni. Dr. Tripuraneni is not present today because his term as a voting member recently ended.

On April 28th the Center for Devices and Radiological Health sent Dr. Tripuraneni a plaque recognizing his efforts as a panel member. Today, I would like to express our deepest appreciation for his bringing to the panel his expertise in radiation oncology and providing us with distinguished service and guidance.

During this panel's last meeting Dr. Tripuraneni made some especially insightful comments on the use of a multiple-reader multiple-case study to investigate intraobserver differences between chest CTs and plain films. We hope that in the future we will be able to have the benefit of Dr. Tripuranei's expertise as a panel consultant.

The success of this panel's work reinforces our conviction that responsible regulation

of medical devices depends greatly on the experience, the knowledge and varied backgrounds, as well as the viewpoints that are represented here. Thank you.

MS. WERSTO: The FDA seeks communication with industry and the clinical community in a number of different ways. First, FDA welcomes and encourages pre-meetings with sponsors prior to all IDE and PMA submissions. This affords the sponsor an opportunity to discuss issues that could impact the review process.

Second, the FDA communicates through the use of guidance documents. Towards this end FDA develops two types of guidance documents for manufacturers to follow when submitting a Premarket Notification application. One type is simply a summary of the information that has historically been requested on devices that are well understood in order to determine substantial equivalence. The second type of guidance document is one that develops as we learn about new technology. FDA welcomes and encourages the panel and industry to provide comments concerning our guidance documents.

I would now like to turn the meeting over to our chairperson, Dr. Elizabeth Krupinski.

DR. KRUPINSKI: Thank you. Dr. Robert Phillips, Chief of the Radiology Branch from the Office of Device Evaluation would now like to give a brief update on FDA radiology activity.

Dr. Phillips.

DR. PHILLIPS: Well, here I am again. As you're aware, the panel has not met for about the last year and a half. In that period of time we have had a lot of interactions with manufacturers but really very little on the PMA area. That is, original PMAs. What we have done is approved supplements for various devices. These have been in the area of CAD devices primarily where manufacturers are making changes in their devices or applying them to new or different display systems.

The changes have been primarily with the CAD devices that are used in mammography. The thing of interest to the panel, though, is we currently have a guidance that is out for comment on bone sonometers. If you will recall, we have had bone sonometers as a

Class 3 PMA product. These devices are devices that measure bone status by means of passing an ultrasound beam through the bone as opposed to what we are more familiar with, bone densitometry where you pass an x-ray beam through the bone.

The bone sonometer guidance has been out for comment for the last approximately 90 days. The period of review has either closed or is very close to being closed. We will, in the near future, be looking at the comments we received on that. It will be used probably as a basis for reclassifying of bone sonometry from Class 3 to Class 2. Other than that, our activities have been rather routine and I'll leave it at that. Are there any comments or questions? Thank you.

DR. KRUPINSKI: Thank you, Dr. Phillips. If no one has any questions, we will now proceed with a presentation on the FDA's Critical Path Initiative in Medical Devices by Dr. Sousan Altaie, Scientific Policy Advisor from the Office of In Vitro Diagnostic Device Evaluation and Safety.

MS. ALTAIE: Good morning. It's a

beautiful day out there and I just wish the pollen count was a smaller amount. You will excuse me if I start coughing and hacking up here. I am the Scientific Policy Advisor in the Office of In Vitro Diagnostics. Also I am the Critical Path Coordinator for Center for Devices.

Today I would like to talk to you about the Critical Path Initiative, what it is, and talk about the FDA interest and why FDA is interested in the Critical Path Initiative and talk a little bit about the critical path tools and talk about the medical device areas of interest in CDRH. Then talk a little bit about the device critical path projects that we have in the center. Then offer you an opportunity to participate in the Critical Path Initiative.

This Critical Path Initiative is now a departmental project and the Secretary of Health has shown a lot of interest in it and hopefully we can get some funding for it at this point. For now there is no funding. We are doing what we can do as a regulatory agency using our collegial interactions

with the outside people on the different projects.

Well, Critical Path Initiative is a serious attempt to make product development more predictable and less costly. The Critical Path Initiative covers -- if you look at the life cycle of a device development or any medical product development, the Critical Path skips the basic research and starts with prototyping, preclinical development into clinical development, and finally marketing of the product. It's a journey from medical product candidates to full-scale production and marketing.

So why is FDA interested in Critical Path? We are interested because we realize the significant benefit of bringing innovative products to the public faster because we have a unique perspective on product development. We see the successes, failures, and the missed opportunities because the Critical Path would help us to develop guidance and standards for fostering innovation.

We like to work together with the industry, academia, patient care advocates to

modernize, develop, and disseminate solutions. These are tools to address scientific hurdles and device development.

So what are these critical path tools that we care so much about? These are critical path tools that are methods and techniques that are used in three regulatory dimensions. That is, in assessment of safety, the tools predict if a potential product will be harmful. In proof of efficacy, the tools determine if a potential product will have medical benefits. In industrialization, the tools help in manufacturing the product with consistent quality.

When we talk about critical tools at the center, we think about biomarkers, Baysesian statistics, animal model biomarkers. We think about computer simulations, quality assessment, protocols, postmarket reporting, and anything else that the public might suggest or people who are interested so it's an open area for finding these tools and trying to follow them and try to establish some removal hurdles in device and medical product development.

Of course, in medical devices we have a

lot of opportunities. We regulate anything from the tongue depressors to band-aids to defibrillators to stethoscopes to MCATs and PET CATs. We have a lot of playing field to improve the product development.

However, I want to note that devices are totally different than drugs. We deal with complex components of these devices. We deal with biocompatibility in durable equipment. We deal with rapid production cycles, and our devices become obsolete very fast. We deal with device malfunctions and user errors, bench and clinical studies, quality system. Regs is what we follow as opposed to drugs following good manufacturing processes.

If we look at device safety tools, biocompatibility databases are one of the ones that we're looking at. We think about affects of products on diseased or injured tissues when we look at the device safety tools.

Under the device effectiveness tools, we think of surrogate endpoints for cardiovascular device trials. We think of computer simulation modeling for implanted devices.

Under device mass manufacturers or industrialization of the tools, we think of practice guidelines for follow-up of implanted devices. We think of validating training tools for devices with a known learning curve.

So here are examples of some critical path projects that are currently under -- currently being done at the Center for Devices. For validation of biomarkers, we are working to qualify biomarkers for personalized medicine in diagnosis and therapy as well as product purity and quality. For peripheral vascular stents, we are working with Stanford University to develop computer models of human physiology to test and predict failure even before going into animal and human studies.

For intrapartum field diagnostic devices, we are working with NIH to develop a clear regulatory path with consensus from the obstetrics community. We are collaborating with NIH on pharmacokinetics and image guided innovations. We are working with University of Stanford in San Francisco to identify barriers to drug diagnostic device co-development. We

are working on the pathways for statistical validation of circuit markers, especially in the area of cardiovascular devices.

We also are working with the Juvenile Diabetes Research Foundation to accelerate development of a closed-loop system using continuous glucose sensors and insulin pumps linked by a control algorithm. Our scientists in the Office of Science and Engineering Laboratories are collaborating with various researchers to develop animal models and computer simulated virtual families to improve predictions of toxic effects for medical products.

There is a horrendous amount of projects going on in the Center. Since we don't have a budget we are working on our own scientific background. We are doing workshops and we are actually using the wet labs outside the FDA to do all these testings that I mentioned.

If you are interested in getting involved in the Critical Path which is something that the Center and the Department encourages everyone, you could add to the National Critical Path Opportunities

list that we have compiled. There is a list that was published in April of this year and it has 76 opportunities. There are two documents.

One is a report describing the opportunities and how they are categorized and where we are going with these tools. The other one lists the projects. You could participate by adding to this list or you could pick up one of these projects and actually help us accomplish that project.

You also can go to the webpage for the Critical Path Initiative if you need more details about it, and you can find a link to the critical Path white paper. That is how the whole ball started rolling. You can see a copy of that in that webpage.

Then I would like to leave you with this concept. The product development has many stages, parts if you like, and they are all interconnected. Here at CDRH we believe in ensuring the public health through the total product life cycle and we think it's everyone's job. Any questions? Thank you.

DR. KRUPINSKI: Okay. Thank you, Dr. Altaie. If no one has any questions, we will now

proceed with the presentation on some of the recent changes in CDRH's Condition of Approval studies by Dr. Thomas Gross, Director of the Division of Postmarket Surveillance in the Office of Surveillance and Biometrics.

DR. GROSS: Good morning. I would like to take a few minutes of your time to talk to you about some recent changes in our Condition of Approval study program. Before I do, I would like to tell you a little bit about the Office of Surveillance and Biometrics.

This is the office that is currently overseeing the Condition of Approval Study program. We have several functions, both pre- and postmarket. On the premarket side we provide support for all statistical aspects of premarket submissions, be they 510(k) or PMAs.

We also have a cadre of epidemiologists who are involved in the review of original PMAs and I'll say a bit more about that in a few minutes. We have an interdisciplinary staff who detect signals of potential public health problems through our

nationwide adverse event reporting system, the medical device reporting system, which gathers reports mostly from manufacturers. These are mandatory reports.

We have another system called MedSun, Medical Product Safety Network, which is comprised of 350 mostly hospitals throughout the United States. We received from them reports of adverse events and product problems. We also characterize the risk of these potential public health problems and other safety issues by reviewing the literature, doing enhanced surveillance, de novo studies, and conducting collaborative studies with academia and professional societies and the like.

We are also responsible for coordinating the center response to these high-profile safety signals. We convene a panel of experts within the center to deliberate these issues and provide recommendations to center senior staff for action. Lastly, we are responsible for interpreting the Medical Device Reporting regulation, what needs to be reported, and also speaking to violations of that reporting requirement.

Now, with regard to our Conditional Approval Study program, we do have legal authority to mandate manufacturers to conduct these studies if provided in the regulation which states that post-approval requirements can include a continuing evaluation and periodic reporting on the safety, effectiveness, and reliability of the device for its intended use. This gives us our broad legal authority to, again, ask manufacturers to conduct these studies.

Having said that, we decided to do an internal evaluation of how well we were doing with regard to oversight of these studies. Our study was done, I believe, in the latter part of 2002, early 2003. We decided to look at original PMAs that were approved from the beginning of 1998 through the end of 2000. All told, there were 127 PMAs. Forty-five of those had Condition of Approval Study orders.

We did extensive review of our documents to try to establish the status of these studies. All told, what we found was disconcerting in the following ways. We concluded that CDRH had limited procedures for tracking the progress or results of these studies,

that our IT and other systems were wholly deficient in this regard.

There's huge turnover of lead reviewers that resulted in lack of follow-up and continuity. Up to 40 percent of those reviewers who were the lead reviewers when the PMA came in the door, were no longer associated with that PMA when we conducted this study. Again, extreme lack of continuity.

Lastly, there was a lack of premarket resources. Those were appropriately devoted to premarket submissions and premarket review and there was very little time left over for the important task of overseeing these Condition of Approval studies.

So obviously, we decided there was a need for a change, and we established goals for our Condition of Approval study programs. These are broad goals. Basically, what we would like to do, is have these studies in place by the time the product is marketed so we can gather real world safety and effectiveness data as the product hits the marketplace.

Secondly, obviously they are there to

better characterize the risk/benefit profile as these products are used in the real world. Of course, they are there to add to our ability to make sound scientific decisions.

So logistically what did we do? Beginning January of '05, we transferred the program from the premarket side of the house to the postmarket side of the house, the Office of Surveillance and Biometrics. We did that principally for two reasons. One, we had the available resources to oversee the program. Two, as I mentioned before, we have a staff of epidemiologists who are expert in the design of observational studies, and these conditional approval studies are essentially that kind of study.

Also, we developed and instituted an automated tracking system to make sure that we could acknowledge receipt of these reports when they came in the door, and we would know the status of the reports throughout the period of study. That tracking system was established in April of '05.

A bit more about the role of epidemiologists. This is unique in the agency.

Actually, we did a pilot study courtesy of Nancy Brogdon and her staff that we piloted this concept of adding epidemiologists to the PMA review team. At the end of about a two-and-a-half-year pilot, we deemed it very successful, and they are charged with the following responsibilities.

Again, working in conjunction with the rest of the PMA review team. They are tasked with the development of the postmarket monitoring plan during the premarket review process. Again, when the product hits the marketplace, we will have a plan in place to help best to monitor the safety and effectiveness of this product not only including condition of approval studies but other tools available.

They lead in developing well-formulated postmarket questions. They lead in the design of condition of approval study protocols, in the evaluation study products, study progress and results after approval, and they work very closely with industry and the rest of the PMA review team in achieving these objectives.

Obviously everybody has to be motivated in

doing these studies, and here are some aspects that we believe will help motivate good studies. First and foremost, obviously, is that we have to have important postmarket questions that need to be addressed in the postmarket period. The essential questions have to be addressed premarket.

There are many times residual important questions that should be addressed postmarket. Those need to be identified and specifically addressed via good study protocol design. It has worked out between us and industry. The tracking system is there to acknowledge receipts of reports on a periodic basis to provide feedback as to how well we think the study is going.

In an effort to be much more transparent, we plan on posting the study status of these ongoing studies on the agency's website. This is currently done with our drug colleagues and biologic colleagues in CDER and CBER. When necessary, we may issue penalties for extreme failure to conduct these studies or failure to report on the status of these studies. This is all laid out in draft guidance that we issued

in September of last year.

Lastly, how does this impact the advisory panel? Well, during our presentations to the advisory panel we will attempt to lay out the important post-approval public health questions and possible approaches for panel consideration. Also, again, this is laid out in the guidance that we hope to update the panel, that is FDA and industry, on the status of these studies as they go forward in time. Many times these studies are suggested or recommended by the panel.

That concludes my remarks. Any questions I would be happy to entertain. Thank you.

DR. KRUPINSKI: Okay. Thank you, Dr. Gross. If no one has any questions, we will now proceed with a series of presentations from FDA staff starting with Dr. Robert Phillips who will lead off with the presentation on the background of FFDMs and the regulatory history of the agency.

Dr. Phillips.

DR. PHILLIPS: Thank you again. What I want to talk to you about today is to start the

discussion about reclassifying full-field digital mammographic systems.

I will cover briefly background, our current situation, the device history, what premarket applications we have, the basis for device approvals, in other words, what basis do we use for approving those PMAs, what kind of equipment problems we have seen in the five years since these devices have been on the market, and then what has changed that has caused us to consider reclassification.

First of all, you are all aware of film/screen systems that are used for mammography. They are analog in that they use a piece of film to directly convert x-rays into an image on a piece of film. Digital systems are new. They came on the market about early in the 1990s. They convert x-rays into an electrical signal that is then translated into a number. This becomes part of a numerical image matrix. A computer can then process this matrix into an image that is either displayed on a monitor or can be printed to paper or piece of film for interpretation.

The devices that we are talking about now, the full-field digital mammography systems are intended as replacements for film/screen mammography systems. Both have the same indication for use. They are intended to generate mammographic images for screening and diagnosis of breast cancer.

Now, as you heard earlier this morning that I will repeat, new devices that enter the market after May 28, 1976 -- and this date is important. It is the date of enactment of the medical device amendments to the Food, Drug, and Cosmetics Act -- these devices are automatically in Class 3. In other words, they need Premarket Approval applications approval to go on the market unless they can be shown to be substantially equivalent to a device that was on the market.

In other words, marketed prior to May 28, 1976, or to a legally marketed device. In other words, another device that we have 510(k)'d and put on the market, or they undergo a process known as de novo which is a way of taking relatively simple devices and getting them cleared for marketing without having to

go through the PMA process.

Currently film screen systems of mammography are classed to their pre-amendment devices. In other words, film screen systems were available prior to May 28, 1976. They secure marketing clearance through the 510(k) process. In other words, they are found substantially equivalent to a predicate which is another mammographic device which is already on the market.

Full-field digital mammography systems are in Class 3. That is, they secure their marketing approval through the PMA process. This is a demonstration of safety and effectiveness for that particular device.

We have been aware of digital mammography systems and full-field digital mammography since about the late '80s. In 1996 we had a panel meeting to discuss full-field digital mammography and how we would go about approving it into the market. Subsequent to that meeting we had several companies submit 510(k)s which use Receiver Operating Characteristic (ROC) curves as their analytic method

to try and show substantial equivalence to film screen systems.

They were unable to do this primarily because of the rather large intra- and inter-reader variability that occurs when mammograms are read. Since they could not be found substantially equivalent, the pathway for getting to the market was the PMA process. To date we have approved four full-field digital mammography using the PMA process. We also have published a guidance document that applies to the Class 3 devices that spelled out what we wanted to see in a PMA submission for a full-field digital mammography system. This guidance was made available in May of 2001.

As you are aware, a major study that was run by the National Cancer Institute and the American College of Radiology Imaging Group, ACRIN, called the DMIST study, Digital Mammography Imaging Screening Trial, these results were published in the New England Journal of Medicine in September of last year, and they are still publishing or will be publishing based on more information.

What are the four devices that we have approved through the PMA process? The first was the General Electric Senographe 2000D, and that was approved January 28, 2000. The SenoScan full-field digital mammography system by Fischer Imaging was approved in September of 2001.

The Lorad Digital Breast Imager (LDBI) by Hologic, Inc., was approved in March of 2002. The last device that we approved was the Siemens Mammomat Novation, and that was approved in August 20 of 2004. Now, if you look at the slide, I also noted what type of detectors they have.

One has a flat panel amorphous silicon detector. One has an array of four charged particle coupling devices. Another has an array of 12 charged coupling devices. The Hologic device used an amorphous selenium detector. We have covered a wide range of the technologies that are available for this digital transducer that are used in these devices.

What do we look at when we are reviewing and approving a PMA? We look at three things. One, the device, secondly what laboratory information we

have, and thirdly, the results of clinical trials.

A PMA will consist of a physical description of the device. It will also contain a significant amount of laboratory data. These could be dynamic range and sensitometric response, image sharpness, and modulation transfer function, image noise and exposure as the noise power spectrum, detective quantum efficiency, how the automatic exposure control operates, what the radiation exposure is to the patient, and how the device performs when scored using various phantoms used in mammographic imaging.

In the clinical area we will see a reader performance analysis. This will be an assessment of sensitivity and specificity of detection on a large enriched study population. This involves double exposure where the same patient is exposed on the analog system and then the digital system.

Secondly, we will see side-by-side mammographic feature analysis, and this is used primarily for assessing the performance of, let's say, a soft image or monitor image displayed on a monitor

compared to the image displayed on film or paper. Then lastly, we will look at a comparison to film/screen systems based on an ROC analysis.

What kind of problems have we had with these devices since they started going on the market? We had five medical device recalls. These are procedures initiated by the company to correct some problem that has occurred. In 2003, we had a recall because the system did not meet accuracy specifications required for milliamperage.

In 2004, we had a device that had a software problem which truncated imaging. We also had a situation where we were having x-ray tube overload, overheating. Lastly, for 2004 we had a device that in its labeling lacked technical specifications for the minimum filtration and maximum line current that could be used with the device.

Then in 2005, we had a recall for a computer problem where overloading caused the interruption of image acquisition. We've had three reports submitted by users for problems with a device. In one case it was a system that just didn't work

properly, and it was completely replaced by the manufacturer.

In another, we had procedures delayed due to error readings in the system. Lastly, we had a problem with the release of the compression panel which caused the patient to be under compression longer than necessary.

Now, what has changed in the last few years that causes us to be here and recommend the reclassification of these devices from Class 3 to Class 2? First of all, we have the initial results of the DMIST study. These were published, as I indicated, earlier. Another speaker, a little bit later will be discussing this with you.

Secondly, our understanding of full-field digital mammography technology has improved to the point where we can develop -- we feel we can develop appropriate special controls that will assure adequate safety and effectiveness if we were to market clear these devices through the 510(k) or substantial equivalence process.

Again, we are talking about devices that

have the same Indication for Use (IFU). That is, to generate full-field digital mammographic images for screening and diagnosis of breast cancer.

Let me just spend a moment discussing the reclassification process itself. You heard a little bit about that this morning, but the process can be initiated either by the agency when we feel there is sufficient information to start the process, or by a member of the public who can petition the agency to initiate a reclassification procedure.

In either case, it requires a justification for the reclassification and the development of a Special Control which would allow us to review the device as a Class 2 device. This Special Control, in this case, is guidance on what we would want to see in submission.

The concept and proposal is then presented to an advisory panel for their recommendation, and that is what we are doing today. Assuming we get a positive recommendation, the proposal to reclassify and the draft guidance is made available for public comment by publication of notices in the Federal

Register.

After tha,t the public gets a period of time to comment on the proposal and the draft guidance, and after we have received those comments, we analyze them and make appropriate changes in the guidance or process. Then, a final action reclassifying the product together with a final guidance would be published in the Federal Register. At this point, the device would be placed into either Class 1 or Class 2.

Now, following me you are going to have several other presentations. Dr. Sophie Paquerault is going to talk about the DMIST Study results. Dr. Robert Jennings is going to talk about the risk to health and the special controls we propose for them. Dr. Richard Kaczmarek is going to talk about the role of MQSA, the medical Mammography Quality Safety Act. Then, we will discuss specific questions that we would like the panel to answer.

Madam Chairman, I am finished. The next speaker can be called.

MS. PAQUERAULT: Thank you, Dr. Phillips.

As was outlined in the previous presentation, digital mammography imaging screening trial provides evidence for reclassification of full-field digital mammographic systems. In this presentation, I will give an overview of the protocol and resulting conclusion.

The trial was funded by the National Cancer Institute through the American College of Radiology Imaging Network. The study was directed by Dr. Etta Pisano from the University of North Carolina at Chapel Hill. Dr. Pisano designed a clinical trial comparing reader performance for full-field digital mammography and film/screen mammography in detection and characterization of breast cancer in the screening setting.

The outcome of the trial was published last September in the New England Journal of Medicine. You were sent a copy of this paper. The trial involved nearly 5,000 (50,000) asymptomatic women presenting for screening mammography at certain free clinical sites. A total of 335 women were diagnosed with breast cancer. All patients participating in the

study underwent both full-field digital mammography and film/screen mammography acquisition.

Reader task were identical to the clinical routine task and consist of reading mammograms using a BIRADS scale providing a binary work-up recommendation, and also reading breast density according to the BIRADS lexicon.

Five digital mammographic systems were used in the study, the Senoscan from Fischer Medical, the Computed Radiography System for mammography from Fuji, the Senograph 2000D from GE, the Digital Mammography System and Selenia Full-Field Digital Mammography System both from Hologic.

Reader performances were evaluated using the area under the Receiver Operating Characteristic (ROC) curves also called AUC. Secondary analyses were performed using sensitivity, specificity, positive predictive value. This first graph illustrates the overall result among all women participating in the study.

The dotted line represents full-field digital mammography. The solid line is for film. The

area under the curve (AUC) is .78 for digital. It is lower for film, .74. The difference between these two curves was not found to be statistically significant.

This is a sub-analysis of the data. Among young women under the age of 50 years digital achieving AUC of .84. It is statistically lower for film, .69. This graph shows advantage of full-field digital mammography among young women.

This is a summary of the study findings. As reported in the paper, the reader performance for digital mammography did not vary significantly from that for film mammography according to race, the risk of breast cancer or the type of digital machine used.

Also, there were no significant difference in diagnosis accuracy between digital and film mammography in the overall population. However, full-field digital mammography was found more accurate in women under the age of 50 years, women with dense breasts, and premenopausal or perimenopausal women.

As an indication of the results of this study, the call-back rate of 8.4 percent for both full-field digital mammography and film/screen

mammography was found similar to or lower than those reported elsewhere for U.S. screening programs.

In summary, digital mammography and film/screen mammography are equivalent. The DMIST study showed advantage of full-field digital mammography for a subgroup of women among the population: young women, women with dense breasts, and premenopausal or perimenopausal.

Again, DMIST provided support for classification of full-field digital mammography. Following this presentation, Dr. Jennings is now going to present the risk to health and special control that has been identified for reclassification.

DR. JENNINGS: There's a formal context that we consider when we look at the issue of reclassification. We identify the risk to health presented by the device and then we look at the measures that are available for mitigating these risks and then ask the panel to decide whether the mitigations are adequate to control the risks in a way that gives us assurance that we'll have a safe and effective device using a 510(k) process rather than

PMA.

The risks to health are essentially the same ones we have with screen/film systems, the possibility of misdiagnosis either false/negative or false/positive, image retakes due to loss of data during acquisition or archiving due to positioning problems.

You might expect to see incorrect exposure here. We don't expect that to be an issue with digital systems because of their dynamic range. Certainly x-ray exposure, excessive breast compression, electric shock, and infection or skin irritation due to the compression.

The methods that we can use to mitigate the risks involve Special Controls. The biggest one is the guidance document. That will be the major thing that I'll be talking about today. Manufacturers also have access to voluntary standards that they can comply with. There are other Special Controls. As you heard about earlier, Quality System Regulations (QSRs) which in the device arena take the place of GMPs.

You have already heard that there's a PMA guidance document. We are in the process of developing a 510(k) guidance. There's a general software guidance document that is already available. There will be a separate guidance for accessories, namely review work stations. That is also under development.

This slide should look somewhat similar to the one that Bob Phillips showed. What we are proposing for the 510(k) clearance, is a physical device description, physical laboratory data which would be similar again to the PMA guidance with some differences. Namely, since we are going to be using substantial equivalence, we will be comparing performance of these devices to some other previously cleared device.

There will be more comprehensive evaluation of AUC systems. I'll explain where that comes from in a bit. More extensive phantom scoring. Then the big difference which we feel goes a long way towards our goal of least burdensome approach to device clearance is that we will use instead of a

large clinical trial simply reader evaluation of clinical films as is done in the ACR accreditation process. Finally, we will use appropriate labeling as another method of informing users about the performance of the device.

In the area of imaging performance we will be asking for the same kinds of things, sensitometry, issues of dynamic range linearity, temporal affects which affect some of these digital devices, image sharpness as expressed by the modulation transfer function, image noise as a function of exposure expressed in terms of the noise power spectrum, and the derived quantity, detector quantum efficiency (DQE), again as a function of exposure and spacial frequency.

The automatic exposure control (AEC) system has a new function these days both for screen/film and digital systems. Namely, in addition to actually controlling the exposure, in some systems, at least, it can make selections of technique factors, can select the anode and filter. We are interested in knowing exactly what those systems do.

They also are capable of operating in different modes so we want to know that information for all of the available modes. In addition, we want to know how the AUC system control signal to noise ratio (SNR) or contrast to noise ratio (CNR) is a function of breast thickness. Obviously, we want to know those as a function of breast thickness in AUC mode.

We do have some preliminary data on patient dose. For June of 2000 until September of 2003 when the agency was certifying full-field digital mammo units there were 337 units cleared. During that same time Government inspectors measured doses on film/screen units so there is an average value available. It turns out that the digital systems produce about 15 percent lower dose than the film screen units.

This is a histogram of the dose values for the digital systems. You see the peak is somewhere around 150. I think screen/film systems are up around 180 now. You also see that there's a high dose tail to that curve so we do want to look at what happens

with individual systems.

In the area of physical laboratory data we have a couple of recommendations. One is that the lab measurements be made by methods that are supported by standards such as those that are being developed by the International Electrotechnical Commission or by recommendations such as those being developed by the American Association of Physicists in Medicine.

Another recommendation that we were considering is that the AUC performance result in patient dose as a function of breast thickness that conforms to the EUREF acceptable level. EUREF is the European Reference Organization for Quality Assurance and Mammography. They have two levels of performance. One is called acceptable, which is the less stringent level, and the other is achievable. In other words, what a good facility ought to be able to do. We are asking, or considering anyway asking, that the performance be at least at the acceptable level as defined by EUREF.

In the area of clinical data, and this, again, is the one where we hope to make a large

difference in the difficulty of getting clearance, we propose that sets of patient films be evaluated by CDRH staff who are trained in the evaluation of clinical films for the ACR Mammography Accreditation Program.

The ACR procedure requires only two sets of films, one set of films from a patient with fatty breasts and one from a patient with dense breasts. We are thinking that we would like to have several sets of films covering a range of patient characteristics and a range of machine settings. Still, these are just normal patients so the accrual of this kind of data is not a major difficulty we think.

Just to remind you what the ACR process involves: positioning, compression, exposure level, contrast, sharpness, noise, and artifacts. Of course, dealing with digital images, exposure and contrast can be manipulated so we might redefine those as ability to obtain optimal contrast or exposure.

In the area of device labeling we would like to see the following: a detailed quality assurance program, an explicit summary of the physical

device description and the laboratory data, and appropriate cleaning and disinfection procedure. Although we can't mandate this, we think it would be a good idea that the labeling recommend that each clinical facility maintain an adverse event log book.

The voluntary standards that are available, the biggest one is not here yet, but we are aware that it is under development and that is a generic full-field digital mammography quality assurance program. If that becomes available, then our recommendation in the labeling for a detailed quality assurance program could be satisfied simply by reference to the ACR NEMA document.

There are voluntary standards covering electrical and mechanical performance and compatibility. There are material standards and biocompatibility standards available also.

Quality System Regulations (QSR) require that all manufacturers, both foreign and domestic, have a quality system that covers design, manufacture, packaging, labeling, storage, installation, and servicing of medical devices. In other words, it

ensures that in production the devices continue to be safe and effective.

QSRs also provide for the monitoring of device problems and inspections of the operations and records of device manufacturers. CDRH has the authority to enforce those QSRs so we think this goes a long way towards covering device safety and effectiveness as well.

Finally, there is the Medical Device Reporting (MDR) Regulation which provides an independent means of obtaining information on adverse events. This is a somewhat complicated summary slide that simply points out the fact that the things that I've mentioned apply to, in many cases, a number of individual risks. At this point I guess the issue becomes one of have the mitigations that we are proposing do they address the risks appropriately to allow us to down classify from PMA to 510(k)?

DR. KACZMAREK: Good morning. The reclassification of the FFDM systems has important consequences for the manufacturers of these devices. It also has significance for the mammography

facilities who are interested in using these systems.

What I would like to do is discuss what bearing the reclassification of full-field digital mammo devices would have on screening mammography.

I am representing the Division of Mammography Quality and Radiation Programs (DMQRP) which is contained within the Office of Communication Education Radiation Programs.

We, the DMQRP, are responsible for the enforcement of the Mammography Quality Standards Act (MQSA) which regulates the clinical practice of mammography. Although we operate under a different authority, our staff works together with the Office of Device Evaluation, Office of Science and Engineering Labs, to try to facilitate the delivery of high quality healthcare to the public.

The Mammography Quality Standards Act (MQSA) was passed by Congress to ensure that all women have access to quality mammography for the detection of breast cancer in its earliest and most treatable stages. FDA was charged with developing and implementing MQSA regulations and interim regulations

became effective in February 1994.

These regulations began being enforced in 1995 when FDA initiated an inspection program and subsequently FDA issued more comprehensive final regulations which became effective in April of '99. The MQSA regulations which appear in 21 CFR 900 are very comprehensive.

They established a program for the accreditation and certification of all facilities performing screening mammography. They also specified training and credential requirements applicable to all facility personnel involved in any aspect of mammography: x-ray technologists, medical physicists, and physicians.

The regulations also address requirements for equipment performance and provision for periodic testing of clinically used mammography systems. It is this aspect, in particular, that I want to focus on here today.

The MQSA regulations essentially are oriented towards film/screen mammographic systems which were considered to be state of the art for

screening when the regulations were developed and was the dominant technology in use at the time. Manufacturers and clinical researchers had spent a considerable amount of time developing and improving film/screen systems to make them as patient and technology friendly as possible. Also, to lower the patient dose to acceptable levels and to improve the image quality to the greatest degree possible.

The evolution of this modality and its ability to provide early detection of breast cancer is why x-ray screening was able to become such a vital part of the MQSA. It is important to note that FDA was aided in writing regulations by the fact that the American College of Radiology (ACR) had developed and implemented an accreditation program for mammographic facilities. This was in wide use and FDA adopted many of the policies and procedures of the ACR program including the equipment performance QC guidelines.

So, although the systems were and still are highly specialized, there was very broad agreement about performance criteria and also what specific QC testing needed to be performed. It was relatively

straightforward to incorporate this into the regulations.

However, full-field digital detectors for screening were not close to being ready for clinical use when the regulations were developed. The statement here, which is in 900.12(e)(6) appears in the Quality Standards Requirements part. It did anticipate dealing with modalities other than screen/film and when FFDM systems became available, FDA and facilities had to consider what equipment performance criteria and what QC testing would be appropriate for these systems.

As part of the PMA process, in addition to the requirements for clinical data, we at FDA have drawn upon our considerable internal experience in diagnostic imaging science and required manufacturers, as part of the PMA process, to provide information about their systems with regard to accepted digital imaging metrics.

Each criteria have already been mentioned, and this process has been very beneficial to the facilities who have purchased these FFDM systems.

This is because what has resulted from all this is that all FFDM systems which have gone through the FDA PMA process and which are in clinical use today have satisfied the agency that they meet our performance requirements for digital imaging technology. We now have the benefit also of the large control study, the DMIST study that Sophie spoke of to reflect on.

Accepting the experience from the clinical trials and the results of the DMIST study, which can be considered to have established the clinical benefits of digital mammography, I want to emphasize the importance of a requirement for a Quality Assurance (QA) program that we are proposing, as heard earlier by the earlier speakers, that this remain as part of the Special Controls.

From our perspective, the perspective of DMQRP, the Quality Control (QC) tests have provided facilities with a comprehensive set of tools to ensure that the equipment is operating in a manner which meets the criteria which manufacturers have specified. We have gone a long way toward achieving a situation which is similar to screen/film mammography where both

the facilities and the manufacturers are aware of the essential parts that they play in providing quality mammography services so we would like to continue with our success in this area.

Those of us involved with the implementation of the Mammography Quality Standards Act (MQSA) would agree with what was said earlier by Bob Phillips, that our understanding of FFDM technology has improved to the point where we can develop appropriate Special Controls so that we can assure active safety and effectiveness through the 510(k) process.

I would like to say that even the proposed guidance, which has been discussed, the proposed requirements for the review of clinical data, the discussion we have heard about how device performance would be evaluated, and the inclusion of the other Special Controls the Division of Mammography Quality and Radiation Programs supports the reclassification. Thank you.

DR. KRUPINSKI: Thank you, FDA staff. Does the panel have any questions for the FDA?

DR. ZHOU: Yes, I have a few questions about the results we reported from DMIST because that's the one you rely on for your recommendation. One of the conclusions from that study is that the film and digital mammography are equivalent.

When I look at the data you show us here, I'm wondering that the two ROC curves you plotted, on page No. 4, I think, on the slides, how that compares between the film and the digital mammography ROC curve changes by readers, also by the centers. I wonder whether that conclusion how we depend on which reader are you looking at or which center are you looking at. That is one question not clear to me.

Also, on the conclusion from the paper, it shows the digital mammography actually is better for the woman under age 50, I think. In that sense, actually for some population of the patients, those two systems are not equivalent.

The third question I have is in order to establish equivalency of two diagnostic tests yearly, you need to establish the range in the ROC curve to say the ROC curve of the two systems within the range

of 0.1 that you can they are equivalent. I would like to see actually somehow we perform or you perform actually bioequivalency test on those two systems.

DR. PAQUERAULT: As you know, we are not in control of the data, and it will remain in DMIST. We are taking the demonstration that Dr. Etta Pisano provide us via the paper and to support reclassification. What was your question about the ROC curve?

DR. ZHOU: That is the implication that, let's say, if you establish equivalency of two systems in some of the centers, there are 34 --

DR. PAQUERAULT: Thirty-three.

DR. ZHOU: There are 33 centers involved, so maybe it's possible that in some centers they are equivalent but in other centers they are not.

DR. PAQUERAULT: Over all, you know.

DR. ZHOU: That's right.

DR. PAQUERAULT: It's an overall study so you are looking at the average and looking at it being kind of small. Quite small.

DR. ZHOU: Yes, but if the results

actually depend on centers, then that's the real issue about the conclusion that the two systems are equivalent.

DR. PAQUERAULT: That's a question you should ask to the principal investigator, I guess.

DR. ZHOU: It would be nice to see additional data.

DR. KRUPINSKI: I had a question as well, I guess, for Bob Jennings. You said that one of the control factors was that you were going to have reader evaluation of clinical films. My question, I guess, is do we have any idea what percentage of systems that people are actually using in clinical service, what percentage are actually reading from films, hardcopy, and what percentage are reading softcopy? Based on that answer -- well, answer that one first. Do we know what percentage of soft versus hardcopy reading in clinical practice now?

DR. JENNINGS: I don't believe we have data that is well substantiated but I have heard numbers like 95 percent read from softcopy.

DR. KRUPINSKI: Then I guess the follow-up

question then is why use film for your control process and shouldn't we actually be using softcopy as your standard there?

DR. JENNINGS: That is certainly an excellent question and certainly a desirable thing to do. You may be aware of the fact that independent manufacturers of review stations are unable to properly display certain proprietary data even though ostensibly it conforms to DICOM. But, yeah, if there is a way to properly display the images to our readers, then that certainly would simplify things and I would be all for it.

DR. KRUPINSKI: Dan.

DR. BOURLAND: I'm not exactly sure who can address this one but several of you have mentioned that there are, for instance, performance standards both for software and then digital detectors. Are those mammography specific? Are they broad enough to cover what is needed to be covered? Can you tell me a little bit of what's in there and how those would be applied to this situation?

DR. PHILLIPS: The software guidance is

not specific to mammography. It's a general software guidance. It is designed to assure that the software has been developed and designed in a structured and journeyman-like fashion. As you are aware, software really can't be tested after the fact to assure that it is safe and effective.

If you don't design it in an organized manner and test it as you are designing it and as you are developing it, what you will end up at the end is something that is unreliable. The software guidance is mainly designed to assure that software that we use in devices is robust. The second question was --

DR. BOURLAND: The digital detector performance standard.

DR. PHILLIPS: Yes, at the present time, the guidance for digital detectors is generic. It's for all solid-state detectors, but that is something that could be addressed in our guidance if the panel felt it was appropriate.

DR. BOURLAND: In a guidance document could it include, for instance, performance specifications that are lab based that, for instance,

were reviewed in part and then things such as this? In other words, the digital detector as well as software, those are something that could be incorporated either in part or by reference or as appropriate?

DR. PHILLIPS: Right now, they are incorporated by reference. If you felt -- when the guidance comes out, the public, the panel, everybody will have an opportunity to comment on it, and I'm sure AAPM will comment as one factor. But if the comments are returned to us indicating that the community feels there is a need for some specific type of guidance, specific to mammography in those two areas, that is something that we would consider then in writing the final guidance.

DR. KRUPINSKI: Any other questions?

DR. BOURLAND: So one question and maybe it's an afternoon one, but impact on manufacturers. Are there some thoughts on that?

DR. PHILLIPS: What's the nature of the question? Where are you going with it?

DR. BOURLAND: This would be, I think, a

change for manufacturers. Maybe we are waiting to hear from them perhaps. Maybe they should be the ones to --

DR. PHILLIPS: There are two things that would happen. One, for the manufacturers who currently have PMAs for their devices, right now, whenever they make a change in their device, they are obligated to submit a supplement, a PMA supplement to the agency for clearance for those changes.

Under a 510(k), that could be done internally by the manufacturer, and the only time they would need to submit a new 510(k) for their device was if the change that they were making had the potential for significantly changing the safety or effectiveness.

For manufacturers who are coming on the market in the future, they no longer will have to go through the PMA process which means they will not have to do a rather extensive clinical study and do all the other major background material that we ask for in a PMA. Hence, the burden on them would be significantly reduced, and hopefully, the time it would take to get

a new product on the market would also be reduced.

DR. KRUPINSKI: Anything else? Okay. Thank you FDA staff. If no one has any questions, we will now proceed with the first of two half-hour Open Public Hearing Sessions for this meeting. The second half-hour Open Public Hearing Session will follow the panel discussion this afternoon. Ms. Wersto will now read a statement prepared for Open Public Hearings.

MS. WERSTO: Thank you, Dr. Krupinski. Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision making. To ensure such transparency at the Open Public Hearing Session of the Advisory Committee meeting, FDA believes it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement to advise the Committee of any financial relationship that you may have with the sponsor, their products, and, if known, a direct competitor to full-field digital mammography systems.

For example, this financial information may include a sponsor's payment of your travel, lodging, or other expenses in connection with your attendance at the meeting. Likewise, FDA encourages you at the beginning of your statement to advise the Committee if you do not have any financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it is not -- it will not preclude you from speaking. Thank you.

DR. KRUPINSKI: I would like to remind public observers at this meeting that while this portion of the meeting is open to public observation, public attendees may not participate except at the specific request of the chair. We can now begin the first open public portion of this meeting.

Ms. Colleen Hittle-Densmore, Anson Group for Giotto USA.

MS. HITTLE-DENSMORE: Good morning. Thank you very much for allowing me to speak here today. I must admit, though, that with the five minutes provided I'm not anticipating providing you with

anything different than what was presented by the FDA. As a consultant I'm in, I suppose, the enviable position uniquely of being a little aligned in the situation with Bob Phillips and his group. A lot of my comments will be just echoing the information that has been presented already this morning.

My name is Colleen Hittle-Densmore. I am managing partner of a firm called the Anson Group. Today, I am here representing two different clients, one the International Medica Scientifica (IMS), medical device manufacturer out of Italy, and their partner Giotto USA.

To Nancy Wersto's point, I am here today as a paid consultant to those firms. Our group, the Anson Group, provides regulatory and clinical strategies to medical technology companies, and we have significant experience in diagnostic imaging.

IMS, as I said earlier, is an Italian-based manufacturer of digital equipment. They have been in business for over 40 years and have worldwide distribution of various products. Giotto USA is their exclusive distributor in the United States, and my

colleague, Bob Rusk, is here today representing Giotto.

I have just put a slide in there for definitions because as a FOIA when you are searching on FOIA sometimes the definitions allude you so I added that slide in. We have talked already this morning about the similarities between full-field digital and film mammography. I think Bob Phillips made the point that it has a similar indication for use and similar clinical populations.

I am referencing various technical articles today, and I have those in full copies if you're interested. Obviously, you are very familiar with the content of those. These are similarities between the two systems. If it wasn't obvious at the beginning, we are supportive, obviously, of the reclassification.

The differences between the two, I think, are important, but I think they all kind of center on kind of the data management aspects of the products. As we have discussed earlier this morning, I think those are the aspects of the products that are well

suited for Special Controls. I take the doctor's point from this morning about the increased detection in women over 50 with dense breasts.

Certainly that's a challenge with the substantial equivalence argument, but I would also suggest that there are many submissions in the 510(k) world where there are slighter various advantages for that product but the limitation in your labeling allows again just the substantial equivalence argument.

I agree with Bob Phillips' report with regard to recalls and adverse events. We didn't see any adverse events reported by manufacturers, but only a few in the user community that we felt were fairly inconsequential.

My closing comments are about Special Controls. I think when you look at ultrasound and other diagnostic imaging modalities, you can see examples of where Special Control reports have been used very effectively to monitor the safety and efficacy of various products. I would suggest that putting effort into the appropriate Special Controls

for full-field digital mammography would be appropriate in this case. Thank you very much.

DR. KRUPINSKI: Thank you. We're going to save questions until the end.

Mr. Andrew Vandergrift from Fujifilm Medical Systems USA.

MR. VANDERGRIFT: Good morning. My name is Andy Vandergrift, and I'm the National Program Manager for Women's Healthcare for Fujifilm Medical Systems USA. I want to thank you for allowing us to make this presentation this morning.

Fuji manufactures the type of devices that are subject to the proposed regulatory action. In fact, Fuji produced the first digital radiographic systems 25 years ago and has accumulated considerable experience in this field. Fuji's full-field digital mammography system was one of the systems proven in the DMIST trial that was discussed earlier today.

In addition, our Fuji CR mammography system is the subject of Premarket Approval application, PMA, currently under review in the FDA. The Radiology Devices Panel role in advising FDA on

its proposed down classification of FFDM is extremely important because it directly impacts diagnostic decisions and women's healthcare.

For its down-classing recommendation FDA has drawn on experience of devices FDA approved in PMAs and those used in DMIST. These devices include fixed array detector systems employing one of two different technologies, indirect and direct detection. Both have been proven clinically.

They also include device types consisting of monolithic sheets of photostimulable phosphorous which are laser scanned known as computed radiography, or CR. Similar to fixed array systems, CR systems of different types are available. In formulating its recommendation to FDA, the panel should be aware that substantial imaging performance differences, such as in detector quantum frequency (DQE), as a function of spatial frequency, exist among various vendors.

For example, although Fuji markets various digital imaging systems, we only recommend the use of our 50 micron system for screening mammography. We do not recommend the use of our other systems for

screening due to our experience in different performances of these systems. These performance differences have significant implications for safety and effectiveness of mammography.

The acceptability of digital mammography below a certain level of DQE has not been proven compared to those commercially available devices submitted at the PMA level. The identification of what are acceptable DQE levels requires much greater clinical investigation.

To conclude, there are technological design and imaging performance differences within fixed array FFDM. Similarly, differences exist within a group of CR devices. Regardless of whether FFDM is categorized as Class 3 or Class 2, any change in regulation of FFDM must ensure that products reaching the market have demonstrated image quality performances equivalent to or better than those devices whose safety and efficacy have been demonstrated through extensive clinical evaluation.

Thank you again for allowing us to present.

DR. KRUPINSKI: Thank you. Ms. Eunice Lin from Konica Medical Imaging.

MS. LIN: Madam Chairman, members of the Advisory Panel, good morning. My name is Eunice Lin. I am here to represent Konica Minolta Medical Imaging. I'm an employee of Konica Minolta Medical Imaging. We are all here today with one common goal, and that is to provide the best possible healthcare services to the millions of women in the U.S., specifically in the area of breast cancer detection.

With innovations and research provided by companies like Konica Minolta and many others, we are closer to reaching our goal every day. The question the panel is being asked today with the proposal reclassification is one to which the answer to the panel must be reasonably assured. The question is, is it possible to demonstrate the safety and effectiveness of a digital mammography system by using standardized methods for measuring performance and safety parameters?

Konica Minolta supports FDA's proposal to reclassify additional mammography systems to a class 2

device. Furthermore, we believe that it is possible to use standardized methods to characterize the performance of a mammography system. I would like to tell you today about two mammography systems that Konica Minolta has commercialized worldwide. The first is the REGIUS 190 CR which is a computer radiography system with mammography applications. The second system is REGIUS PureView mammography system.

This is a combination of phase contrast mammography and computer radiography (CR). Phrase contrast mammography uses an innovative approach to improve breast cancer detection. It utilizes x-ray refraction and modification to amplify the contrast within the breast tissue, therefore making it more visible for the microcalcification and making a more sharp -- increasing the sharpness, as well as increasing the definition and visibility of the fibrils and fringes of masses.

I do not have enough time to tell you more about the science behind this breakthrough technology. I would like to share with you, however, the benefits we have observed both in the laboratories and at

clinical sites outside the U.S.

The benefits of the digital mammography system have been well documented. Like other digital mammography systems, both REGIUS 190 CR and REGIUS PureView mammography system contribute to the overall benefits of the healthcare by reducing the number of retakes, by improving the contrast which is particularly useful in dense breasts, by producing more consistent image quality, and by making data more available electronically.

Specifically, the REGIUS 190 mammography system also offers high resolution among its kind at 43 points by micron. Also, REGIUS PureView mammography system offers more benefits due to the age affect and magnification process. These benefits include: high special resolution of 20 by micron, improved sharpness from age affect, and reduced noise.

To assess the performance of a digital mammography system, many data are gathered in the laboratories prior to testing it on clinical patients. I list some of them here as you have seen earlier during the FDA presentation. As it was also

indicated, many of these tests have been well established and were accepted as industry standard, and organizations such as IEC are including some of these as part of the evaluation for digital mammography system. Some of this has also been included in the FDA guidance document.

We believe that clinical studies are not necessary and, furthermore, as seen in the DMIST trial and other PMA publication studies that we observe, that the clinical studies validate the data, the scientific measurements. However, they do not add additional information to the performance of the systems.

I show you two examples of a physical test that we have measured in our laboratories, and you can see the red dotted line there represents the computer radiography system performance and the blue lines are representing the phase contrast mammography PureView image. The one on the left is a sharpness measurement, and that is represented on our MTF curve. The one on the right is the noise power spectrum which measures the noise and the image. Both of these have

been alluded to by FDA earlier.

Another physical test is a phantom test. For this test we used a standard ACR 156 phantom for subjective evaluation and comparison of multiple mammography system. This test was done by one of our clinical sites in Japan. As you can see, across the board, most of these systems performed pretty equivalently.

The test was done using two types of film/screen combinations, a computer radiography system, 50 micron computer radiography system, a flat panel detection system, and PureView mammography system. As you can see, the total scoring here that PureView mammography system actually performed pretty equivalently to the best film/screen system in the industry. We also notice that it outperformed all the other systems in detecting masses.

I would like to show you an example of a clinical image. On the left, we have the PureView mammography system image acquired by PureView mammography system. On the right, is acquired using film/screen. Although the projector does not do

justice to the image quality here, we can still see a much visible and clearly defined and more detailed fibril with sticklers up here using the PureView mammography system.

As well as well-defined margin on the fringe of this mass comparing to the formless mass that you see on the film/screen. This obviously presents a great deal of potential for improved image cancer detection. This result also is consistent with the data that we have measured in the laboratories.

In the preliminary observer study conducted by a major university in Japan, 38 patients have been examined, and we were able to observe by using PureView mammography system two masses and three classifications were overlooked using film/screen but were picked up by the radiologist by using phase contrast mammography. This study was reported in the Investigative Radiology in 2005.

In conclusion, we believe that test data provides accurate measurements for clinical performance. Clinical data collected in the U.S. through the DMIST trial was data from the PMA

submissions that we have seen outside of the U.S. have provided equivalent performance of digital mammography system to film/screen. Therefore, no additional clinical study is necessary.

Our recommendation is to support the reclassification of digital mammography system which we believe will provide healthcare professionals in the U.S. rapid access to new technologies that are already available to their overseas counterparts. It will accelerate improvement in healthcare for the millions of women in the U.S. We fully support the use of physical tests recommended by FDA to form a basis for the 510(k) device evaluation. Thank you.

DR. KRUPINSKI: Thank you. Last representative, Dr. John Sandrik from GE Healthcare.

DR. SANDRIK: Good morning. I am John Sandrik. I am an employee of and a stockholder in the GE Company. I fully expect that they are going to pay for my travel expenses today. I want to thank the organizers of the meeting for giving us the opportunity to offer some comments on the reclassification of full-field digital mammography or

FFDM.

From the time of its introduction in 2000, FFDM has been shown to provide effectiveness equivalent to screen/film mammography for both the screening and diagnosis of breast cancer. This has been demonstrated in the clinical studies performed to develop PMA submissions as well as those done after the device has entered the market.

In the most extensive study performed to date, the ACRIN DMIST, the diagnostic performance of FFDM was again shown to be similar to screen/film mammography when considering the entire population of women in the study. However, FFDM demonstrated significantly better performance for particular subgroups of the study.

One of the concerns regarding device reclassification is demonstration of reasonable safety and effectiveness. As mentioned, many studies have demonstrated effectiveness of FFDM at least equivalent to that of the most commonly used mammographic modality screen/film mammography.

At this time, we have had over six years

of clinical experience using FDA approved systems, and just over 10 percent of the systems in use at MQSA-certified facilities are FFDM systems. From the point of view of safety, there are many technical and clinical similarities between digital and screen/film systems which is a Class 2 device. We expect that sufficient data are available to verify the safety and effectiveness of FFDM.

Another concern for reclassification is the availability of Special Controls. An FDA guidance document has been published for Premarket Applications for digital mammography systems and we recommend that this guidance remain in effect, perhaps modified as suggested earlier, but we basically support the guidance.

Clinical data should be acquired on the product proposed for entry into the market. The certification and accreditation programs of the MQSA not only provide for oversight of the practice of mammography but might also serve as a source of data on device performance. Mammography has a long history of the application of quality assurance both through

voluntary programs and MQSA mandatory programs.

With regard to devices, every FFDM unit is operated under an FDA approved quality control plan developed by the image receptor manufacturer as part of the PMA submission. Data on the application of these, as well as a more generic QC plan, were gathered as part of the ACRIN DMIST.

NEMA, the National Electrical Manufacturers Association, has developed standard QC planned templates for displays and printers used with FFDM systems. These templates are intended for use by manufacturers of these devices to ensure that all components of an FFDM system are covered by a QC plan.

As it has done in the past for screen/film mammography, the American College of Radiology is also developing QC plan for digital mammography. We do not say that the task is accomplished, but we do believe that sufficient data are available to proceed.

GE Healthcare supports the reclassification of FFDM from Class 3 to Class 2. The evidence to date does not suggest that any regulatory purpose is being served by retaining FFDM in Class 3.

We suggest that the principle of the least burdensome approach be applied to the case of FFDM reclassification. We have no doubt that advances are yet to be made in digital mammography. We believe that patients will more readily benefit from these advances if they can be brought to market in a more timely manner. I will be available if you have any questions later. Thank you.

DR. KRUPINSKI: Okay. Thank you. Does the panel have any questions for these speakers? Okay. Is there anyone else who would like to present to the panel? Please raise your hand and come forward to the microphone. Please identify yourself and tell of any device company involvement.

MR. TOHKA: My name is Sami Tohka. I'm employed by PLANMED, a device manufacturer from Finland. I just want to briefly say regards to the Panel, and I agree with the previous presentations that PLANMED also supports the reclassification of FFDM to Class 2 device. Thank you.

DR. KRUPINSKI: Thank you.

Again, please identify yourself and tell

of any device company involvement.

MR. WINSOR: My name is Robin Winsor. I'm the Chief Technical Officer at Imaging Dynamics. We are a company that makes general x-ray digital systems just now. We have development of a digital mammography system underway. We hope to show work and progress later in the year and get our regulatory filing started later on.

One thing that hasn't been mentioned, and just for the panel's consideration, is that by declassifying down to Class 2 with all the good scientific data that we've had here and the well-established scientific guidelines, removing the barriers-to-entry for other companies that have less resources than the giants that are in digital mammography today, the GEs and the Fujis and Siemens and so on.

Smaller companies like Imaging Dynamics have made a difference in availability of digital x-ray in general by bringing to market innovative lower cost devices. Today, my company is producing systems that are now marketed in 25 countries around the world

and extensively in the United States. With access to market through the 510(k) system that allows us to get systems on the market quicker and, most importantly, to bring good quality devices to the market at much lower cost.

Today, we have systems that are a quarter to a fifth of the cost of systems produced by the majors, and by reducing cost, we could not only accelerate the time to market for new technology but make it far more available to women in the United States and around the world by making it much more economical for facilities to get there. Obviously, we want to have good scientific guidelines that would prevent poor quality products coming on the market as we have certainly seen coming out of Asia and Russia.

There are a number of systems that are based along similar technical lines but don't have the quality controls so we must maintain those controls. Good established guidelines allowing innovative technologies to market will improve access by the economic portion which today is the largest single barrier to widespread adoption of facilities. We

wholeheartedly support the reclassification with appropriate checks and balances for quality. Thank you.

DR. KRUPINSKI: Anyone? Come on. Again, identify yourself and any company involvement.

MS. RYERSON: I'm Carol Ryerson. I'm Director of Regulatory and Clinical Affairs for Eastman Kodak Company. Our company has brought to the worldwide market products for radiology and improvements in technology specifically for women's health and mammography for over 100 years. We have progressed in also bringing to market not just the traditional screen film products but also products in the digital radiography area and some specific to mammography.

We do support the down classification for digital mammography products. We think that the experience that we and other manufacturers have had with a variety of products in the digital area for mammography applications supports the down classification and making that technology available to medical practice.

We do have a long history of developing products using quality assurance methods and using standards. We do think it's the right time for the panel to be considering such a down classification for digital mammography.

DR. KRUPINSKI: Is there anyone else? Any final questions from the panel? Okay. Before we adjourn for lunch, I would like to remind you that the open committee deliberations will resume in one hour at 1:15 in this room.

(Whereupon, at 12:17 p.m. off the record for lunch to reconvene at 1:29 p.m.)

DR. KRUPINSKI: Good afternoon. Sit down, now. I would now like to call the meeting back to order. Remind public observers of the meeting that while this portion of the meeting is open for public observation, public attendees may not participate unless specifically requested to do so by the Chair. We will now continue with the Panel's general discussion after which they will focus their deliberations on the FDA questions. Following that, we will conduct the second Open Public Hearing session

to give the public an opportunity once again to direct questions to either the panel or the FDA. Then Ms. Shulman will guide the Panel in the completion of the Reclassification Questionnaire and Supplemental Satasheet Forms. We will conclude our deliberations by voting on the completed forms which will formulate our recommendation to the FDA.

The Panel may ask the FDA questions at any time. We will now move to the general discussion portion of the Panel's deliberations. Does anyone on the panel have questions for anybody this morning, or any points for discussion? At this time, we can begin to focus our discussion on the FDA questions. Copies of these questions are located on the tables outside this conference room.

Question 1: Do you believe that the risks to health from the device have been identified, and that the mitigations for these risks are appropriate? If not, what additional risks to health are presented by the device? What mitigations for these risks would you provide a reasonable assurance of safety and effectiveness?

Go ahead.

DR. POTCHEN: Do you want us to respond to the question?

DR. KRUPINSKI: Yes.

DR. POTCHEN: I believe that the risks to health from the device have been identified, and that the mitigations for these risks are appropriate. Yes, I think we have had very good discussion of this specific issue, and I think they have been identified, and I saw a magnificent list and a nice matrix, so I'm satisfied.

DR. DESTOUET: I agree.

DR. MITTAL: Go ahead.

DR. DESTOUET: I agree. I think the risks have been identified, and we understand what they are, and we see that this reclassification would pose no risk to human health.

DR. MITTAL: I also believe the risks to health from this device have been identified, and I do not believe there are additional risks to health from this device.

DR. KRUPINSKI: I agree, as well, and

especially the reduction and potential reduction in dose is a great mitigating factor.

DR. ZHOU: Yes, I agree.

DR. GOLDBERG: I agree, as well. I was also going to mention that the 15 percent decreased radiation dose to patients was very important. And I also agree there are no additional risks to health.

DR. POTCHEN: I would like to rekindle that and say that there is more than I saw up there, and that I think it's going to make it more effective and efficient to diagnose breast cancer with this increased modality because of the fact that you don't have to worry about the films and a variety of other things that makes it considerably more efficient and effective, at least in my experience.

DR. KRUPINSKI: Any other comments? Okay. Dr. Brogdon, in regards to questions 1, the panel generally believes that the risks to health from the device have been identified, and that the mitigations for these risks are appropriate. The Panel has no other concerns or opposing opinions. Is this adequate?

DR. BROGDON: Yes. Thank you.

DR. KRUPINSKI: Question 2: Do you believe that the information to be required for 510(k) clearance will be sufficient for determining substantial equivalence between a new device and the predicates?

DR. POTCHEN: Answer two. Yes.

DR. BOURLAND: I agree as well. And we have had some discussion about the guidance document. And I think the one issue was raised, for instance, about what is the appropriate, so to speak, gold standard type of film to use, and that perhaps digital is the way to approach this. So I think there are some very interesting aspects to the digital components that the guidance document can be devised to include some flexibility, but also important aspects, relative to, in particular the digital aspects.

DR. MITTAL: I agree with Dr. Bourland's comments.

DR. DESTOUET: I think the 510(k) process will be adequate to evaluate any additional units that

come to market.

DR. KRUPINSKI: I agree as well.

DR. ZHOU: I have a small concern here. Like I raised the question in the morning about the variability of the accuracy among the readers. So I would like to see actually if there is some evidence that diagnose the accuracy of digital mammography is similar than the existing film in terms of the readers. So there is variability among the readers because those two systems are similar, and that's the data we can see from the published studies.

DR. KRUPINSKI: I think if we do get that data, I mean, Craig Beam did a wonderful study a number of years ago just on that issue, and it was with film, and there was huge variability.

DR. ZHOU: How about the digital system?

DR. KRUPINSKI: He hasn't done it, but I'm sure it's at least as variable as that. If it decreases variability, I'm sure that would be great, but I don't think anybody has done that study. I mean, if the DMIST trial could give us that data, I think it would be worthwhile, as well. I have doubts

that it would be any more variable than film, though.

DR. ZHOU: Yes. If they can show it's not as big as the existing one, that would be great. Then I would be satisfied.

DR. POTCHEN: Is it appropriate to share data, our experience in studying the two techniques? Is that appropriate? Observer performance?

DR. KRUPINSKI: Yes, go ahead.

DR. ZHOU: I think so, yes.

DR. POTCHEN: Initially, if an observer performance was done, it was not as good, but when people gained experience it became superior very rapidly. And I think the difference, initially, was lack of experience. When we studied residents over four years of time looking at digital and looking at this, they learned much quicker with digital than they do with film/screen. I think it's an improvement if anything, just like we found for the others.

DR. ZHOU: You say --

DR. POTCHEN: But there was a big barrier initially. People who had no experience with digital at first, had trouble making the jump, but that

quickly is overcome.

DR. DESTOUET: I think part of the problem may be that you are looking at softcopy as opposed to looking at film. Radiologists are trained to look at hardcopy images, and there's a learning curve to look at monitors.

DR. KRUPINSKI: And the DMIST trial was with film, by the way. Everything was put into film there.

DR. POTCHEN: But that is absolutely true. The experience gleaned from softcopy now has gotten so much ubiquitous across radiology that people have gained the ability to do this without the error rates that we had previously. It's all imperfect.

DR. ZHOU: But that is actually very easy to see from this published data because you can have an AUC or ROC curve for each reader by both systems. You can just pause it and see how much variation there is.

DR. POTCHEN: Have you done that?

DR. ZHOU: No, I'm talking about this paper.

DR. KRUPINSKI: Okay. Any other comments?

DR. PHILLIPS: I would just like to point out that the information that FDA has available is the paper that you have in front of you. We do not have the raw data or access to it that supports that paper. At this time we would not be able to go back and analyze the individual readers in that study.

DR. ZHOU: Is there anyone here actually familiar with this study which might answer that question?

DR. PHILLIPS: Is that the DMIST?

DR. ZHOU: Yes.

DR. KRUPINSKI: Later on, Etta Pisano will be here, so she can address that.

DR. MITTAL: I would like to ask a question that was asked in the morning by Dr. Krupinski. I think it was a very important question. FDA is planning to review the hardcopies instead of softcopies, and there are propriety issues as it relates to reading soft films.

Could you approach Radiology and talk to them if different vendors can come to a conclusion so

that you can read the softcopies because one of the advantages of digital mammography is to be able to make a contrast and be able to see some of these images that you may not be able to see from mammography.

DR. KRUPINSKI: I think we can get a comment on that. Introduce yourself and say how you --

DR. CHAKRABARTI: Kish Chakrabarti, FDA. First question, you know that ACR currently are using hardcopy film only because there are complexities that Bob Jennings pointed out. Myself and Aldo Badano have been involved with IHE. There is a handbook available, and I talked to Bob Phillips already that is there anyway we can accommodate that in our guidance. So, definitely we are aware of that.

DR. POTCHEN: I would like to speak strongly in favor of that so you can get comparable studies across vendors, and we can do comparable studies over time, so it is increasingly important as we go to softcopy that we develop some standards. DICOM apparently is not quite good enough to bridge all the different vendors yet, but I would like to see

this standardized so we can do that.

DR. KRUPINSKI: Any other comments with regards to question No. 2? Okay. Dr. Brogdon, with regards to question No. 2, the panel generally believes that the information required for 510(k) clearance is sufficient to determine substantial equivalence between the new device and the predicates. The panel had some concerns about system variability and reader variability that hopefully we will be able to address this afternoon. Is this adequate?

DR. BROGDON: Yes. Thank you.

DR. KRUPINSKI: Question No. 3: Do you believe the materials presented support reclassification of FFDM devices?

Jim?

DR. POTCHEN: Yes.

DR. MITTAL: I agree.

DR. GOLDBERG: I'll also agree, too. I think we do have sufficient information here for reclassification.

DR. BOURLAND: Agree as well.

DR. DESTOUET: I agree.

DR. KRUPINSKI: I agree as well.

Andrew?

DR. ZHOU: Yes, I think I get satisfaction from this afternoon's answers.

DR. KRUPINSKI: Any other comments?

Okay. Dr. Brogdon, in regards to question No. 3, the panel generally believes that the materials presented do support reclassification of FFDM devices, and there are no additional concerns. Is this adequate?

DR. BROGDON: Yes. Thank you.

DR. KRUPINSKI: Question No. 4. If reclassified, are there any concerns that you believe need to be addressed in the labeling (includes direction for use, indications, and contraindications) of these devices?

Dr. Mittal?

DR. MITTAL: My suggestion would be to have, besides the general requirement, the special requirements including the document we talked about. I'm just trying to remember the name of the document.

DR. KRUPINSKI: There's the MQSA, the ACR.

PARTICIPANT: The guidance document?

DR. MITTAL: The guidance document. As you indicated earlier, the guidance document is in that form. We would like to see the guidance document implemented along with the reclassification of the device from Class 3 to 2.

DR. KRUPINSKI: I guess my question is, does that include soft copy as well as hard copy? And if not, we do want them both, especially soft.

DR. PHILLIPS: Just a reminder. The process from now on, the guidance document and the reclassification process go in parallel. The next step you'll see will be a notice in the Federal Register announcing our intention to reclassify full-field digital mammography, and also the availability of a guidance document for comment. Then, that will go through in parallel throughout the entire process. Besides the guidance documents for full-field mammography, we have another guidance for the accessories, work stations, etc., that go along with that. So that is essentially a package, the reclassification and the two guidance documents.

DR. KRUPINSKI: Great. Any other comments?

DR. BOURLAND: Yes, I have a comment concerning new things. I know that's always the problem, what about new, but mostly relating to the digital side. The question is, what would constitute the type of, for instance, digital detector that would satisfy the guidelines, basically, the guidance document? Can that be written such that, do we add definition to define types of detectors?

There will always be new detectors. The x-rays will stay about the same but, for instance, there could be changes there relative to beam sector, for instance. So, I think these are things to think about when preparing the guidance document.

DR. KRUPINSKI: So in a sense, how different is different?

DR. BOURLAND: Yes, that's the issue.

DR. PHILLIPS: Once we go ahead and reclassify these to Class 2, the 510(k) process itself gives the agency a great deal of flexibility as to what is equivalent, and what is not. If you go all

the way back to the congressional discussion that accompanied the original law, their comment on the 510(k) process was, it was not intended to have devices that were identical, but to have devices that were substantially equivalent. And the agency was not only allowed but directed to use common sense in making these kind of decisions. Since then, we have -- I'm afraid we don't have the slide here -- but we have a very laid-out process for the various types of questions that we ask in a 510(k) review. Is it the same indications for use? Is it the same technical characteristics? Are there new issues of safety and effectiveness, etc., etc., that we ask on every 510(k) before we make a decision.

And I would just point out to you other devices, such as magnetic resonance, where a great deal of innovation has occurred through the 510(k) process. There is a lot of judgment there in deciding what is going to be an acceptable change that we can still accommodate under the 510(k) process, versus what is significantly different enough that we have to go back to a PMA. But that is done almost on a case-

by-case basis. It's very difficult to try and prejudge what happens there.

DR. GOLDBERG: Just one question about that. If the device is reclassified into a No. 2, would it be under the same stipulations as film/screen mammography regarding use, indication and contraindication?

DR. PHILLIPS: If it's reclassified into Class 2, the four approved devices that have PMAs right now would become the predicate devices for the 510(k)s. So the labeling for our new device would be equivalent or consistent with the labeling that accompanies the four devices that have been PMAed.

DR. GOLDBERG: Thank you.

DR. KRUPINSKI: Any other comments or questions? Okay. Dr. Brogdon, in regards to question No. 4 the panel generally believes that there are no concerns that need to be addressed in the labeling of these devices other than incorporating the guidance documents into their wording and everything. Is this adequate?

DR. BROGDON: I would like to ask the

staff if we have any specific questions of the panel.

Dr. Phillips, anything that you know of?

DR. PHILLIPS: I just have one clarification, because this was brought up during lunch. In this reclassification process, we are including in the package both digital mammography, in other words, the direct detectors, and computer radiography (CR), the indirect detectors. We are regarding both of those as being under the paradigm of digital mammography.

DR. BROGDON: I guess we have no further questions. Thank you.

DR. KRUPINSKI: Thank you. We will now hold the second half-hour Open Public Hearing session. You are reminded that the same identification processes, disclosures, suggestions, and five-minute maximum time limit announced for the first Open Public Hearing session this morning applied to this session, as well. We can now begin the Second Open Public hearing session of this meeting. Margaret - or, Etta Pisano.

DR. PISANO: I'm happy to go second.

DR. KRUPINSKI: Okay. Etta Pisano, M.D., P.I., and principal author of the DMIST paper.

DR. PISANO: I just brought a few slides to share data, and I understand there are some questions so I'll try to go through these pretty quickly.

We did find that digital had better diagnostic accuracy in three subgroups. This was published in the New England Journal, but there was no difference in diagnostic accuracy across the entire population.

I have the ROC curves for the entire population. This is this slide. These are the AUC differences. Some of this data is not in the paper. This particular slide, everything in this slide is in the paper, but some of the following slides are not in the paper.

You can see that the AUC difference was quite small for the entire population with a nonsignificant p value, and those are the actual numbers with the standard errors for digital and film.

These are the curves for women who are

extremely dense. The solid lines are for the extremely dense breasts. The dotted lines are for the fatty breast. We dichotomized on the ACR four point scale for density. Solid lines are for dense breasts, blue being digital every slide, red being film every slide. And you can see that there is a large difference in the curves for the dense breasts, and that the curves are closer for the fatty breasts with film being slightly better than digital in the fatty population but not significantly different. I'll give you the raw numbers right now.

Here is the AUC difference for the dense-breasted population including with the p value that was significant. Here is the number for the fatty-breasted population. The AUC difference is a negative number, meaning film was slightly better than digital, but p was not significant.

Here are the curves for women with age. Solid lines were for women under 50, dotted lines for women over or equal to 50. Again, a large difference in the women under 50, blue always being digital, red always being film. The two curves for women over 50

practically overlapping.

These are the results for women under age 50, a significant p value .15 difference in area under the ROC curve. For women over 50, an insubstantial difference in area under the ROC curve, not significant. These are the curves for women who are pre- and perimenopausal, solid lines, postmenopausal, dotted lines, and again blue, digital, red, film. A big difference between digital and film, practically overlapping in the postmenopausal group.

Area under the curve (AUC) difference for the pre- and perimenopausal group, p value significant. Here is the postmenopausal, again a negative number suggesting film was ever so slightly better than digital but, again, a nonsignificant p value.

Here are the sensitivities. I'm reporting these at 365 days. For the other data it was 455 days. That gave us an extra 82 cancers approximately by waiting out to 455 days. There were 335 cancers all together in the study. You can see that these are the sensitivity numbers using BIRADS scale between digital

and film, so big differences 27 percent difference. In women under 50, 15 percent difference. You can translate these percentages.

Here, the specificities really did move, suggesting that the reason the areas under the ROC curves were different were really because we found more cancers with no difference in false positives. That was borne out by the actual numbers of callbacks and was insubstantially different between the two modalities. Positive predictive values also really didn't budge.

Here are the number of cancers per machine type which has not been published anywhere as far as I can remember yet. You can see that we really don't have much power for individual machines, especially for Hologic and Trex, the numbers are really tiny. For GE and the other machines, we do have a fair amount of power, although you can see it's limited. The fewer cancers, the less power. Certainly for GE, we can make pretty strong statements.

Here I am going to show you now -- these are in alphabetic order, so I have to remember which

one this is. This, I believe, is Fischer. These are basically overlapping. Next slide will say the machine. Yes, this is the Fischer system. You can see that the difference in area under the ROC curve was slightly in favor of film, but really tiny difference and not significant. Remember, this was the second most cancers of any of the machine types.

This is for Fuji. Again, blue is digital, red is film, and the curves are separated. Not significantly so, however, but film was better than digital. Again, we only had 60 cancers in the Fuji population, so that is going to limit the power, but you can see the ROC curve numbers. The differences do overlap zero, and the p is nonsignificant, but just because we only had 60 cancers.

Here is GE, blue over red, again digital above film, but not a significant difference. Very small difference in area under the ROC curve, nonsignificant. I am not going to show you curves for Lorad because they are so unstable with so few cancers, but I will tell you, and you can take it or leave it for what it's worth, you can see the width of

the confidence intervals much greater as you would expect with that few cancers. Same thing with Hologic. Tiny little difference between the two technologies, but not significant, and large confidence intervals around the estimates.

So I am here as a private citizen today not representing any one organization. Obviously, with a lot of information about digital mammography, and I am here today to recommend that digital mammography be changed to a 510(k) from PMA.

I also think we could and we should probably change tomosynthesis to 510(k), as well. I think that probably one should treat tomosynthesis, however, only that way if they can produce a two-view mammogram that is a digital mammogram and then additional data on top of it. In other words, if the two-view mammogram is substantially equivalent to another digital technology, then the additional information provided by tomograms should be, if anything, more helpful to radiologists.

So, I think I would like to see both technologies classified as 510(k). So, I think that's

my last slide, and I understand there are a lot of questions about DMIST which I am happy to answer if I can. I also am happy to answer them offline if that would be helpful to the Committee. I have a lot of data that I don't have in my brain, but I have in another place that I could access and look at and e-mail you or call you or whatever you need me to do. So, I'm happy to entertain questions if you have any.

DR. ZHOU: So do you have the data on the reader availability inaccuracy between those two systems? Which system has bigger reader variability?

DR. PISANO: Neither. You mean digital and film? They were equivalently variable. Readers behave similarly for both digital and film in terms of variability. The question though, I think, you know of course, each reader in DMIST didn't see that many cancers, so we know in terms of their callback rate, etc., that they were equivalent. The readers behaved very similar with both modalities, but in terms of sensitivity per reader, if you think about it we don't have a lot of data per reader for sensitivity. Each reader only saw two or three cancers. There were 160

some readers in the study.

DR. ZHOU: How large a variability by centers?

DR. PISANO: We are just now looking at that. We have not looked at that yet so I don't have an answer to that. Remember, every center did both digital and film.

DR. ZHOU: Yeah, so you could compare them.

DR. PISANO: Yeah, we will, but we haven't yet.

DR. ZHOU: Okay.

DR. KRUPINSKI: If the individual readers were fairly consistent, you would assume that the centers were probably fairly consistent as well.

DR. PISANO: If you are asking about cross-center variability, it's possible there was some, but I don't have any information about that, but I don't expect there to be a difference, categorical or any sort of systematic difference, between digital and film given the overall results of the study.

Just having looked at a huge amount of

data about this, I mean, obviously we only shared a little bit today. That particular question, how much variability there was between centers, we just now are starting to look at. I don't expect a big difference.

DR. ZHOU: How about the gold standard issue there in your study? Is the gold standard unique for every patient?

DR. PISANO: The gold standard was biopsy proof. If the patient had a biopsy, we knew about the biopsy, benign or malignant. Then we had a year follow-up, either a mammogram at a year or information about their breast cancer status at a year. The vast majority actually had a mammogram at a year.

DR. ZHOU: So you have two levels of a gold standard so one is real gold but --

DR. PISANO: You mean pathology?

DR. ZHOU: Yes.

DR. PISANO: You can't do a screening trial and expect everybody to have pathology because only 1 percent get biopsied. The normal in a screening trial -- the normal gold standard in a screening trial is to watch the patients for 12

months. In fact, we did more than that. We watched the patients for 15 months and called it true. Most screening trials only watch a patient 12 months. That is pretty well accepted standard for a screening trial.

DR. GOLDBERG: Was the 15 percent reduced radiation dose to the patients regardless of the breast composition whether it was dense or fatty?

DR. PISANO: I don't know the answer to that question off the top of my head. I would have to check. I believe that's true, but I don't know that for sure. We were trying to match those, by the way, but we could not because the machines just produced the images with less radiation and the radiologist didn't want to over-penetrate or overexpose the breast, so we ended up doing that as part of the study.

DR. MITTAL: How is the radiation dose measured?

DR. PISANO: We actually use a TLD chip for some subset of the patients. We imposed it in the mammogram for part of a subset of our patient

population. I don't remember the exact number but it was multiple hundreds of patients for both digital and film.

DR. KRUPINSKI: The details of that are reported in Dr. Yaffe's paper.

DR. PISANO: I believe it's -- yeah, it's in Medical Physics. It's been published already, I believe, this month, I think.

DR. KRUPINSKI: Are there any other questions for Dr. Pisano?

DR. PISANO: I just want to repeat that I am willing to answer questions later if you have others that you need more technical responses or more detailed responses. If that is going to help you make a decision, I am happy to share additional data with you, so please don't hesitate to call me.

DR. KRUPINSKI: Thank you. Now, we will go back. Margarita Zuley, M.D., American College of Radiology (ACR).

DR. ZULEY: Hi. I'm here representing the College today. I'm a private practitioner. I've been a member of the College for many years, and I'm here

representing over 32,000 members. The College started the voluntary accreditation program for mammography in 1987 and was the foundation of what turned to the MQSA and is now the only named accrediting body for MQSA. They have been a leader in safety and quality standards not only for mammography but for all of radiology for a long time.

They strongly support the reclassification of digital mammography to a Class 2 device. The reasons for that are the studies that have already been discussed, the ACRIN being the largest and some smaller ones predating that really showing clinical equivalence of the two modalities and, in some instances, increased accuracy.

Most radiologists feel and have become comfortable with, and the College feels that this modality is safe and effective for patients. The community has really embraced it with all these studies that have come out.

This slide is showing from the FDA's score card, the number of facilities getting digital units and the number of digital units. You can see the

incline in both. The digital units is red, and the blue is the number of facilities. It is really becoming very accepted in the community.

There are several reasons that the College thinks this should be reclassified, and one of them is patient care. It is very hard as a clinician to try and recruit a patient for a study that is to fulfill a PMA requirement, and double expose a patient when you feel that the technology that you are trying to get data for is in some respects better than the technology that you are using as the gold standard. That is probably the most significant reason to me, as a radiologist.

The other more practical reasons, you know, the vendors have had very slow response to innovate and to change their products because everything is a PMA supplement, and it requires, again, double exposing the patient and requiring a lot of data and reviewing those cases. It is long and drawn out for them so it has been very slow for them to adjust to what we feel that they need as radiologists.

Not only does the ACR feel that it should be reclassified as a Class 2 device, but the ACR would like to recommend that it be broken into two devices: the first being the acquisition unit and the second being processing algorithms. The separation logically could occur after detector corrections are made from the raw data because that would allow vendors who are going to be performing processing algorithms to have a very clear understanding of what they are going to be starting with to provide better processing.

This is just a schematic showing where that would happen so you acquire the raw information. You detect it, do all the detector corrections and then from there forward via a separate device. The reason for this is primarily clinical and practical. Better comparison between images.

I am going to show you examples of why that is true. Then work flow improvements. The way it is right now is that facilities that have digital mammography are trying to schedule patients to go to the same unit every year because the images look so different coming out of the units so it is virtually

impossible to run a busy facility in that kind of work flow environment. But clinically is really where the information is.

This is just some examples to show you. In the screen/film world we could buy any acquisition unit that we wanted and even if there were different energy spectrums coming out of those units, we could achieve a similar look because the screen film combination and chemicals were the same. This is an example of a real patient from my practice done two different years in a row out of different units with the same screen/film and chemical combination.

You can tell that is the same patient. It looks very similar so my job as a radiologist reading current and prior is not that hard. I am just looking at the patient's tissue changing and there is no technical difference between these two images.

This is another example of the same thing yet two different units. Again, the only changes that I'm looking for are in this patient, not in the technology. So here is a situation. I have two problems that are going on right now with digital.

One is the vendors when they do change processing algorithms. This is the same vendor two different processing algorithms. You can see how now my job just got harder because now I'm trying to not only find a difference in the patient but now I have to take into account the difference in technology.

This is another example of a different vendor, two different processing algorithms applied to the same patient two consecutive years in a row. Even if an organization only has one unit, the radiologist is at the mercy of the vendor, and every time the vendor changes the processing algorithm, the radiologist can never go back and use what they had before. They just have to keep on the roll and keep adjusting. I can't help but believe that that is going to decrease our accuracy. Even though that is not shown yet, it's pretty clinically apparent to me.

This is an example of all different processing algorithms that I am dealing with right now. These are all normal mammograms. These are four different looks. These are all units that I have in my office right now, all FDA approved pieces of

equipment. Not only do I have to judge as a patient moves from one unit to another, gets a new processing algorithm what's changing, but every one of those is normal and I have to set my threshold of number all the time, every day, constantly as I read patient from vendor A, patient from vendor B, patient from vendor C. I am constantly adjusting my mindset.

This is an example of the same patient done on two different units with the exact same detector with different processing algorithms because it's from two different vendors. You can see how different that picture looks. Now I'm adjusting for patient difference from year to year and vendor difference from year to year.

Another example, different patient -- this is the same patient two years in a row different from the last picture I showed you. Look how different that is. Very difficult to make a comparison. There were some clinical issues that arose when the acquisition unit was separated from the work station. There were clinical issues that arose when that separation was made because of incompatibility that

has been worked out.

Our concern from the college is that now we are still facing quite a bit of technical differences, and it would make the radiologist's job much easier and would be more safe and effective for patients if you allowed the separation to occur so that we as radiologists could choose one or two processing algorithms, apply them to all the mammograms so that the only variability we are dealing with is in our patient's tissue, not in technology. Thank you.

DR. KRUPINSKI: Thank you. Are there any questions for Dr. Zuley? Thank you.

Our third representative, John Goble from Sectra.

DR. GOBLE: Tough spot to follow a couple of esteemed physicians who have seen more mammograms than I'll ever think about. Real briefly, I'll use this spot.

I still teach a little at Yale. One of the things I talk about is that technology in the medical marketplace is only acceptable for just one of

three things: improve patient outcomes, reduce the cost of care, or improve access of quality care to under-served populations.

We think digital mammography has a superb capability to handle all three of these aspects of technology innovation in the medical marketplace and believe that declassification is the right thing to do to make these advantages happen.

We know that just as in the expedited handling of anti-retrovirals in the AIDS crisis, we know that we can expedite technology innovations into clinical improvements. Our own company builds a detector with significantly reduced radiation exposure with respect to either screen/film or existing digital mammography devices.

Certainly in Europe this has been seen as a real advantage to substantially reduce radiation exposure without reducing clinical effectiveness. We also know of companies which are, as Rita indicated, producing image processing algorithms that optimize observer performance and normalize that performance across multiple vendors and multiple years.

We know there are high performance compression algorithms that can be used to provide the expertise of our mammographers into under-served communities that don't have access today to the quality of mammography that they should.

There are cancers going undetected because these patients do not have access to quality care. These are just a few of the many, many innovations that we need to expedite into the marketplace and certainly declassification into a Class 2 device will help us get these things into your hands as clinicians faster.

I won't beat this dead horse. Next please. We also believe, though, that even today digital mammography technology is sufficiently well understood that adequate special controls may now be developed and quickly. Dr. Yaffe, one of Dr. Pisano's colleagues, developed quality procedures across all the 30 some facilities that participated in DMIST and ensured that the quality of that study stayed very, very high.

These types of procedures exist today to

maintain physical quality assurance across multiple facilities. Rather than invent these things again, what we recommend is that the guidance documents that come from the MQSA side of things don't send this on an endless ACR, AAPM, NEMA dance that will effectively end up with the same thing and that is the withholding of important technologies from the marketplace.

We would ask that the Committee recommend expedited handling of this so that these technology improvements can be in the hands of our clinicians sooner rather than later. We also believe that existing QSRs can ensure overall device compliance. We think a lot of the basics are already out there, what Dr. Yaffe has done as part of DMIST, other standards that are already available. Let's work hard and expedite these improvements in the clinical practice.

As my father would have said, "Hey, the innovation ain't done," okay? There's lots going on just as it was in the early days of MR. Lots of companies with lots of smart ideas are coming to the marketplace and these will, in fact, result in

impacting the cost of care, quality of care, access to under-served populations that we ought to address.

So our recommendation is, of course, the reclassification. Since I went through fast, I want to steal one more minute. IHE is very, very important. Bob can probably address this, but in the initial certification process the entire imaging chain was certified. There are people better qualified than I to speak about this.

Then there was this Homer Simpson moment when a patient called and came to me with my Hologic stand and they had their priors on a GE disk. There was this, "Duh, we've got to separate this." How can I look at the priors when they come from another vendor?

I would hope, and I address this to my FDA colleagues, that the guidance document will clearly separate and push whatever processing is done, á la Dr. Zuley's comments, back onto the acquisition station and make it simple for you as clinicians to be able to compare a patient who has Fuji exam and compare that to their priors who happen to be on GE or

Hologic. Because of my corporate career my wife has priors spread up and down the east coast.

Trying to compare those in a digital world, fitting the films is bad enough but as Dr. Zuley much more graphically than I pointed out, to compare those in a digital world is a real challenge. We would urge the FDA to include in their guidance some of the IHE guidelines, which many of our companies are actively involved in, but we would encourage to push that and prioritize that so that the kind of pain that Dr. Zuley is seeing on a daily basis now goes away as quickly as possible.

That's really all the comments I had. Thank you very much for your attention and we appreciate the work that the Committee is doing.

DR. KRUPINSKI: Thank you. Are there any questions for Dr. Goble? Jim.

DR. POTCHEN: Comments on this?

DR. KRUPINSKI: Yes.

DR. POTCHEN: I strongly support the last statement made. If I see a big problem coming, for those of us who read a lot of mammograms and digital

mammograms, there is a wide variation of what we see. Anything that we can have to make it conform so that there is enough similarity that it doesn't disturb us as the observer would be very helpful. This is an opportunity to do so so I strongly support the last speaker's comments.

DR. MITTAL: I have a question for Dr. Pisano. I think the last presentation from ACR on processing algorithm was an important issue. Could you please comment on the DMIST trial? Did you see that issue or anybody brought that to your attention?

DR. PISANO: Not as part of DMIST. It was not a big issue because at that point most of the vendors were relatively new. The machines were relatively new and most of the sites had just installed digital, and we were comparing to film. It really wasn't a big issue for DMIST. It was also only one time.

We did one screen. We weren't doing repetitive screens. Although I agree with the comments that have been made by the two previous speakers that this is a big issue, image processing is

something that as it varies from year to year can really mess up an interpretive process and has to be carefully watched.

I think it really is bad if we can't compare images from one year to the next because of a change in image processing. It's very confusing, and I should think -- my own concern is more inter-vendor variability, not being able to compare between vendors because of the work station issue.

I think that is a real big problem. A work station should have to handle each other images. There should be DICOM compatibility, and they should have to show them. I am not happy about that even more than the image processing.

DR. KRUPINSKI: Were the digital printed to film or read softcopy?

DR. PISANO: It depended on the vendor. GE was all softcopy. Fuji was all hardcopy. Fischer was a combination of hard and softcopy. Hologic was when it was Trex Lorad, it was softcopy -- I'm sorry, hardcopy, and when we switched to Hologic, it was softcopy, but it stayed the same within vendor.

DR. KRUPINSKI: Any other questions?

DR. POTCHEN: Can they put something in the guidelines that would specifically address this issue of the different variations in vendors from year to year so we could develop some standards?

DR. KRUPINSKI: I think that's what part of DICOM and IHE is addressing. I mean, that could be incorporated in the guidelines.

DR. POTCHEN: Can we have that as part of our recommendation if we do vote to approve this?

DR. KRUPINSKI: Can we put that language in? Yeah, we can put that language in there.

DR. BROGDON: Yes.

DR. BOURLAND: I think the issue is a very interesting one because the suggestion is to decouple, for instance, processing algorithm from the digital data set that it's applied to. When you have a digital detector, in fact, there are differences between digital detectors, different designs, for instance, so there are algorithms that perhaps do a few things based on the characteristics of that actual detector so you have to be careful about how much can

you decouple this.

Maybe it is processing algorithms that, in fact, are related to the raw capture and the particular physical characteristics for the detector, and then algorithms beyond that as well so there are multiple stages. More than two, if you actually go through the imaging chain and count the number of quanta per step.

DR. PISANO: I just have one comment about this. In terms of proving an algorithm is useful to readers or not, we're not talking about gigantic level of evidence. We are talking about the number of studies you have to do, and the number of readers you have to do. We actually did a study in 2000 comparing different image processing algorithms, and we used 27 mammograms with a variety of cancer/noncancer and normal tissue.

We found statistically significant differences between algorithms with, I think, eight readers. It was a relatively small study using a Liker scale, not using ROC performance. In other words, it is not an overly burdensome thing to require

the vendors to make the algorithms substantially equivalent in my opinion.

DR. KRUPINSKI: Any other questions or comments for the three?

DR. ZULEY: I just wanted to make a clarification. I am also the clinical co-chair of the mammo IHE subgroup. The IHE work that we are doing is working on making sure that the mammography acquisition units can display everybody's images correctly. It is doing nothing about the processing differences. That is out of scope for IHE.

DR. KRUPINSKI: Any other questions or comments? Okay. If there are any individuals wishing to address the panel, please raise your hand and identify yourselves at this time. Please state your name and your affiliation.

MR. UZENOFF: Hi. My name is Bob Uzenoff, and I'm with Fujifilm Medical Systems. I would just like to comment on the idea of making mammograms look the same for ease of comparison. I am not sure if what I heard before I understood correctly, but I would comment that the differences in mammograms that

Dr. Zuley showed between digital machines, I think exist between the kinds of imaging that are done on screen film currently.

There are different types of film, different techniques that are used, different radiologist preferences in what a mammogram could look like from institution to institution. While a clinician, I think, rightfully would like to see the same kind of appearance year after year on their patients, clinicians differ in what they find is a comfortable film to interpret.

Similarly, there are different levels, and we are talking about preserving innovation here in our work. There are different image processing algorithms. Different companies have access to different technologies. Some of them are proprietary. Some companies have more experience in image processing in another.

I think you should be careful in this guidance document to look at and separate areas of practice which may be more properly left to recommendations from the American College of Radiology

to requirements for the device themself. In other words, I think you want to preserve the flexibility for clinicians to have the kind of image that they prefer to interpret rather than to, if I could use the phrase, dumb down imaging to the lowest level of performance.

If everything has to look the same and somebody has a different look, that might be a matter of professional practice of whether that look is something that a clinician wants to follow or not. I think in whatever guidance you're asking for you want to preserve the prerogative of the clinician to make some of those judgments rather than to dictate that they all look the same. Thank you.

DR. POTCHEN: I believe the Mammography Standards Act require very similar looking images, particularly if you send out the films to the American College of Radiology for review. They have pretty strict limitations as to how variable that should be. Most of us have accepted a standard that is national.

DR. DESTOUET: Absolutely. The difference from year to year is not that dramatic from patient to

patient. As Dr. Potchen points out, we have specific guidelines as to what the film should look like, what density there should be. I think it's not as dramatic as what we saw from Dr. Zuley.

DR. KRUPINSKI: Again, state your name and affiliation.

MR. WINSOR: Robin Winsor, Chief Technical Officer of Imaging Dynamics. I would agree with the last speaker that we have to be careful on this issue but some very real concerns were raised there in terms of the look. As a suggestion, I would like to see the approvals go through for device with software because really raw data without software isn't really a device, it's half a device.

However, our approach at Imaging Dynamics is that as well as sending processed image through from the device to the system on where it's going to be viewed, we also store a version of the image that has been data processed. We separate for definition data processing from image processing.

Again, I'm talking at the moment in terms of general radiography, but in data processing we do

things like flat field corrections, pixel nonuniformities and so on, things that don't change in imaging a hand, a head, a hip, or breast for that matter.

Then we layer image processing that is specific to the particular view by holding onto the things that are corrected, a base image that is corrected for the device itself which would have no value to another vendor's image processing, and taking the base data that is not raw but has been properly data processed and making that available if an institution then wanted to apply other image processing assuming the appropriate DICOM standards. That could be done, and that gives us the flexibility. I think to separately approve a device without its associated software might be only looking at half the picture.

MR. MARSHALL: My name is Julian Marshall. I'm with R2 Technology which is being consumed by Hologic Corporation. All of the prior speakers, I think, have very good points, but if you go back to Dr. Zuley's images, the reality is that when a patient

turns up with prior mammograms from another institution and the radiologist that has to read those prior mammograms as part of the study did not have a choice how those mammograms were produced, what image acquisition unit was used, what processing was applied.

That doctor gets precisely the films that come on that CD-ROM from the site. The comparison of current priors is prohibitively difficult in digital because of the variance in image processing algorithms.

Now, as Dr. Zuley suggested in her diagram, if you properly define the point at which the acquisition modality is done with detector corrections for dead pixels and flat-fielding and so on, when you define that as a standard output of an image acquisition device, then it is possible to take those images and regardless of the source -- we have actually done this ourselves -- regardless of the source, you can make one image look very much like another.

If we fail to define that point accurately

or we allow there to be a lot of slop in what the definition of that point is, it will make life a lot harder for the radiologist.

DR. KRUPINSKI: Okay. Does anyone else have any comments? Any questions from the panel? Okay. This concludes the second Open Public portion of the meeting. We will move on to the Reclassification Questionnaire and Supplemental Datasheet.

Now that we have addressed the FDA questions, we will complete the Classification Questionnaire and Supplemental Datasheet. Ms. Marjorie Shulman of the Office of Device Evaluation will assist us as we go along.

After panel discussion of each question, I will note our answer for each blank on the datasheet, and Ms. Shulman will record it on the PC for us. We will vote on the completed Questionnaire and Supplemental Datasheet. It will become the Panel's recommendation to the FDA. Are there any questions on how we will proceed? Let's begin.

Ms. Shulman, will you proceed with the

Questionnaire, please? We're starting with the General Device Classification Questionnaire that was in your notebooks. Put your name on the top one, the date which is, what, the 23rd? The generic type of device. Ready when you are.

MS. SHULMAN: Question 1: Is the device life sustaining or life supporting? Go around however you choose.

DR. KRUPINSKI: Let's just start with, I guess, Dr. Bourland.

DR. BOURLAND: No.

DR. MITTAL: No.

DR. DESTOUET: No.

DR. KRUPINSKI: No.

DR. ZHOU: No.

DR. GOLDBERG: No.

DR. POTCHEN: No.

MS. SHULMAN: Thank you. Is the device for a use which is of substantial importance in preventing impairment of human health?

DR. BOURLAND: Yes.

DR. MITTAL: Yes.

DR. DESTOUET: Yes.

DR. KRUPINSKI: Yes.

DR. ZHOU: Yes.

DR. GOLDBERG: Yes.

DR. POTCHEN: Yes.

MS. SHULMAN: Thank you. No. 3: Does the device present a potential or reasonable risk of illness or injury?

DR. BOURLAND: No.

DR. MITTAL: No.

DR. DESTOUET: No.

DR. KRUPINSKI: No.

DR. ZHOU: No.

DR. GOLDBERG: No.

DR. POTCHEN: No.

MS. SHULMAN: Thank you. No. 4: Did you answer yes to any of the above questions? We did, so now we may go to No. 6. Is there sufficient information to establish Special Controls in addition to General Controls to provide reasonable assurance of safety and effectiveness?

DR. BOURLAND: Yes.

DR. MITTAL: Yes.

DR. DESTOUET: Yes.

DR. KRUPINSKI: Yes.

DR. ZHOU: Yes.

DR. GOLDBERG: Yes.

DR. POTCHEN: Yes.

MS. SHULMAN: Thank you. Okay. If yes, classify in Class 2 and go to item 7. No. 7: If there is sufficient information to establish Special Controls to provide reasonable assurance of safety and effectiveness, identify the special controls needed to provide such reasonable assurance for Class 2.

DR. KRUPINSKI: Do we just start with each one and say yes or no to each one?

MS. SHULMAN: Or, if you want to start with the guidance document, and then see if anyone has anything to add.

DR. KRUPINSKI: Okay.

DR. BOURLAND: At this point I would have guidance document.

DR. MITTAL: Guidance document only.

DR. DESTOUET: I agree.

DR. KRUPINSKI: Guidance document.

DR. ZHOU: Guidance document.

DR. GOLDBERG: Guidance document.

DR. POTCHEN: I agree.

MS. SHULMAN: And is there anything to add to the Special Controls?

DR. DESTOUET: No.

MS. SHULMAN: Thank you. So question 8 and 9, we may skip because that only has to do with performance standards. Question 10: For a device recommended for classification or reclassification into Class 2, identify the priority for inquiring -- I'm sorry. Question 10 we skip. Question 11: Identify the needed restrictions. Again, this is the prescription question. The first one is the prescription statement, and then the additional ones are added on. You may answer prescription only or if you have nothing else to add.

DR. MITTAL: I think the main issue is the persons who are trained to be able to read the films like you, have the second one here, that is the only thing that is really applicable here.

MS. SHULMAN: Okay. Thank you.

DR. KRUPINSKI: Is that covered -- I mean, in our guidance document we are saying that MQSA must be followed so is that already covered by --

PARTICIPANT: That covers it.

DR. KRUPINSKI: So we are not -- if we say that, that means we are adding something additional. Aren't we?

MS. SHULMAN: Correct.

DR. KRUPINSKI: So we don't check that since it's already covered by MQSA.

MS. SHULMAN: Correct.

DR. POTCHEN: MQSA covers it.

DR. KRUPINSKI: I think we are just deciding whether it's just the first box, only upon the written or oral authorization basically to prescription, or do we need the others checked as well?

DR. BOURLAND: Just a clarification that MQSA is within guidance document.

MS. SHULMAN: Correct.

DR. BOURLAND: Then, yes, upon

prescription.

DR. MITTAL: I agree with Dan's comments.

DR. DESTOUET: I agree.

DR. KRUPINSKI: I agree.

DR. ZHOU: Agree.

DR. GOLDBERG: Prescription only. I agree.

DR. POTCHEN: I agree.

MS. SHULMAN: Thank you. Now we can move on to the Supplemental Datasheet. Again, the generic type of device, the Advisory Panel of Radiology, and No. 3 is the device an implant? No. Okay. Question 4: Indications for Use. Would you like to see them again or is that agreed on the Indications for Use that were presented during the panel meeting?

DR. DESTOUET: As presented in the panel meeting.

DR. POTCHEN: Yes, as presented.

MS. SHULMAN: And everyone agrees to that? Thank you. No. 5: The identification of the risk to health presented by the device. Again, as presented in the panel meeting or was there anything

else that you would want to add?

DR. MITTAL: As presented.

MS. SHULMAN: Thank you. Question No. 6: Recommended Advisory Panel classification and priority. The classification is Class 2, and the priority is a high, medium, and low. Basically, that means how fast would you like us to work on this? To move it to the top of our workload would be high, medium, or low. Of course, there are no time frames associated with that.

DR. KRUPINSKI: High.

DR. DESTOUET: High priority.

DR. POTCHEN: I would say high. Quite high.

DR. GOLDBERG: High.

DR. MITTAL: Just high.

MS. SHULMAN: Thank you. If device is an implant, life sustaining or life supporting. Let's see. We answered --

DR. DESTOUET: General and Special Controls are sufficient.

MS. SHULMAN: Yes, we can say General and

Special Controls can handle the risks, or not unreasonable risk. Is there is anything else you wanted to add?

DR. DESTOUET: No.

DR. BOURLAND: No addition.

MS. SHULMAN: Thank you. No. 8: The summary of the information including clinical experience or judgment upon which classification or reclassification recommendation is based on. Again, you may say as presented in the panel meeting or add anything else.

DR. DESTOUET: Yes.

DR. POTCHEN: As presented.

DR. BOURLAND: As presented.

MS. SHULMAN: Okay. Identification of any needed restriction, Question 9: Special labeling, banding. We already have the prescription use. Anything that you wanted to add at this point?

DR. DESTOUET: No.

MS. SHULMAN: Thank you. No. 10 we may skip because it is just for Class 1 devices. No. 11: If the device is recommended for Class 2, recommended

whether FDA should exempt it from Premarket Notification.

DR. KRUPINSKI: Could you explain what that means?

DR. MITTAL: Yeah, what does that mean?

MS. SHULMAN: If we exempted it from premarket identification, we would not see 510(k)s for it. It would still be a Class 2 device subject to other Special Controls such as design controls, but we would not see 510(k)s for it.

DR. DESTOUET: Not exempt.

DR. KRUPINSKI: Not exempt.

DR. POTCHEN: Not exempt.

MS. SHULMAN: Thank you. And then, if you know of any -- Question 12, any other existing standards to the device, assemblies, components, devices materials, anything other than what was presented today or anything you would like to add.

DR. BOURLAND: As discussed, meaning software, digital detector, these types of things.

MS. SHULMAN: Great.

DR. POTCHEN: Where would we put in the

idea we would like to see it standardized across -- somehow standardization more appropriate to the user? Where would that fit in? It has been discussed, you know.

MS. SHULMAN: We could go back and amend.

DR. POTCHEN: Maybe that's in the guidelines. I don't know.

MS. SHULMAN: On the first page, you can under No. 7 under 'Other' because the General Device Classification Questionnaire, we have the guidance document under 'Other', and you can specifically say that you would like the standardization.

DR. POTCHEN: That's No. 7?

MS. SHULMAN: On the General Device Questionnaire. The first one.

DR. ZHOU: That should be part of the guidance document?

MS. SHULMAN: It could be part of the guidance document, but if you specifically want to point that out, that is where that would be added.

DR. POTCHEN: I would like to add it because I think there is a consensus that is really

relevant to making this work best for patients.

DR. KRUPINSKI: Standardization of a default image should we call it?

DR. POTCHEN: Standardization so you could look at multiple images from year to year, and you would have something that is similar. That would be nice. That is really important, I think.

DR. KRUPINSKI: Dr. Zuley, the classification is between, you said, raw data versus for presentation? Was it raw data versus for presentation? Is that where the split was?

DR. ZULEY: Yes. After detector correction but prior to any other processing. I guess to the point that was made already is we are not looking for one look mammogram. We are looking for just the ability for the radiologist to choose a look that suits them or their practice but not one standard look for everybody in the country or the world.

DR. POTCHEN: How does that differ from the standardization in MQSA already?

DR. ZULEY: Well, because --

DR. POTCHEN: We already standardized it.

DR. ZULEY: The screen/film combination and chemicals that I use doesn't have to be the same that you use. It is just that you have to have the same thing for you all through your facility. If we separate them into two different devices, then we can each process them differently as long as those processing algorithms have some sort of quality to them.

DR. POTCHEN: If we were to put standardization under 'Other', would that meet that need? Would that communicate the essence of what we discussed?

MS. SHULMAN: It would, and then we would take it back and then we could see if it would be included in the guidance document or not.

DR. ZHOU: I don't think this is so simple issue. There are a lot of technical issues here.

DR. BOURLAND: I think that's the question, and that is we need to be careful that we don't define essentially technology or limit it in some fashion. I have drawn three little boxes. You have data, data processing, and the question is: Is

that the raw image after that? Was it the raw image halfway through? Was there one more box before you get to a deliverable image that then applied other image processing? The question is how many boxes are there, and where that line is drawn? I don't necessarily disagree with the idea of having a line drawn somewhere. I don't know that I could say today where to put that.

MS. SHULMAN: Certainly, because this is a recommendation, and then we'll take it back and see if we can --

DR. BOURLAND: I think with that qualification that is the thing to do.

DR. DESTOUET: So what do we say, standardization of image processing?

DR. BROGDON: I've lost track of whether you're discussing provisions for a guidance document or whether you are seriously considering breaking this one device up into two devices or more.

DR. KRUPINSKI: No. I think it's for the guidance document. That would make things too complicated I think.

DR. ZHOU: I think the software is -- I mean, I think I agree with one of the speakers, it's part of the system so you can't standardize software because some companies are better than others who produce software so that should be part of it.

DR. POTCHEN: We have DICOM standards, and we can compare images. The DICOM standards work pretty well for a lot, and I have seen it work as well here as I would like to see it.

DR. BOURLAND: And I think what this suggestion is to an image which is before the DICOM image, and then what is its standard?

DR. KRUPINSKI: So the message is being taken back. Do we have to write anything down?

MS. SHULMAN: No, we'll read it from the transcripts.

DR. KRUPINSKI: Okay. So that is the end of the forms, and we are going to vote one more time on the forms as completed as being reclassified into Class 2 requiring Premarket Notification. Are there any questions from the panel before we vote on the completed forms? Is there a motion?

DR. POTCHEN: I so move.

DR. MITTAL: Second.

DR. KRUPINSKI: It has been moved and seconded that the motion to reclassify the FFDM device from Class 3 into Class 2, that the Special Control for digital mammography be a guidance document. All in favor of the motion please raise your hand. Dr. Bourland, yes.

DR. BOURLAND: Yes.

DR. KRUPINSKI: Dr. Mittal, yes.

DR. MITTAL: Yes.

DR. KRUPINSKI: Dr. Destouet.

DR. DESTOUET: Yes.

DR. KRUPINSKI: Dr. Krupinski, yes. Dr. Zhou?

DR. ZHOU: Yes.

DR. GOLDBERG: Yes.

DR. KRUPINSKI: Dr. Goldberg, yes. Dr. Potchen?

DR. POTCHEN: Yes.

DR. KRUPINSKI: Okay. All opposed? None. Anyone abstaining from the vote, please raise your

hand.

DR. BROGDON: After the vote is complete, you probably ought to get comments from the Industry and Consumer Representatives also.

DR. KRUPINSKI: Okay. Go ahead.

MS. HOLLAND: My comment is that I am satisfied at this point that we are meeting the needs of the general population with this particular reclassification. I have nothing to add.

MS. MOORE: And I second that. I think I fully support FDA's position that has been presented by industry today, industry classification. I think this will allow companies to innovate and bring this technology available to more women. In fact, make a technology that is, in fact, better in some cases.

DR. KRUPINSKI: Thank you.

MS. SHULMAN: Thank you very much.

DR. KRUPINSKI: Okay. The motion carried seven to zero. There were no abstentions. It is the recommendation of the panel that full-field digital mammography systems (FFDMs) be reclassified into Class 2 with the guidance document to be developed for the

device containing the information agreed upon today.

I am now going to ask each panel Voting Member the reason for his or her vote starting with Dr. Bourland. Or, if you just have any comments to make.

DR. BOURLAND: Well, the answer is yes, I agree with this vote. I think the level of technology has been, one, developed, two, tested, and shown clinical effectiveness, and that this is a means for better propagational technology to the community and for public health and well being.

DR. MITTAL: I have nothing else to add except what has already been said.

DR. DESTOUET: The technology, as it exist today, is very expensive and prohibitive for many users, and if there is anything that the manufacturers can do out there to give us technology that is less costly but effective, it will help save women's lives.

DR. KRUPINSKI: I agree, and I feel that by doing this reclassification we have opened it up to some of the smaller companies that should be able to accomplish that and reach women in rural areas by

direct digital telemammography and so on.

DR. ZHOU: I agree. I think the evidence presented to us convinced me that this device actually poses equal or less risk than the previous one also effective.

DR. GOLDBERG: I agree with the vote and have nothing further to add.

DR. POTCHEN: I think the two major reasons that I think I would favor it is that it is improved care in some patients, and it decreases radiation dose for all patients. I think the most compelling argument given to me was that by eliminating the need for subsequent PMA studies, we have eliminated the need for double exposure to patients undergoing those studies. That is a very important concept to put forward in this type of approval.

MS. HOLLAND: I have nothing further to add.

MS. MOORE: Nothing further.

DR. KRUPINSKI: Dr. Brogdon, do you have any further comments?

DR. BROGDON: Nothing further. Thank you.

DR. KRUPINSKI: Having addressed the FDA questions on the reclassification of full-field digital mammography systems, the Panel has completed its charge. I would like to thank the Panel for its deliberations, the FDA staff and the public for their comments. This meeting is adjourned.

(Whereupon, at 2:48 p.m. the meeting was adjourned.)