SurFACTS in Biomaterials

June/July 2008 Volume 13 Issue 1

BioInterface 2008 Heading Back to Minneapolis, Oct. 27-29

By Bill Monn

The BioInterface Workshop and Symposium is heading back to its roots in 2008, with this year's program slated for Oct. 27-29 at the Millennium Hotel in downtown Minneapolis. The very first BioInterface was held in Bloomington, a suburb of Minneapolis.

The program committee is nearing completion of its work to develop topics that are relevant and timely for the Workshop and Symposium. Information will be posted as soon as it is available on the Surfaces website at www.surfaces.org

Oct. 27 is dedicated to the Workshop; the technical program follows on Oct. 28-29.

Highlights of the three-day conference include the Excellence in Surface Science Award, Student Town Hall Meeting, a Student Poster Award competition and a lively Point-Counterpoint debate session! As always, these events provide participants with great networking opportunities. Bioscience entrepreneur and philanthropist Alfred Mann was the Surface Science Award winner in 2007. Mann's luncheon address riveted attendees with a discussion of companies he has founded or been involved with over the past several decades. As an example, Mann was an early pioneer in cardiac pacemakers — including heading Pacesetter, which was sold to St. Jude Medical Company.

BioInterface Continued on Page 5

On My Microscopic Soapbox

By Steve Goodman
SurFACTS *Editor*

Several issues ago, this editorial addressed the topic of why microscopy is not only a research and development tool, but should also be considered a "Sales" instrument. That editorial defined microscopy as the family of scientific instruments that not only provides information on things that are too small to be seen with the naked eye (the classical definition), but that microscopy is the only scientific instrument family that provides information on spatial relationships. Thus, microscopy not only enables viewing of the size and position of features or components (again, "classical microscopy"), but today microscopes

Editor Continued on Page 2

What's Inside

...From the Editor

By Steven Goodman, Editor

also reveal chemical composition, molecular orientation and many other physical properties. The second aspect of that editorial addressed "Sales." The thesis was that microscope images are perhaps the single most important scientific tool for "selling" your device or technology. In that context, sales were defined as selling yourself and your colleagues by providing functional evidence that a device works. This image information is then utilized to sell your device or device concept to obtain the necessary funds for development from management or perhaps from outside investors. Eventually, microscope images are likely to be used to actually sell to the true customers: the physicians and the patients themselves. Frankly, I cannot imagine a single sales document (such as a brochure or website) that does not use images, drawings or photographs based on optical or electron micrographs, or at least close-up photography. Of course, you must also convince the FDA (and other regulatory bodies) that your device is safe and effective so that it can be approved and made available for sale. Since FDA approval is required to make these real sales, it is imperative that you provide FDA with the microscope data that they need to enable your device approval.

Over the last several months, my firm has provided microscopy consulting and services for all these purposes to multiple medical device clients. As discussed above, the initial or primary need is to find the best analytical methods to address R&D questions. Should device development be successful, often the next need is to have a suitable methodology and standard operating procedure (SOP) to enable microstructural assessment for quality control, and possibly for intellectual property prosecution, and then to use this microscopical information for preparing regulatory submissions, such as 510(k)s. As a best practice, it is my firm's goal to select, develop and execute analytical methods to cost-effectively address the technical questions as well as the follow-on needs. Clearly, having the necessary microscopical data to provide acceptable data for FDA is a central need. Therefore, my firm would be clearly remiss if we did not evaluate the demands of the FDA for acceptable data.

To be relevant to SurFACTS readers, I will address the evaluation of some medical devices. Since almost every medical device company with which my firm has worked has analytical issues related to coatings, these will be briefly addressed. It turns out that most of the questions related to device coatings are universal for any medical device:

- Is the coating there?
- Are there holes or imperfections?
- How thick is the coating?
- Is this thickness uniform?
- How strongly adherent is the coating?

Note that all these questions are readily addressed with microscopy. Of course, depending on the nature of the device there will undoubtedly be additional questions. For example, with multicomponent coatings such as those containing drugs, there are questions regarding the uniformity of the distribution of these components. Additional specifics will also differ depending on the device application. For example, the required strength of adhesion to a substrate will be greater for an orthopaedic bearing than for a lubricous coating on a urinary catheter, or for a drug

From the Editor Continued on Page 13

SurFACTS in Biomaterials is the official publication of the foundation and is dedicated to serving industrial engineers, research scientists, and academicians working in the field of biomaterials, biomedical devices, or diagnostic research.

FDA is Crystallizing Standard Template for Press Releases on Recalls

FDA is proposing a new template for all product recalls, from medical devices to pet food, that seeks to have firms put recalls into the proper context. It also offers some flexibility in wording the announcements made in response to safety reports.

The agency's Office of Regulatory Affairs (ORA) presented FDA's Risk Communication Advisory Committee with a model of the proposed template, which the agency has been developing for several months.

An internal working group will take the committee's suggestions into consideration as it finalizes the form, said David Elder, director of ORA's Office of Enforcement, at the inaugural committee meeting, held Feb. 28-29 in Gaithersburg, Md.

FDA sought advice from the committee on the structure and content of the template, whether it will actually reduce risks to patients and whether standardization is appropriate across all FDA products.

"I heard a lot of support for the basic approach, for standardization," said committee chair Baruch Fischhoff, Ph.D., Carnegie Mellon University, "with a recognition that one size probably won't fit all."

While the risk communication experts liked ORA's draft template overall, many agreed that consumer alerts involving medical devices, particularly implanted products, pose a unique challenge.

New Template Offers Some Flexibility For Industry

Essentially, the new template would structure the way FDA presents information about product issues, in hopes of getting the message through to consumers and health care providers. "One of the goals of the proposal was to reverse the procedure of a one or two or three page narrative and put the information in a more useful way," Elder said.

He says the template will allow the agency to get information out faster.

The proposed template includes subsections for detailing the problem, who is at risk, how to identify the product, where it is distributed, what the symptoms are and who should be contacted.

For the purposes of the release, the action can be dubbed a recall, correction or market withdrawal.

The Heart Rhythm Society (HRS) applauded FDA's efforts to create a precise and effective recall template, but noted, "This hasn't been done yet."

HRS recommends that FDA eliminate the term "recall" from all public communications about implantable cardiac devices and other implanted products. It says FDA should change "class I recall" to class I "advisory notice" or "safety alert," and change class II and III recalls for non life-threatening malfunctions or potential malfunctions to "safety notices."

HRS is concerned that the term "recall" confuses patients about whether or not they should have their device explanted.

Panel consultant Michael Wogalter, a psychology professor at North Carolina State University, shared his research on the topic with the panel. Wogalter found that people prefer to see the word recall for everything except for medically implanted devices.

"We're well aware that there is some information on implantable products that may need to be handled differently," responded Michael Verdi, senior recall coordinator at CDRH.

But he maintains the word "recall" is needed to alert patients and doctors to the situation. More nuanced product information can follow in the body of the document, Verdi adds.

FDA also says the press release should include useful information to put the risk into perspective. For example, the proposed template says, ICD or pacemaker notices could include: "This is a life-saving device. Malfunctions and failures are rare. Even if the device fails to work properly, it usually will not harm the patient."

"Certainly we don't want the risk downplayed," said Elder, "but we want to characterize it." He said his office is still seeking advice from industry on the template. "Step one is please advise us how we can do this, whether we're on the right track."

Experts Offer Clarity on Confusion Surrounding Stents

To stent or not to stent? Which type of the artery-opening device is best? When is heart bypass surgery smarter than getting a stent?

These are the questions many heart patients are left asking themselves and their doctors, as dozens of recent high-profile -- and often conflicting -- studies have compared the performance and safety of various types of coronary stents.

But experts say a consensus on the safest and most effective use of the devices is slowly emerging.

For the majority of patients undergoing angioplasty to clear a blocked artery, newer, drug-coated stents are preferred over bare-metal ones, mainly because they reduce the risk of artery re-closure, cardiologists say.

And it may not matter which of the two established brands of drug-eluting stent you get -- Boston Scientific Corp.'s paclitaxel-coated Taxus or Cordis Corp.'s sirolimus-coated Cypher.

"The truth appears to be that whatever differences exist between these two drug-eluting stents are so small that there's not a compelling reason to select one over the other," said Dr. Kirk Garratt, clinical director of interventional cardiovascular research at Lenox Hill Hospital's Heart Vascular Institute, in New York City.

He said that in very special circumstances, a patient may be better suited for one type of drug-coated stent over another, "but for the average patient out there trying to make sense of this, he or she can be comfortable that whatever stent their doctor recommends is going to be a good choice."

The tiny mesh tubes known as coronary stents were first developed in the mid-1980s, and, within a decade, the insertion of bare-metal stents to prop open narrowed vessels had become standard procedure for many patients at risk of heart attack.

However, the rate of artery re-closure, known as restenosis, after the insertion of a bare-metal stent was close to 30 percent. To circumvent that problem, researchers developed drug-eluting stents, which emit medicines that prevent restenosis. A majority of patients who need a stent now receive one of these devices, which cost about $2,000 each, double the price of a bare-metal stent.

In recent years, the Taxus and Cypher drug-eluting stents have dominated the field, and conflicting studies comparing their relative effectiveness appear regularly in major medical journals. A third drug-coated stent, Medtronic's zotarolimus-coated Endeavor, has received U.S. Food and Drug Administration approval.

But even drug-coated stents aren't perfect. Soon after they gained widespread use, experts began to notice that rates of fatal or nonfatal blood clots were more likely in patients who received a drug-coated stent versus those who did not. This excess clotting risk was confirmed in later trials. For that reason, the FDA recommends that patients who receive drug-eluting stents be placed on dual anti-platelet therapy -- typically Plavix (clopidogrel) and aspirin -- for a year after they receive the device.

But are stents always the best option when arteries narrow or is bypass surgery sometimes a better choice?

In many cases, the answer to that question must still be decided on a case-by-case basis, the experts said. Studies suggest that in cases where only one vessel is blocked, stent placement (during minimally invasive angioplasty) may be a safer and equally effective option.

But a study published in the January issue of the New England Journal of Medicine found that when multiple vessels are blocked, bypass may be a better choice.

"This is really a hazy issue," Garratt said. In more complex clinical situations, a surgeon must carefully weigh the pros and cons of each procedure before making a choice, he said.

If your cardiologist does suggest a stent, it will most likely be a drug-coated one.

The accumulated research is "uniformly very positive and has shown a benefit for drug-eluting stents" versus bare-metal stents in keeping arteries open, Garratt said.

Some patients will still receive bare-metal stents in certain scenarios, he noted. These would include people whose arteries are simply the wrong size for a drug-coated stent, for example. In other cases, patients may need to avoid the excess bleeding risk that comes with a year or more of anti-coagulant therapy.

"This would include patients who are expected to need some surgical procedure in the next few months -- maybe they want a hip replacement or they have a tumor that needs to be removed," Garratt said. "We don't want then to implant a product that requires them to stay on dual anti-platelet drugs for an extended period of time if we know that that is coming."

For these types of reasons, bare-metal stents still make up 40 percent of the coronary stent market, said Dr. Charles Davidson, director of the cardiac catheterization laboratory at Northwestern Memorial Hospital, in Chicago.

When it comes to drug-eluting stents, the Taxus and Cypher models perform equally well, he said.

"I think they are very similar," Davidson said. "There's different drugs, different polymers, platforms. But if you look at the long-term clinical results and the short-term clinical results, they're very similar."

Many of the studies that have pitted the Taxus stent against its rival, Cypher, have been funded by the makers of either one of the devices, Davidson added. Patients should "not put too much stock into what's been out in the press, some of which may have been biased in one direction or another, for whatever reason," he said.

Instead, patients may want to focus on the steps they can take to ensure a long healthy life after receiving a stent.

"The most important thing that patients need to be aware of is that the anti-platelet therapy that is prescribed them by their physician needs to be adhered to," Davidson said. All too often, he said, patients either stop taking the anti-clotting drugs on their own or on the advice of a doctor who may not realize the patient has recently received a stent.

"That's where they have run into some real problems. Good communication and adherence to therapy is the number one thing they can do," Davidson said.

Positive lifestyle changes are also key, Garratt added.

"The really dangerous thing is for patients to leave the angioplasty laboratory feeling like they have had their problem fixed, and then it's back to the cheeseburgers," he said.

"I think that happens all the time. We can fix them up temporarily [with a stent], but if they go back to their old habits, new blockages will form, and they'll have the same risk of death and heart attack in the future."

Davidson concurred. He said the major cause of mortality after stent placement is a narrowing of another artery -- not the one that received the stent.

"Remember, the angioplasty is only treating the most severe lesion, it's not treating the 50 percent [closed] lesions that are very likely to go on and cause heart attacks," he said. "So, maybe with good lipid-lowering therapy, with healthy diets and exercise, these things could also be prevented."

BioInterface Continued from Page 1

The Surface Science Award Winner for 2008 is Ken Stokes from Medtronic. Stokes has been integrally involved in many of the breakthroughs at Medtronic. We look forward to his views on the industry today and into the future.

Seven student posters were submitted in 2007 in the Student Poster Contest. Large and active programs at the University of Minnesota promise to make 2008 another successful year for Student Posters. The posters are a method for the Foundation to open its doors to students to interact with professionals in the field. Karin Straley from Stanford was the 2007 Student Poster Award winner and recipient of $1,000 from the Foundation.

Students also benefit from the popular Student Town Hall meeting, which provides an opportunity where technical students can "meet the industry" during a luncheon. This Q&A plus networking session has been a very popular component of the BioInterface conference.

The Minneapolis area offers a number of opportunities to learn more about companies involved in the bioscience industry. One venue of interest is the Bakken Library and Museum in Minneapolis. It is named for Earl Bakken, the founder of Medtronic and traces many of his and the company's developments including early pacemakers. To learn more follow this link: http://www.thebakken.org/exhibits/exhibits.htm

Biointerface attendees will be enriched by the science, debate sessions, open accessibility of the speakers, by the Minneapolis area and by the unique blend of industry, academic, regulatory and clinical attendees. We look forward to seeing many of you in Minneapolis this October. Registration materials will be posted on the website shortly. Attendees can register and pay online. The board has made a number of revisions this year to make registration simpler and easier.

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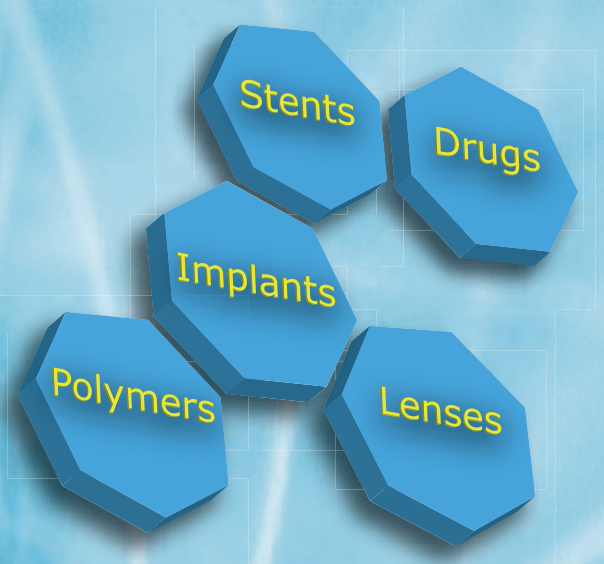

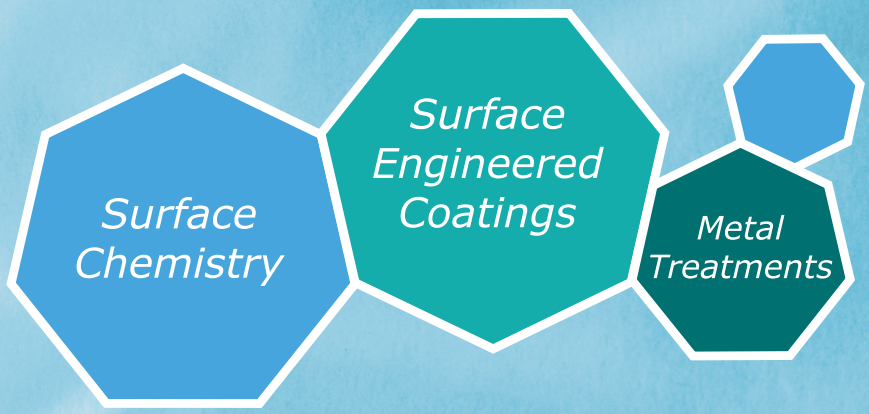

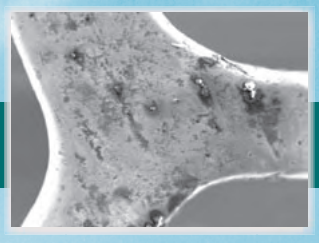

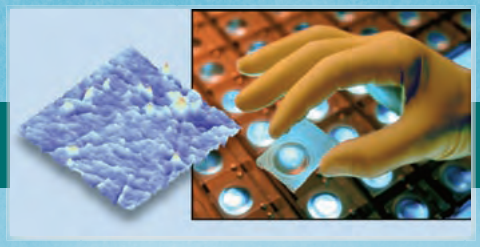

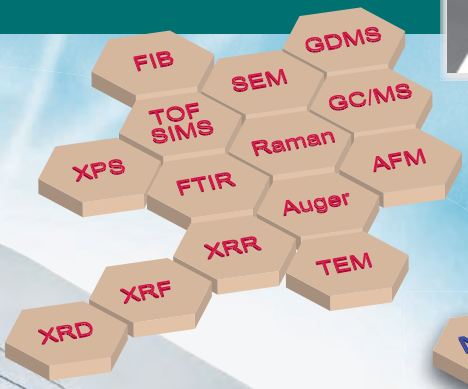

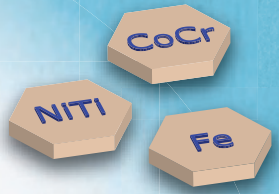

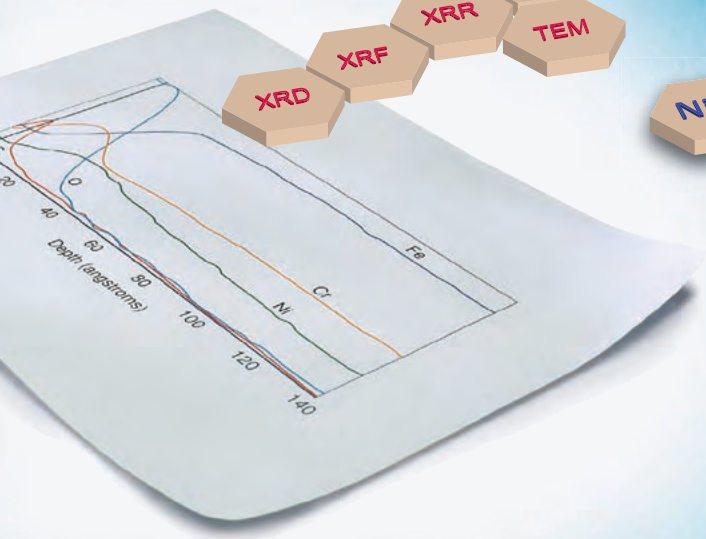

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FDA Plans to Open China Office in May

By Gillian Wong

U.S. food and drug regulators will start working in China once Beijing gives its final approval, the top U.S. health official said recently.

Health and Human Services Secretary Mike Leavitt said the Food and Drug Administration plans to open an office in China as part of a change in strategy following product safety problems in Chinese imports that prompted several health scares and have been linked to some deaths.

"In the past, the United States and many other countries have employed a strategy of standing at the border trying to catch things that aren't safe," Leavitt said in an AP interview during a visit to Singapore.

However, he said it is impossible to inspect all of the massive amounts of goods that enter the country.

"So we're changing our strategy from one of trying to catch unsafe products to building safety into the products," Leavitt said. "Our purpose is not just inspection, it's building capacity and maintaining relationships between regulators."

The FDA's China office will be headed by Christopher Hickey, currently director of the Asia and the Pacific office at the Department of Health and Human Services, Leavitt said.

Hickey, who was with Leavitt in Singapore, said Washington is still awaiting final approval from the Chinese government on the opening of the FDA's office there, but that the agency expected to begin work in May before the official opening of the office in October.

No further details were given, but the agency had earlier said they planned to establish eight permanent FDA positions at U.S. diplomatic posts in China. The FDA also said it would hire five Chinese employees in Beijing, Shanghai and Guangzhou.

U.S. regulators have recalled a number of contaminated products made in China: toothpaste, pet food, the blood thinner heparin and others. Heparin, a commonly used blood thinner, has been linked to 62 deaths and hundreds of allergic reactions in the U.S. and Germany.
About 40 percent of pharmaceuticals and 80 percent of the chemical ingredients in drugs are imported, according to U.S. government statistics. A growing share comes from developing countries such as China, India and Mexico that are still building their own drug safety systems.

Leavitt said the U.S expects to build a presence in a number of other countries, including India and those of the Central American region. He said the safety of food and product imports is "a global problem" driven by a rapid increase in goods being produced and consumed across borders.

"We've started a conversation with the Indian government but no conclusions have been reached," he said, adding that the amount of pharmaceutical trade between the United States and India has grown rapidly and that there are now up to 100 FDA-inspected facilities in India.

"Many of the products that are innovations of American science and American pharmaceutical companies are now being produced in India," he said. "So that requires us to be where products are being developed and being produced."

Stryker Launches Partial Knee Resurfacing System

Stryker Corp said recently it has launched a partial knee resurfacing system in the United States. The system preserves the most amount of natural bone, making it a less invasive way to treat diseased joints.

Kalamazoo, Michigan-based Stryker, one of the top makers of reconstructive implants, said its system, called Triathlon PKR, is beneficial because it allows surgeons to provide personalized solutions by only shaving off diseased parts of the knee rather than replacing larger parts of it, or the entire knee joint.

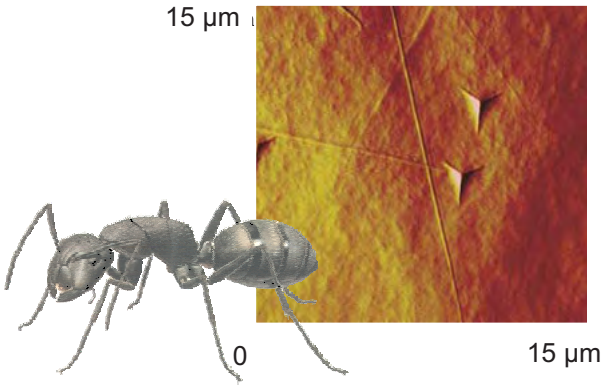
Partial knee resurfacing requires less operating time than total knee replacements and there is a shorter recovery period, with some patients leaving the hospital in less than 24 hours, Stryker said.

Because less bone is removed, there is often less trauma to soft tissue during surgery, which may leave the patient with a more natural feeling knee than with a total knee replacement, the company added.

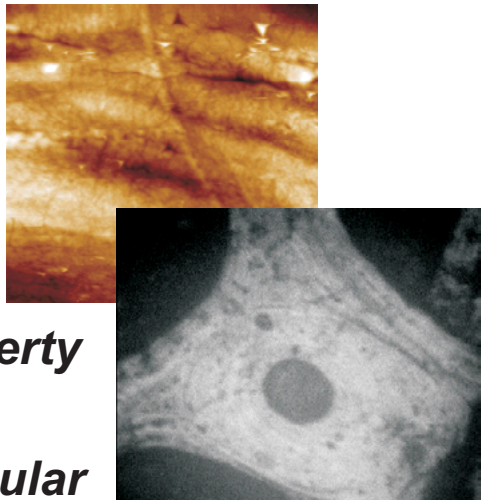
Nano Testing for Natural & Artificial Structures

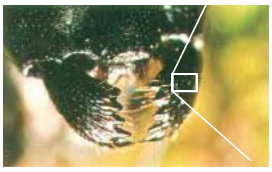
Hard or Soft Materials
Nanomechanical Testing Delivers Results

Hardness of ant mandible



Nanoindentation of the lamellar structure of trabecular bone

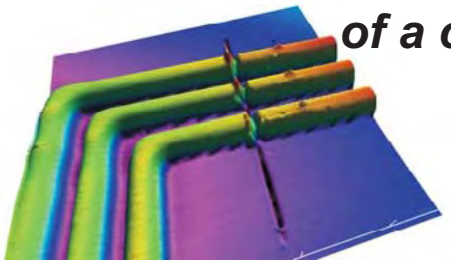




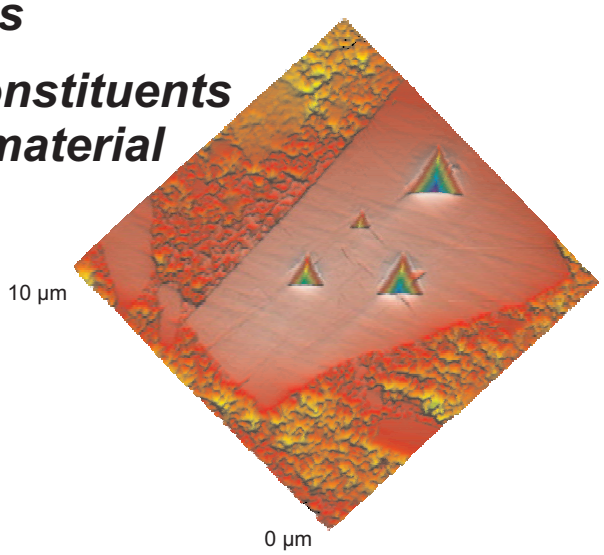
Determine structure-property relationships

Test specimens with irregular geometries

Probe individual constituents of a composite material



Scratch and indents on a MEMS structure



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Highlights include the Excellence in Surface Science Award, Student Town Hall Meeting, a Student Poster Award competition and a lively debate session! As always, these events provide participants with great networking opportunities.

We once again host the popular Student Town Hall meeting where technical students can "meet the industry" during a luncheon. This Q&A plus networking session has been a successful introduction for students to industry perspectives over the past few years.

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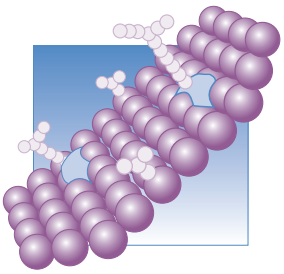
For more information, please contact Ashley Crunstedt at ashleyc@ewald.com or call her at 651-203-7248. Also, you may visit our Web site at www.surfaces.org for updates.



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BIO INTERFACE 08

Abstract Guidelines

Electronic Abstract Submission
Authors are encouraged to submit their abstracts as an email attachment addressed to ashleyc@ewald.com by September 1, 2008.

Submitted abstracts are considered final when submitted. Your email message will serve as your abstract submission form and should identify one topical session from the session list, your preferred method of presentation, and keywords for each abstract submitted; see abstract submission form. Send one email per abstract being submitted. Authors are asked to activate "return receipt" before sending email in order to receive confirmation of receipt of abstract.

Submit only ONE abstract for each presentation; do NOT submit multiple copies of the same abstract, and do NOT submit in blinded format.

Failure to Present
The presenting author is expected to present the paper. If emergencies at the time of BioInterface 2008 prohibit the participation of the presenting author, the Chair(s) of the session and the Program Committee Chair must be notified as soon as possible. It is the presenting author's obligation to ensure that the abstract is presented.

Notification
Notification of acceptance or rejection will be mailed on or about September 15, 2008. The final selection of abstracts for presentation and placement of accepted abstracts in the program format will be made by the Program Committee.

Abstract Format
Abstract information must not appear on or outside the margins. Format a single 8.5x11-inch (21.59cm x 27.94cm) document to the image specifications below. All information must fit on one page.

Top & Bottom 0.75 inch (1.9cm)
Left & Right 0.75 inch (1.9cm)
Column Width 3.25 inches (8.25cm)
Between Columns 0.5 inch (1.27cm)

Title
Type the abstract title in upper and lower case letters. Use a short, substantive title. Title should be centered over both columns.

Authors
The presenting author's name must be underlined. This person is expected to present the paper. If emergencies at the time of BioInterface 2008 prohibit the participation of the presenting author, the Chair(s) of the session and the Program Committee Chair must be notified as soon as possible. It is the presenting author's obligation to ensure that the abstract is presented.

Type name(s) of author(s) and institution with complete mailing and email addresses, including country. Do not use titles, i.e., MD, PhD, etc. Use upper and lower case type. If the affiliations of the other authors are different from the first author, use superscript to note differing affiliations.

Abstract Body
Text should be typed single-spaced. Do not skip a line between paragraphs. Type should be 8 to 10 points using only the fonts named: Arial, Courier New, Helvetica, Marlett, Modern, Symbol, Times, Times New Roman, or Wingdings. ***The abstract is required to include a section on surface characterization/analysis.***

Podium or Poster Preference
The preferred method of presentation (podium or poster) should be noted. Final determination will be made by the Program Committee.

Abstracts accepted for podium presentation will be provided 15 minutes for didactic presentation, followed by 5 minutes for discussion. The nature of the multiple session format makes it imperative that these time limits be strictly observed by all participants. Audio-visual is a single LCD projection. Your presentation must not include animation or sublinks to other programs. No laptop or wireless mouse will be provided. You must provide your own laptop for LCD presentation.

Abstracts accepted for poster presentation will be provided a poster board that is 4 ft. high x 8 ft. wide (1.22m high x 2.44m wide), for mounting the descriptive material. The presenting authors must be at their panels during the scheduled Poster Session listed in the Final Program and adhere to Set Up/Tear-Down instructions included in the acceptance notification.

Outside Support
Support from outside sources must be listed in the abstract. In adherence with standards of the Accreditation Council for Continuing Medical Education, and guidelines of the Food and Drug Administration as endorsed by the American Medical Association, any conflict of interest must be clearly recognizable. Check "Outside Support" if a potential conflict of interest exists. The indication of outside support does not affect the decision of abstract acceptance or rejection.

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From the Editor Continued from Page 2

releasing coating on a stent. Therefore the appropriate test methods will clearly differ, as will the imaging methods use to monitor adhesion.

So how should a company address the evaluation of its devices, such as coatings, to satisfy the FDA regulatory review? One litany I tell my clients with regard to microscopy is: "Do it the right way, not necessarily the way it was done before." Of course, almost all clients want to know what the FDA wants for data. So, what does the FDA have to say about the microscopic methods to evaluate such medical device coatings materials? Well, officially, not very much.

A search of the FDA Medical Device website database lists over 2,500 documents with the word "microscope" or "microscopy." Clearly, this is a great many documents; however, most are not relevant to *SurFACTS* readers. When "Guidance" is combined with "microscopy" the documents become much more relevant, but here there are only a couple of dozen. Surprisingly, these documents are not very specific on the nature of microscopical analysis. Three examples follow, two of which relate to coatings:

1. One of the most recent documents, Guidance for Industry: Coronary Drug-Eluting Stents — Non-clinical and Clinical Studies March 2008 (document is marked Draft - Not for Implementation), states that "The extent of endothelialization should be assessed..." and that "scanning electron microscopy should be considered" for this assessment. This draft guidance document also states that "Acute coating integrity of a DES should be assessed via some visualization" method and again indicates "(e. g., scanning electron microscope)." While I might suggest that there are better methods than SEM for evaluating endothelialization, clearly the FDA is not very specific, and furthermore provides no details on how such SEM should be done. It is important to note that this FDA document does not exclude the use of methods other than SEM.

2. The guidance document "510(K) Information Needed for Hydroxyapatite-Coated Orthopedic Implants March 10, 1995 (revised 2/20/97)" indicates that, "scanning electron microscopy pictures of the metal particle- and the HA-coated implant surfaces as well as the cross-sectioned area of the device including measurements of the coating thickness and tolerances..." Here a specific method is also indicated, but no details are provided on how this should be executed. (I could also question why SEM was chosen for measurement of coating thicknesses, but that would be different topic.)

3. One of the more specific documents that turned up is not for a specifically coated device: "Guidance for the Submission of Research and Marketing Applications for Permanent Pacemaker Leads and for Pacemaker Lead Adaptor 510(k) Submissions." This document indicates that, "Leads should be removed intact and examined for structural integrity and biostability. Biostability of the insulator should be documented by using a state-of-the-art analytical technique(s) e.g., scanning electron microscopy (SEM), infrared (IR) spectroscopy, molecular weight analysis, stress-strain, etc. This document also indicates there should be, "Thorough visual inspection of polymer using light microscopy." While certainly more comprehensive, this document is not very specific and provides at most only minimal details on how analysis should be executed.

Additional examples could be provided but this is sufficient for discussion. In my view, the FDA is absolutely correct in not being very specific. Methods and instruments are evolving, as are the devices that are evaluated. Each device will have its own particular characteristics that will necessitate different methods for specimen preparation. Thus, it is not reasonable or even possible for the FDA to proscribe methodologies in detail since for each device there will be unique characteristics that require different analytical instruments and specimen preparation methods. (In my experience, it is most often specimen preparation that is problematic for an analysis.) Therefore, it is up to the medical device company to apply, and in many cases develop, the microscope evaluation methodology. It should be noted that organizations such as the ASTM also provide guidance, and that the FDA often recommends ASTM test methods. However, these are generally recommendations, and while ASTM methods are generally more specific, the ASTM methods are also rarely explicit with the detail of how microscopy and specimen preparation is done.

In summary, the FDA is not very specific for a very good reason. It is not possible to provide for every contingency. The FDA simply wants, and demands, valid and relevant information. The onus is therefore on us to determine the best method to use, to then adequately explain why these methods and instruments were used, and to present this information clearly. In other words, "Do it the right way, and explain why this is the right way."