Boston Area Chapter
ENGINEERING PHARMACEUTICAL INNOVATION

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IN THIS ISSUE

"Nanotechnology: No Small Matter" - Big Success

by Pietro Perrone

The title of the 9 March ISPE Boston Area Chapter program, "Nanotechnology: No Small Matter" appropriately describes this newest of technologies. Although still in its infancy, you'd be surprised at its presence in everyday products. So no wonder an enthusiastic crowd gathered at the Royal Sonesta Hotel in Cambridge to hear the latest from experts in the field.

The presenters were Dr. Julie Chen, Professor of Mechanical Engineering, Director of the Nanomanufacturing Center of Excellence and Co-Director of the Advanced Composite Materials and Textile Research Lab at UMass Lowell, and Mr. Paul Mraz, Chairman and CEO of Woburn-based Angstrom Medica, Inc. Together they presented an overview of nanotechnology and what it offers in an interesting, clear and practical manner that held the attendees' attention throughout. Our appreciation goes to the speakers and to Chapter Board Member Marita King for organizing this extremely interesting and timely program.

The articles that follow are based on the speakers' presentations and provide a brief introduction to nanotechnology, its current state of development and the challenges involved in commercialization. A follow-up article in a future issue will provide additional information about this exciting field.

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2006 Calendar of Events

ISPE Boston Area Chapter Educational Program
"Water, water everywhere but nary a drop to drink"
23 May, Royal Sonesta, Cambridge, MA

ISPE Washington Conferences
5-8 June, Crystal Gateway Marriott, Arlington, VA

ISPE Boston Area Chapter Annual Golf Tournament
17 August, Granite Links Golf Club, Quincy, MA

2006 ISPE Boston Classroom Training and GAMP Americas Forum
11 - 15 September, Hyatt Regency Cambridge, Cambridge, MA

ISPE Boston Area Chapter Product Show
18 October, Gillette Stadium Clubhouse, Foxboro, MA

President's Message

Dear Boston Area Chapter Members,

Now that summer is upon us, once a week I venture out of my office and onto the streets of Cambridge for lunch. No matter what restaurant I choose, it's impossible not to overhear conversations about technology, breakthrough science, and what are the hot emerging biotech companies to invest in.

With buzzwords like RNAi, synthetic biology, personalized medicine, and nanobiotechnology being tossed about, it got me thinking: what are the life science engineers of today going to be faced with producing tomorrow? Alvin Toffler professed in his 1970 book Future Shock that technology would proliferate exponentially on its own success. He also believed that knowledge would have an ever-decreasing shelf life, to the point where if people couldn't keep up with the unstoppable advance in knowledge, they would become technologically extinct.

So here we are 36 years later, on the cusp of Toffler's future. Are you prepared to deliver the therapeutics of tomorrow today? How will you ensure that you can meet the engineering challenges on our doorstep? Will you be a leader or a follower when it comes to exploiting the ever more rapidly expanding opportunities in therapeutics, genomics and medical devices?

If you intend to participate in this brilliant technological future, start by investing in your continuing education, and become a more active member in the ISPE Boston Area Chapter. Being in the midst of a life science cluster – the greater Boston area – that's home to so many world-class universities and institutes, our chapter is uniquely poised for its members to stay current with cutting edge science and technology.

The overwhelmingly positive response to last winter's highly successful educational program, "Nanotechnology: No Small Matter", which covered topics from high level concepts about nanotechnology to the ground-breaking challenges of commercial marketability and regulation, has spurred us to plan many more programs on breakthrough and developing life science topics. In the quest to provide more discussion about emergent technologies, the chapter has formed a new committee on Process and Product Development (P&PD). This exciting committee is designed for members whose craft is getting science off the bench top and into commercial scale. Stay tuned for upcoming P&PD educational programs this fall.

But the Chapter is not **all** about science and engineering. We know how to break out and have fun, too. Please join us for our annual Chapter Golf Tournament; held once again at Granite Lakes Golf Club in Quincy, MA. Last year's event was a sold-out success and the same is true for 2006. Big thanks to the entire Social Committee which is leading this, and other networking events. And coming in October, we're taking over the clubhouse at Gillette Stadium and hosting a bigger, better Chapter Product Show with 250 vendors and service providers. Keep checking the Chapter Web site for developing event details.

Our Chapter has lots of ambition, but we need support from you, our members, to keep it fresh and active. Visit the Chapter Web site from time to time to see how you can keep your mind fresh and on top of what the future will bring.

Niall Johnson
President, ISPE Boston Area Chapter

Over 100 Attend January Program: "Real-Time Quality in Manufacturing and Just-In-Time Validation"

by Mary Wojtyk

On 30 January 2006, the Boston Area Chapter's Educational Program Committee presented a program aimed at fast-tracking quality assurance decisions and validation projects. The purpose of this program was to discuss a common theme in biopharma: closing the gap between the significantly different pace of manufacturing as compared with quality systems (QS).

The program consisted of presentations by Greg Killian (Real-Time Quality in Manufacturing), Katie Henchir (Optimizing the Client-Contractor Relationship) and David Vincent (Fast-Tracking Validation Projects through Effective Commissioning). Attesting to the relevance of the subject matter, over 100 Boston Area Chapter members attended despite the winter cold snap and threatening weather forecast. And thankfully, so did all three presenters - even David Vincent who had flown in from San Diego especially for the event.

As Pharmaceutical Program Manager at the Siemens Center for Global Competence, Greg Killian focused on RTQ (Real-Time Quality) tools to extract instrument information and trend live data for reliable batch-to-batch forecasting. He outlined multivariate techniques to drive a process to desired operating conditions within operating constraints on the basis of best available knowledge and process characteristics.

A longtime validation engineer and project manager, Katie Henchir offered insights from her experiences as both a validation contractor and as a client of validation firms. She presented a "how to" guide for setting up validation contractors initially, in order to ensure they add value to the client company as quickly as possible. She also discussed the structure of bids and contracts (e.g., time and materials vs. guaranteed not-to-exceed) and efficient ways to alleviate the challenges faced by contractors. She emphasized that expecting the best, holding to high standards, providing immediate feedback and reiterating the end goal all promote high performance on the part of contractors.

As CEO of Validation Technologies Inc., David Vincent stressed that commissioning is the key to fast-tracking validation projects. Leveraging a company's Validation Master Plan and data collected prior to the inception of validation activities are critical to creating streamlined pro-

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Industry News in Brief

by Patti Charek

Industry News in Brief, *a regular feature of the Boston Area Chapter Newsletter, presents news items concerning companies in the pharma, biotech, medical device and related fields with an emphasis on companies with a local presence and topics of special interest to our readers.*

Shire Expansion in Cambridge Adds 100 Jobs

Shire PLC is hiring 100 people to work at its Human Genetic Therapies division in Cambridge, expanding the number of employees at the former Transkaryotic Therapies Inc. by 25 percent. Among those hired will be sales people, scientists, manufacturing staff, and general corporate staff, according to David Pendergast, general manager of the genetic therapies unit. "We're expanding on two fronts," said Pendergast. "We're launching a product and building a pipeline. We're alive and healthy as a business unit within Shire."

Shire purchased TKT for $1.6 billion in 2005 in order to gain its expertise in developing and manufacturing protein-based therapeutics. Shire, based in England, has US headquarters near Philadelphia. Shire is gearing up in anticipation of FDA approval of Elaprase, a treatment for Hunter syndrome, a rare genetic disease. The FDA is expected to rule by May 25 on Shire's application to market the drug.
(Source: Jeffrey Krasner, The Boston Globe, 14 March 2006).

"Orphan" Drug Status Propels Local Startups

More than a half-dozen emerging New England companies have recently earned orphan-drug designation, which essentially bars competitors from selling the same substance for a specified period of time. Biotechs are seeking a shorter, less expensive route to the goal of an FDA-approved drug and the orphan route has been their answer. According to Eric Schmidt, a life-sciences analyst for SG Cowen in Boston, "The successful company can get seven years of exclusivity, and that is a valuable asset for both the company and investors."

Despite the prevalence of orphan-drug status among startups, Genzyme is by far the largest holder of such compounds in New England, with 21 compounds designated, according to FDA data. "Genzyme is probably the great industry story about a small company becoming big as a result of its early work in the orphan-drug area," said Steven Dickman, chief executive of CBT Advisors, a life-sciences consultancy in Cambridge. Other companies with significant orphan-drug designations include Serono Laboratories with 18; Biogen Idec with 16; Bristol-Myers Squibb with 10 and Bayer Pharmaceuticals with six.

Local startups whose drugs have recently received orphan status include: TolerRx, Molecular Insight Pharmaceuticals, Therion Biologics, Vion Pharmaceuticals and Ariad Pharmaceuticals. The U.S. Orphan Drug Act was signed into law in 1983. More than 1,500 drugs and biologics have been designated as orphan drugs, according to FDA data, and more than 250 have been approved for market.
(Source: Dyke Hendrickson, Mass High Tech, 27 February - 5 March 2006).

Amgen to Expand Research Unit Here, Adding 400

Amgen, Inc. of California plans to increase to 400 the number of scientists and support staff at its Kendall Square laboratories over the next few years, substantially expanding its footprint in Cambridge, according to chief executive Kevin Sharer. Amgen, with more than 14,000 employees, is the largest biotechnology company in the world. It had revenue of $12.4 billion in 2005.

Quick Takes

by Janet Tice

While state government officials anxiously await **Bristol-Myers Squibb**'s verdict regarding location of a new $1.1 billion manufacturing plant (Devens in central Massachusetts is still on the "short list" of possible sites), **RenaMed Biologics** has made their decision. The 95-person company, which makes a device to treat kidney patients, will relocate from Rhode Island to Westborough with the move to begin in July. Coincidentally, RenaMed recently signed a deal worth $23 million to split profits and development costs with **Genzyme**… Entering an expansion mode, **Hyaluron** has secured a $1.5 million financing package it plans to use to purchase packaging equipment and construct additional clean room space for its Burlington facility… After hitting a roadblock in its quest for FDA approval for MRI contrast agent Vasovist, **Epix Medical** has announced plans to purchase **Predix Pharmaceutical Holdings** of Lexington for $90 million in stock... **Paratek Pharmaceuticals** has entered into an agreement with **Merck & Co.** to develop an antibiotic against a number of drug-resistant infections that strike hospital patients. Merck paid an undisclosed amount up front and will pay as much as $127 million should the experimental antibiotic win FDA approval… As part of an ongoing research collaboration begun in 2001, **Vertex Pharmaceuticals** will receive an additional $22 million from the Cystic Fibrosis Foundation to further develop "corrector" compounds that act to restore the function of the defective cell membrane protein responsible for the disease... **Genzyme** has announced a new program for "neglected diseases" affecting the developing world and has said it won't profit from commercialization of resulting products, granting commercial and intellectual property rights to nonprofit groups instead.
(Sources: The Boston Globe and Mass High Tech).

Industry News in Brief

Continued.

In Cambridge, Amgen has 135 employees in a 300,000 square-foot building that Amgen opened in 2001. The expansion, however, will gradually move its Cambridge facility to among the top dozen pharmaceutical and biotechnology labs in Massachusetts. The company said that 200 people would be hired by the end of this year. The reason they decided to expand here, according to Sharer, is the concentration of academic medical centers, universities, and biotechnology companies.

(Source: Christopher Rowland, The Boston Globe, 2 March 2006).

Idenix to Get Up to $525 Million from Novartis for Drug

Novartis AG, Switzerland's biggest drug maker, has agreed to pay as much as $525 million for an experimental hepatitis C drug in an effort to reduce its reliance on blood pressure medicine Diovan. Novartis agreed to pay Idenix Pharmaceuticals Inc. of Cambridge as much as $465 million in milestone payments and $70 million in licensing fees for the rights to valopicitabine, the companies said. Idenix is 56 percent owned by Novartis.

(Source: Bloomberg, The Boston Globe, 30 March 2006).

Medicare to Pay for Heart Test from Local Device Maker

In a decision that could have long-term implications for Boston Scientific Corp. and its rival heart device makers, Medicare has decided to pay for a $400 test that could limit the number of patients who receive implantable defibrillators. Defibrillators, which prevent the heart from stopping suddenly, are priced at $20,000 or more - plus the cost of the implant procedure - making them among the most expensive medical implants in wide use. The noninvasive cardiac test made by Bedford-based Cambridge Heart Inc. uses a machine to measure nearly undetectable fluctuations in a person's heartbeat during mild exercise.

The top three manufacturers of defibrillators, Medtronic Inc., St. Jude Medical Inc. and Guidant Corp., share a $10 billion worldwide market, with sales expected to grow significantly in the next several years. Boston Scientific recently won a $27 billion bidding war to buy Guidant, the number-two manufacturer in the US, chiefly as a way to get into the business.

Manufacturers estimate that about 1.3 million Americans are potential candidates for a defibrillator. If the new test were widely used to make decisions about whether to implant defibrillators, it would cut about 465,000 patients out of the eligibility pool, an estimated Medicare savings of about $700 million.

(Source: Stephen Heuser, The Boston Globe and Sylvia Pagan Westphal, Wall Street Journal, 22 March 2006).

Microbia Lands $75 Million in Financing

Cambridge biotech company Microbia Inc. said it has received $75 million in new venture capital financing - the biggest biotech venture deal in New England since 2004. The 70-person company is pushing two experimental drugs through clinical trials, one for constipation and the other for high cholesterol. "It's a great new set of investors," said Bryan Roberts of Venrock, who predicted that Microbia could see a large-scale public offering in a year and a half.

The anti-constipation pill is now in Phase 2 human trials to see if it works as intended, and the cholesterol-blocking pill is currently in Phase 1 human safety tests. With potential patients numbering in the tens of millions, the diseases that Microbia is targeting are a long way from the usual biotechnology targets of rare cancers and other severe, uncommon diseases.

(Source: Stephen Heuser, The Boston Globe, 27 February 2006).

FDA Delays Decision on Biogen Idec's Tysabri

The FDA has delayed its decision on whether to return the multiple sclerosis drug Tysabri to the market by up to three months, citing concerns about plans to safeguard patients from potentially deadly side effects. Biogen Idec and Elan Corp., the drug's makers, said the FDA may take until June 28 to review a risk management plan intended to prevent further cases of a rare brain disease found in three patients taking the drug in trials. The disease, called progressive multifocal leukoencephalopathy, caused Tysabri to be pulled from the market in February 2005, after just three months on sale. The FDA's postpone-

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ISPE Student Chapter – Poster Contest 29 March 2006

by Sean Lyons

The ISPE Boston Area Chapter held its annual Student Poster Contest at Northeastern University on 29 March 2006. The contest provides graduate and undergraduate students the opportunity to present research they have been working on throughout the 2005-2006 academic year. Congratulations to this year's winners and runners up:

Undergraduate

Dawn Eriksen

Cell-density Dependent Lycopene Production in Escherichia coli.

Graduate

Lilian E. van Vlerken

Modulation of Intracellular Ceramide using Multifunctional Polymeric Nanoparticles to Overcome Multidrug Resistance in Tumor Cells

Defending Research!

2006 ISPE Boston Area Chapter Poster Contest Winners – Ms. Lilian E. van Vlerken and Dawn Eriksen.

First Runner-Up

Rishikesh M. Sawant

Constructing Double-Targeted ph-Response Nanocarriers

Second Runner-Up

Mayank D. Bhavsar

Formulation Optimization and Oral DNA Administration using Nanoparticles-Microspheres Hybrid Delivery Systems

Good luck to our undergraduate and graduate winners as they participate in the ISPE International Student Poster Competition on 6 November 2006 in Orlando, Florida.

Mark Your Calendar!
ISPE Annual Meeting
5 - 8 November 2006
Walt Disney World
Swan & Dolphin
Orlando, Florida

2006 ISPE Boston Area Chapter Poster Contest participants.

ISPE Student Chapter – University of Massachusetts, Amherst

by Sean Lyons

The UMass Amherst Student Chapter was established in the Spring of 2004 and currently has 22 undergraduate members, evenly split between upper and lower classes. Mr. Cheng-Yuk Lee serves as the Chapter President and is supported by Mr. Daniel Hines – Vice President, Ms. Dawn Erikson – Treasurer, Ms. Caitlin Blacker – Secretary, Mr. Paul Robinson – Membership Chairman, Ms. Prerana Katti – Sophomore Class Rep. and Mr. Jeremy Sauer – Freshman Class Rep.

The chapter has hosted several guest speakers over the course of the 2005-2006 academic year including Ms. Mary Wojtyk of Biogen Idec who spoke on the roles and opportunities for chemical engineers in the pharmaceutical industry. In addition to speakers, students head out into the field to participate in plant tours that allow them to experience the industry hands-on. The group has participated or looks forward to tours at Biogen Idec in Cambridge and Wyeth Biopharma in Andover.

All students agree the largest benefit to membership is the opportunity to network with industry professionals. Attendance at various ISPE events, including the Boston Area Chapter's Product Show and the National ISPE Conference, has allowed students to make industry contacts that would otherwise be unavailable by simply attending class.

Like most of our student chapters, UMass is looking for methods of raising money in order to support chapter activities. If you would like to help the chapter or would like more information on the UMass Student Chapter or are interested in participating in student member events, please contact Cheng-Yuk Lee – Chapter President (chengl@student.umass.edu) or Mr. Rick Pierro, Chairperson, Student Affairs Committee (rpierro@supercontrols.com).

The Boston Area Chapter would like to take this opportunity to congratulate all of our Chapter's graduating seniors. Congratulations on an excellent job and we all look forward to working with you in the future. Good Luck!

"Nanotechnology: No Small Matter"...

Continued from page 1.

Boston Area Chapter Board of Director Member Marita King introduces our speakers.

Introduction to Nanotechnology and Challenges in Transitioning from Lab to Manufacturing
– Dr. Julie Chen

Dr. Chen opened the program by providing an informative and stimulating presentation covering everything from the basics of nanotechnology to the latest innovations. She also highlighted some of the challenges to be surmounted as the field evolves. A summary of her presentation follows.

Nanotechnology began to receive greater attention about 20 years ago when development of the scanning electron microscope allowed us to "see" at the nanoscale level, typically defined as 1-100 nm (1 nm = 10^{-9}m). For reference, the diameter of a red blood cell is 2,000 nm and a human hair 10,000 nm; the 1 mm spacing on your ruler is equivalent to 1,000,000 nm.

Dr. Julie Chen presents an overview of nanotechnology.

Dr. Chen described nanotechnology as an "enabling" technology useful for many applications, with the potential to impact all sectors of industry. Though the field is still in its infancy, a number of products already on the market have been enhanced by nanotechnology. Examples include golf balls that shift weight to travel further, fabrics coated to repel liquids, tennis balls that retain pressure for longer periods, special sunscreens and enhanced car wax. Potential products include flexible electronic components, sensors, implants, nanocapsules for drug delivery, biosensors (for radiation exposure, cancer, anthrax and insulin, to name a few), reinforced materials and fabrics with unique properties. She stated that by 2015, nanotechnology is projected to yield new products valued at $1 trillion annually, with $180 billion in the pharmaceutical sector. This will result in an explosion of new jobs as a market of this size is estimated to require about 2 million nanotechnology workers.

Support for Nanotechnology

Dr. Chen went on to describe the three main modes of support available for nanotechnology – small business innovation programs (SBIR/STTR), academic programs, and centers/networks. The government programs are driving the development with fifteen Nanoscale Science & Engineering Centers that include the Center for Integrated Nanotechnologies (CINT, Sandia) and the Center for Nanophase Material Science (CNMS, Oak Ridge). More than twenty states also have their own programs.

Since 2001, investments in nanotechnology through the National Nanotechnology Initiative (NNI) have been growing at 20-30 percent annually, exceeding $1 billion in 2005. These investments are in the science, manufacturing, and societal impact of nanotechnology.

"Nanotechnology: No Small Matter"...

Continued.

Unique Behavior of Materials in the Nanoscale World

What's different at the nanoscale level? In order to answer that question, Dr. Chen touched on a number of the features and challenges that are unique to nanoscale dimensions:

- The smaller particles in nanostructures result in more surface area per given volume, creating important implications for chemical reactions, drug delivery processes and catalytic activity.

- Van der Waals and electrical forces are more of a factor than gravity; this affects buoyancy and the interactions between surfaces/materials. Controlled patterns of nanofibers can be used to make fibers with high surface area and fabrics with fine porosity that will repel liquids.

- Nanosize particles can pass through small pores and interfere differently with light transmission. As an example, the common sunscreens consist of microparticles that block UV light only if the light hits the particle straight on, allowing the rest to pass through the spaces between the particles. The higher packing density that occurs when nanoparticles are used in place of microparticles in sunscreens results in a higher blockage of UV light.

- Encapsulating therapeutics in nanospheres or in a polymeric coating can provide for the release of drugs at the site of treatment over an extended time period. This minimizes the amount of therapeutic compound needed, focuses the drug at the target location for maximum effect, and eliminates the drug interactions and side effects of systemic drug treatment.

- The small size of nanodevices allows nanosized sensors to detect with less material and at greater sensitivity.

- At the scale of nanotechnology there is a convergence of disciplines. Biology, chemistry, and physics combine to be equally critical and create unique properties that can be exploited to advance science and develop new products.

The Path to Commercialization

According to Dr. Chen, the path to commercialization consists of four major segments, which she described as follows:

- **Nanoscience**
  Scientific discovery, basic theory, test hypotheses.

- **Nanomanufacturing science**
  Creation of models, discovery of process methods, reliability theory, enabling tools. This segment is supported at UMass Lowell via the National Science Foundation (NSF) Center of High-Rate Nanomanufacturing (CHN).

- **Product prototypes and scalable processes**
  Process development for specific products, production of prototypes. This segment is supported at UMass Lowell via the Nanomanufacturing Center of Excellence (NCOE).

- **Process scale-up**
  Short production runs, scale-up debugging.

As in all manufacturing processes, once a high volume product is identified, methods must be developed to produce it at a high rate and at a high yield in order for the product to succeed commercially. Dr Chen concluded by stressing that success in nanomanufacturing is dependent on support from the technical centers as well as from industry. This cooperation is needed to ensure that ideas evolve into practical, commercially viable products.

Commercialization of Nanotechnology – The Development of a Nanomedical Device
– Mr. Paul Mraz

The second presentation, by Paul Mraz, Chairman and CEO of Woburn-based Angstrom Medica, described the critical process of securing FDA approval and commercializing a "nanomedical device," using his own company as an example. He also elaborated on what is important in directing a start-up business based on nanotechnology. He stressed that

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"Nanotechnology: No Small Matter"...

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one of the key elements is to focus on a limited number of products to maximize the probability of success with the finite resources available.

Angstrom Medica has achieved various milestones and received formal recognition at several points during the commercialization process, most notably:

- 2001 MIT $50K Business Plan Competition Award
- 2005 Frost & Sullivan Excellence in Technology Award
- FDA 510(k) clearance in February 2005 for Bone Void Filler, reportedly the first nanotech medical device cleared by the FDA.

Three New Products – Three Ways to Succeed

Angstrom Medica's NanOss™ is synthetic bone composed of calcium phosphate nanocrystals. It is produced by densifying or compressing the nanocrystals to form a structure that has superior strength and excellent biocompatibility. The manufacturing process starts with controlled molecular assembly. The resultant NanOss™ product is the basis of the company's three targeted product areas of: (1) structural medical devices, (2) injectable cement and (3) bioactive coatings.

Stainless steel has the strength needed for bone repair. However, it can cause problems since it is a foreign material to the body. NanOss™ has an equivalent strength (85-90 percent that of stainless steel) and the ability to become bone after a period of time since it is made up of the same microstructure as bone. It provides for the best of both worlds – strength and assimilation into the bone structure. It has the potential to replace a variety of medical devices such as pins, plates, screws, suture anchors, spinal fusion devices and ACL interference screws.

The injectable bone cement offers 100MPa of compressive strength, a minimal application time (15-minute working time plus 15-minute curing time) and needs no initiators or accelerators, making it easy and straightforward to use. The bioactive coatings consist of micron(s) thick layers applied to metals, composites and polymers to increase surface area or act as carriers.

Paul Mraz describes the process of securing FDA approval.

As in many start-ups, it is critical to scale-up the process so that commercial quantities of material can be produced. The production process is presently scaling up the 50-liter reactor to a 4X capacity. Growth projections place the long term expansion needs at 50X the current capacity with the ultimate goal (at least for now) of having a 5000-liter reactor in the process. These products need to undergo regulatory compliance; for NanOss™ the strategy is to obtain 510(k) clearance.

Angstrom Medica's Growth Potential

Mr. Mraz went on to present some of the business criteria important in the exciting and developing market of nanotechnology products. He characterized NanOss™ as a disruptive and enabling technology that has applications in large, existing markets that are profitable with growing demographics and an unmet need for weight-bearing biomaterials. He further forecasted exponential revenue growth for Angstrom Medica over the next five years.

He explained that the projections are contingent on meeting critical milestones such as commercializing first products by 2007 and maintaining availability of funds as the business develops. In addition, key decisions will need to be made along the way. These include defining the optimal business model of license/OEM or produce/sell, assessing potential acquisitions, and determining the best way to present the company's case to the marketplace.

In closing Mr. Mraz presented key takeaways for playing and succeeding in the nanotechnology business (or probably any other business). These are:

1. Develop products, not just concepts.
2. Focus on getting one product to the marketplace at a time.
3. Optimize how the product can bring value to the marketplace.
4. Build value by minimizing risk. ●

Industry News in Brief

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ment led several analysts to lower their 2006 revenue estimates for Biogen Idec and Elan.
(Source: Jeffrey Krasner, The Boston Globe, 23 March 2006).

British Launch Probe of Parexel after Six Hospitalized in Drug Trial

After six patients suffered adverse reactions to an experimental drug, British authorities have launched a "full-on investigation" of the Waltham company running the tests and the German biotechnology firm that invented the drug. Two of the patients remained in critical condition and four appeared to be recovering, according to the hospital treating them.

The affected patients were among eight subjects for tests of an antibody designed to fight leukemia, rheumatoid arthritis, and multiple sclerosis. The two patients unaffected were in a control group that did not receive the drug. The experiment, run by Parexel International Corp., was designed to measure whether the drug is toxic to humans. Such testing is standard for potential new treatments, but the almost immediate hospitalization of the men who received the antibody set off alarms. "We've never had anything like this, ever, and we never want to have it again," said Sara Coakley, spokeswoman for the British agency that regulates drug trials.
(Source: Stephen Heuser, The Boston Globe, 16 March 2006).

The ISPE Boston Area Chapter Communications Committee Needs You…

The Chapter Communications Committee needs your help! We're responsible for communications between the Boston Area Chapter and its members — that includes the Chapter newsletter, published 6 times a year, and the Chapter Web site. In addition, we network with other Chapter Committees to assist with publicity for flagship Chapter events such as the annual Product Show coming up in October.

We need creative folks who will help write articles, maintain the Chapter Web site and come up with new and exciting ways to keep our members up-to-date and promote Chapter events. Committee members need to be deadline-driven individuals willing to make a commitment to the Chapter. A technical background is not necessary.

To join our Committee, meet other hard-working Chapter members and help the Boston Area Chapter succeed, contact ISPE via email at ispe@camihq.com.

Regulatory and Legislative Highlights

by Sean Lyons

Regulatory and Legislative Highlights, *a regular feature of the Boston Area Chapter Newsletter, reviews recent actions by the FDA and other regulatory agencies and governmental bodies, both federal and regional, with the potential to impact the pharma, biotech, and device industries, and related fields.*

FDA and Northfield Laboratories Questioned over Clinical Trial of Blood Substitute

Iowa Senator Charles Grassley has begun an inquiry into the handling of a clinical study by the FDA and Northfield Laboratories, Inc. The clinical study involved the use of Northfield's blood substitute Polyheme in hundreds of hemorrhaging trauma patients. In the study, severely injured trauma victims receive the blood substitute or a saline solution containing human red blood cells. Sen. Grassley has focused on whether patients in the study were made aware of all adverse events with the product and whether it was appropriate to conduct such a trial without the patients' consent. (The FDA occasionally allows exceptions to the usual informed-consent rules under the rationale that it would otherwise be impossible to test a medical product designed to treat trauma patients who may be unable to give informed consent.)

The senator's questions arose based on a report in the Wall Street Journal. The article noted that Northfield had not publicly disclosed the full results of an earlier study in which ten aneurism patients receiving Polyheme had heart attacks, two of whom died. It further noted that anyone choosing not to participate in the study must wear a blue bracelet obtained from Northfield to indicate they have "opted out." Any trauma victim without a blue bracelet may be used as a study participant. Sen. Grassley said he is skeptical that participating medical centers "managed to conduct effective, practical outreach to the community" before beginning the study.

(Source: Thomas M. Burton, The Wall Street Journal, 24 February 2006).

FDA Debates ADHD Treatment Labeling

The Pediatric Drugs Advisory Committee of the FDA is recommending health care providers and patients be better informed about potential (though rare) cardiac and psychiatric side effects associated with drugs used for the treatment of attention deficit hyperactivity disorder, or ADHD, in young people. Medications cited include Ritalin (Novartis), Adderall (Shire PLC), Concerta (Johnson & Johnson) and Strattera (Eli Lilly). The committee stopped short of calling for a "black box" label warning endorsed by an earlier agency panel.

Manufacturers stated they will work with the FDA to address the committee's concerns. Novartis believes its current Ritalin label "accurately reflects" the psychiatric events observed in patients; Johnson & Johnson said it would "wholeheartedly support the FDA's efforts; a Shire spokesman stated the committee's recommendations were "reasonable and fair;" and Eli Lilly said it "supports the FDA's efforts to remain vigilant in reviewing drug safety."

(Source: Jennifer Corbett Dooren, The Wall Street Journal, 15 March 2006; and Anne Wilde Matthews, The Wall Street Journal, 23 March 2006).

FDA Proposing to Charge Fees for Repeat Inspections

The FDA has requested $22 million of its $1.95 billion budget be raised through fees charged to medical device manufacturers requiring re-inspection to ensure that problems identified by the agency are corrected. The proposal must be approved by Congress prior to the beginning of the 2007 fiscal year which starts in October 2006. The FDA spent $22 million on follow-up inspections in 2005; this figure includes staff time, laboratory analysis fees and incidental expenses.

According to Daniel Troy, FDA Chief Counsel, the money is incon-

Briefly Noted

by Janet Tice

The following information briefly describes a few recent regulatory actions affecting local life sciences companies. It is based on an informal review of the local print media only and should not be viewed as a comprehensive survey of local regulatory activity.

Product	Application	Activity
Biovest International		
BiovaxID	follicular non-Hodgkin's lymphoma	seeking "conditional" FDA approval
Cytosol Laboratories		
saline solution	cataract surgery	FDA recall
Cubist		
Cubicin antibiotic	expanded use for Staph aureus bacteremia and endocarditis	FDA "approvable" letter received; amended application for approval submitted
GTC Biotherapeutics		
Atryn	blood thinner	product launch delayed based on expected negative decision by EMA
Alkermes		
Vivitrol	Alcoholism	FDA approval received

Regulatory and Legislative Highlights

Continued.

sequential for large device manufacturers because costs are only incurred as a result of repeat inspections and "the fees are the least of your problems." As an example, Boston Scientific is currently responsible for correcting quality control issues identified by the FDA and could face significant charges if the proposed fee structure is approved; Paul Donovan, a company spokesperson, states Boston Scientific "has long supported user fees as a means of providing the FDA the resources it needs to do its job."

(Source: Diedra Henderson, The Boston Globe, 20 February 2006).

FTC to Subpoena Drug Manufacturers

The Federal Trade Commission has announced plans to subpoena nearly 200 pharmaceutical companies as part of an investigation into anticompetitive pricing practices. The FTC will investigate whether pharmaceutical companies are stifling competition by releasing authorized generic copies of their own brand-name drugs to coincide with the debut of generic challengers made by competitors.

Currently federal law allows generic drug manufacturers a six-month period of exclusivity following a successful challenge to brand-name patent holders during which it is supposed to have the generic marketplace to itself, free from competition. Generic manufacturers rely on this period to recoup costs and begin turning a profit. However, a loophole in the law allows brand-name manufacturers the opportunity to authorize their own generic versions, which hit the market at the same time as the generic challengers. The FTC plans to investigate whether this practice dissuades generic manufacturers from challenging patents and offering competition to brand-name drugs, ultimately leading to higher drug prices.

(Source: The Wall Street Journal, 30 March 2006).

FDA Issues Guidelines for Accelerated Flu Vaccine Approval

The FDA has issued a set of draft recommendations for the development and submission of clinical data showing the safety and effectiveness of new vaccines. The guidelines are contained in two documents, one directed at seasonal flu vaccine makers and the other at companies developing vaccines for pandemic influenza; both are designed to speed the development of new vaccines. Boosting the capacity to produce vaccines against the seasonal flu, which kills 36,000 Americans a year, should put the US in a better position to respond to a potential global outbreak of pandemic flu, which could kill millions, said Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, in remarks he made to a congressional subcommittee.

To some extent, the new guidelines build on FDA policies already in use such as the accelerated-review procedure. This procedure can cut one to two years off the vaccine development and approval process by

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Dates and topics subject to change

Regulatory and Legislative Highlights

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allowing companies to submit clinical data showing that patients developed an immune response to the vaccine rather than waiting for clinical data that shows the vaccine actually prevents the flu. This data would still be required but could be submitted later, after the product is offered to the public. The accelerated-review procedure was used during last year's flu vaccine shortage to allow quick approval for GlaxoSmithKline's Fluarix. The draft guidelines are available at the FDA's Web site www.fda.gov.
(Source: Jennifer Corbett Dooren, The Wall Street Journal and Andrew Bridges, The Boston Globe, both 3 March 2006).

Easing of Biotech Grant Limits Sought

Massachusetts officials and biotech leaders are lobbying in Washington for a law that would permit small companies that are funded primarily by venture capitalists to compete for government research grants that help small businesses fine tune new medical breakthroughs. With the support of the National Institutes of Health, Bay State lawmakers are pushing for passage of bipartisan legislation that would lift current restrictions that disqualify many small biotech firms across New England from receiving Small Business Innovation Research (SBIR) grants. New grant requirements approved in 2003 effectively shut out companies that receive more than 51 percent of their funding from venture capitalists.

Proponents for changing the guidelines say too many Boston-area biotech firms and medical device manufacturers with fewer than 500 employees can't get necessary federal dollars. They contend that the Small Business Administration (SBA) changed the rules to boost so-called "mom and pop" enterprises that have promising ideas but limited access to private investment capital. The consequence has been that small, investor-backed companies with some of the most promising innovations can't get access to federal money that could sustain them during the years of research and fine tuning necessary before these innovations benefit the public.
(Source: Bryan Bender, The Boston Globe, 24 March 2006).

Over 100 Attend January Program...

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tocols and reducing risk of failure. David also brought considerable levity to the evening with his engaging, easy manner with the crowd and a surprise raffle of GMP-related items.

The program ended with healthy applause, and a contingent of attendees lingering about to share ideas with the presenters and one another. These discussions quickly became focused on the next and even more important step: using the practices described by the presenters to reduce project timelines and improve both quality and efficiency within our own organizations and throughout our industry.

Call for Technical Articles

Share your Knowledge with ISPE Members

The Boston Area Chapter Newsletter offers a great opportunity for you to share your technical expertise with fellow members. Authors receive a byline plus a 1-2 sentence profile describing their credentials and company affiliation. So when you submit a technical article for publication you gain visibility for yourself and your organization as well.

Any topic of interest to members is fair game. Members are eager to learn from your experience whether you're directly involved in research, pilot production or scale-up, or provide products or services to the industry. Suggested topics include:

- 21 CFR Part 11
- basic microbiology
- CIP
- chemical sanitization/steaming
- cleanroom technology
- disposable technology
- mixing
- process filtration
- passivation and electropolishing
- Riboflavin testing
- sterile connections
- vessel design
- water quality/water purification

Requirements are simple. Your article must be 1000 words or less (750 words or less with two charts, graphs or photos) and technical, not promotional, in nature. ISPE will provide light editing to correct any spelling and/or grammatical errors. You will be consulted if more extensive editing is required. ISPE reserves the right to accept or reject articles based on technical merit. (Note: Please be sure to review your employer's policy concerning publication before submitting your article.)

To submit an article, email it (in text format with any graphs, charts or photos as attachments) to ispe@camihq.com with the subject header: **Communications Committee - Tech Article**. Your contribution will provide valuable information to your fellow ISPE members, strengthen the Boston Area Chapter and provide publicity for you and your organization - so don't delay!

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