Boston Area Chapter
ENGINEERING
PHARMACEUTICAL
INNOVATION

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NEWSLETTER
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Chapter Tours Massachusetts Biologic Laboratories (MBL)

by Allan MacDonald

ISPE Membership certainly does have its privileges. More than 60 members toured the newly opened Massachusetts Biologic Laboratories (MBL) facility in Mattapan on 16 November 2005. The 150,000 square foot facility was built on a 15-acre portion of the former Boston State Hospital. The cost of the facility once it has been equipped and started up will be about $100 million. Although MBL is publicly owned, the facility is expected to be self–supporting based on the income from the vaccines and other therapeutics to be manufactured there.

Larry Weiner presents to an eager group of tour participants.

Our hosts for the evening from MBL were Larry Weiner, Director of Engineering and Doyle Johnson, Facilities Director. Larry and Doyle gave an excellent presentation before the tour that described the project from conception through construction and commissioning. We were guided through the facility in groups of about 10. In each of the main areas toured, there were stations where Subject Matter Experts (SMEs) explained the features and functions of the equipment and facility. Many stations were enhanced by video clips of a process in operation.

The organization of the tour was superb. Each group was able to tour both the production areas as well as the utilities areas that support the facility. The production areas include a monoclonal antibody manufacturing operation within Class 10,000/100,000 clean suites. Bioreactors as large as 2500 liters are installed in the suites.

As commissioning was not complete, we were able to enter areas that allowed better views into the clean suites than will be possible for visitors once the facility is in full production. The fill finish operation includes automated vial filling that operates at more than 300 vials a minute with fill weight checking. Automated controls are used extensively throughout. Each vial can receive a UV visible 2D matrix label, which is verified using a UV strobe and camera arrangement. Other vision systems verify that the packaging includes the appropriate inserts.

The materials handling and inventory systems are run from hand held devices that are tied to an inventory control system. These units instruct staff in the handling and disposition of all items from receiving dock through storage, dispensing, and delivery to the user. The warehouse and refrigerated storage incorporate a multi-tiered pallet rack system that was 35 feet tall. Computer systems allow documentation of all of the components that have gone into a particular batch and tracking of all the products that have

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President's Message

Dear Boston Area Chapter Members,

During this holiday season, I am pleased to report that the Chapter held a very successful Toys for Tots benefit at our annual Boston Area Chapter holiday bash which took place this year at F.E.L.T. in Boston. This well-attended event attracted many Chapter Members and guests who enjoyed an evening of networking and sharing holiday cheer. I'd like to thank all who attended and contributed toys and donations for children in need from our area. And thanks to the Marines who once again collected our donations at the event for this worthy cause.

As we begin the New Year, our Chapter Committees continue to work hard in their pursuit of excellence in providing educational and networking opportunities for our Members. A lot of work happens behind the scenes to make our events possible. Here is a summary of some of their activities and achievements.

The Student Affairs Committee has been busy maintaining five Student Chapters (a record high for our Chapter!), located at Northeastern University, UMass Lowell and Amherst, Tufts University, and the University of New Hampshire; and as result of the diligence, our Chapter won an ISPE excellence award for Student Chapter Development. Also, please join me in congratulating Bhawna Gupta from Northeastern University. She won the Student Poster Contest in the Graduate Student category at the competition held during the ISPE Annual Meeting in Scottsdale, Arizona this past November. Congratulations Bhawna!!

The Educational Programs Committee delivered two Talking Shop programs at the 14th Annual Product Show held on 25 October; Disposable Process Systems and Commissioning as Project Quality. And, on 16 November the Massachusetts Biologic Labs (MBL) graciously opened their doors for us to tour their new state-of-the-industry production facility in Mattapan. Big thanks to the entire MBL staff who work hard to bring us the highly successful plant tour. Keep an eye out on our Web site at www.ispe.org/boston for details on our upcoming educational and social programs. Lots of great events brewing for 2006.

The 2005 Product Show Committee wrapped up another successful show this year. Our 14th Annual Product Show featured a keynote address by the Lieutenant Governor Kerry Healey. 590 attendees joined us for the event despite the unexpected nasty weather that day. The show featured 150 company exhibits as well as the usual good food and company. And, the Product Show Steering Committee has already started planning for next year. The 2006 event is going to be bigger and better than ever; stay tuned for details over the coming months.

The Member Services Committee has been diligently working to grow our Chapter. Their efforts are showing as we approach 1200 this year. Another task of the Member Services Committee is to make sure we're offering programs and events that are in line with our membership's interests. If there is a topic that you would like to have addressed, we'd appreciate hearing from you.

And last, but certainly not least, I'd like to recognize the Communications Committee whose tireless efforts produce this informative newsletter every two months.

Best regards and Happy New Year!

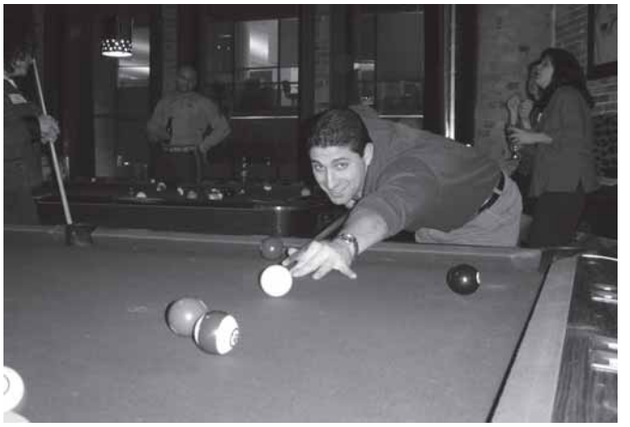
Niall Johnson
President, ISPE Boston Area Chapter

Holiday Social and Toys For Tots Event

by Doyle Johnson

On Wednesday, 7 December, the Boston Area Chapter held its annual Holiday Social and Toys for Tots Event at F.E.L.T. Boston. Seventy-four people enjoyed appetizers, drinks, pool, and the presence of three Marines – Staff Sgt. Thomas Miles, Sgt. Omar Maldonado, and Sgt. Norm Colon. In addition to a sizeable collection of toys, attendees also donated $285 to the Marines' Toys for Tots program. ISPE logo shirts and two $100 American Express gift certificates were given away as raffle prizes. Although the party officially concluded at 10 pm, there are reports that some Members stayed out dancing until 4 am! This would represent a new record for the ISPE Boston Area Chapter. ●

From left to right: Marine Staff Sgt. Miles, Sgt. Maldonado, and Sgt. Colon



Playing Pool!

Cleaning In Place

by Pietro Perrone

This section highlights subjects that are related to the biotechnology or associated industries. It features items that are of general interest as well as articles that could be directly applicable to your job.

Introduction

This article introduces CIP operations, the top-rated technical topic identified by a recent readers' survey (see June 2005 newsletter). It is intended as a general introduction to CIP and identifies general, but important topics that are considered in defining appropriate CIP protocols. The more in-depth CIP issues and concepts and how they apply to specific unit operations will be featured in future newsletters.

Since cleaning is a big part of any processing plant, there should be many readers experienced in CIP operations. If this describes you, we invite you to submit an article that could be used in a future column. The article should deal with CIP and focus on specific unit operations such as vessels, fermentors, filtration systems, heat exchangers, chromatography equipment, etc. Please forward your article to christine_lindberg@yahoo.com.

Cleaning In Place

Cleaning is one of the most prominent operations in pharmaceutical/biotechnology plants. Although it is often one of the first operations done during a processing plant's commissioning activities, it typically gets addressed after the processing functions are defined and detailed. This can result in an operation that does not use the equipment at its optimum design point relative to all of its operating situations.

Most processing equipment spends a substantial amount of its lifetime in a cleaning mode. The best operating process can consist of a cleaning time in the range of 10 to 20 percent of the processing time. However, it is more typical that the cleaning time is in the range of 30 to 50 percent of the processing time. In some extreme cases where batches are small, the equipment could spend more time cleaning than processing. This causes a significant impact in the efficiency of the operations and one that warrants attention. A proper cleaning design will minimize the time (and cost) that the processing equipment needs to stay in clean mode while maximizing the productivity of the equipment.

During the design of processing equipment, it is best to keep the critical parameters that can impact the cleaning of the equipment at the forefront of the PFD and the P&ID development. An understanding of the primary factors of a proper cleaning should help in identifying areas that need attention during the design phase of a process.

Contributors to Effective CIP Protocols

Contributors to effective CIP protocols include the following:

1. Temperature
2. Chemical Concentration
3. Fluid Motion/Agitation
4. Time

These factors and their interdependence have a direct impact on the effectiveness of the cleaning operation. Although each factor may take a leading role in a specific step of the cleaning cycle, they are all interactive and all contribute to overall cleaning effectiveness. For example, in a rinsing protocol, the temperature of the solution and fluid motion have the leading roles. The chemical concentration and time, although important, have a secondary role.

A chemical solution protocol is most dependent on the chemical concentration. However, temperature is a close second as the activity level of the chemical solution is impacted by the temperature: a higher temperature results in higher chemical activity. Once the chemicals loosen the contaminants, maintaining the level of chemical activity depends on moving the contaminants away from the surface. The fluid motion/agitation comes into play for this function. At the base of all these actions is the amount of time the surface to be cleaned is exposed to the chemical solution. A longer amount of exposure time is not always best since re-deposition can occur if the contaminants removed are allowed to re-circulate on the surface. An optimum time of exposure is usually developed for the cleaning operation. This time is optimized for getting the most chemical exposure activity in the fastest time.

Cleaning Protocol

A generalized cleaning protocol consists of the following steps:

1. Rinse
2. Chemical Solution
3. Rinse
4. Chemical solution
5. Rinse

This simple protocol is the foundation upon which most cleaning programs are based. Although variations (more steps) may be implemented, the return-on-investment for the additional steps is often only justified for very difficult-to-remove contaminants or the need for an extremely low level of residual contaminants. A brief description of each step is provided below.

Rinse

This is the initial rinse that flushes out any residual process fluid. Promptly executing a rinse operation after finishing processing maximizes cleaning effectiveness and minimizes the chemical solution concentration needed in subsequent steps.

Chemical Solution

Typically, the first chemical solution consists of an alkaline (NaOH or

Cleaning In Place

Continued.

equivalent) solution that removes proteinaceous components from the surface. The high pH level is most effective at removing oils, fats, and proteins. Other additives such as detergents and/or sodium hypochlorite (NaOCl) also may be added.

Rinse

This rinse is to flush out any chemical solution remaining after that cycle is complete and the solution drained.

Chemical Solution

Typically, the second chemical solution consists of a low pH solution that targets the removal of mineral components that become soluble in acidic conditions.

Rinse

This final rinse is to flush out any chemical solution remaining after that cycle is complete and the chemical solution drained. Complete drainage at the end of this step will minimize the presence of any residuals contaminants.

The effectiveness of the chemical cleaning is dependent on the quality of the chemicals used in making up the solutions. It is important that any additives and their effects be understood before incorporating them into the cleaning protocols. Additives, such as chelating agents or detergents, may resolve one issue while creating another. It is also important that the water used for the cleaning protocols be of reasonably good quality.

Two deleterious effects can result from poor quality water. The first is that the chemical cleaning solution may be impacted by the chemicals/components present in the source water. The second is that the effectiveness of the rinsing steps may be compromised by contaminants present in the water. The quality or purity of the rinsing water is especially critical during the later rinses. The final rinse is best done with WDI or WFI to eliminate any trace of chemicals.

Conclusion

Efforts directed at developing and properly executing cleaning programs can pay significant dividends. These efforts include: addressing CIP concerns at the design phase of projects, selecting cleaning operations consisting of a combination of: 1. proper chemical selection, 2. sufficiently elevated cleaning temperature, and 3. high fluid turbulence, and using these in CIP sequences that systematically remove the various contaminants. Following these simple rules will maximize equipment utilization and minimize operating costs. ●

New Member Spotlight - Greg Troiano

__New Member Spotlight__, a regular feature of the Newsletter, seeks to introduce a new Member of the ISPE Boston Area Chapter to our existing membership.

Where did you grow up?
New York, just north of Manhattan.

Where did you go to school (college)?
I received a BS and MSE in biomedical and chemical engineering at the Johns Hopkins University in Baltimore, MD.

What are your hobbies?
Most anything sports related, especially rock/ice climbing and mountaineering when I have time.

How do you spend time with your family?
Hiking, cooking, eating, and reading stories to the little ones.

What do you do?
I'm an engineer and manager for Alkermes, a mid-sized pharmaceutical drug delivery company. We work on process development from pre-clinical to commercial manufacturing.

What do you like best about your job?
I enjoy the unique challenges that come with every project. My favorite activity is designing new processes or unit operations.

How did you get to where you are today?
I've worked in a formulation or process development group for two companies over the last eight years.

Where do you see yourself in 5-10 years?
Hopefully, still helping Alkermes mature its processes into world-class commercial production plants. We should have a number of products moving into late stage clinical or commercial manufacturing over the next decade.

Greg Troiano and his children.

What ISPE activities have you participated in?
Most recently, I attended the 2005 Annual Meeting in Scottsdale. I especially enjoyed the education sessions at the meeting. These sessions provided good information on pioneering technologies in the topics most interesting to me, such as aseptic processing and Process Analytical Technology (PAT). I've also attended a number of small seminars in the Cambridge area over the last five years.

Where do you see the pharma/biotech industry going over the next five years?
I think the biggest change will be the move to more efficient manufacturing processes. I believe the FDA's PAT initiative as well as the desire for more cost-effective plants and products has helped drive this effort. I believe we will continue to tap into other industries to share their expertise in manufacturing excellence.

What changes have occurred in your field?
The change in the FDA's philosophy over the last decade to a more reward/risk based approach has helped ease many of the inefficiencies in our industry. I think we still have a long way to go, but I think we are moving in the right direction.

What is your favorite biotech term, product, or process?
I love the processes to make microspheres for controlled release therapeutics, which has been the main area of focus for my entire career. These processes and products are stimulating to me because of the challenges each Active Pharmaceutical Ingredient (API), polymer, excipient, and solvent brings to the table.

How do you balance the demands of your career while continuing to stay current?
I try to attend training sessions or seminars that are both relevant to my company, but also provide perspective on the rest of the industry.

What publications do you read?
A number of monthly chemical engineering publications, *Pharmaceutical Technology*, *Drug Delivery Magazine*, and the newsletters from both ISPE and the American Association of Pharmaceutical Scientists (AAPS).

Which publication do you find the most worthwhile to read?
I enjoy the chemical engineering publications because they provide information and ideas spanning multiple fields of study that can often be applied to our processes.

What is the biggest challenge in your current position?
Balancing the desire as a scientist to gather as much information as possible with the desire as a manager to be efficient and meet timelines.

Currently, what do you see as the biggest challenge for the pharma/biotech industry?
Trying to break out of the current mold of rushing products through the clinical trials and neglecting the appropriate process development before building commercial facilities. If we invest a little more up front, it will go a long way toward saving us manufacturing headaches.

If you weren't in the pharma/biotech industry, what other profession do you see yourself in?
Probably the food industry. Or if I had enough money in the bank: a climbing guide.

How do you balance the demands of your career and the needs of your family?
Having two children in the last three years has forced me to change my schedule and routines. I now get up before the roosters crow so that I can get to the gym by 5:30 am, and I try to be as efficient and effective as possible at work. This usually allows me to get home and enjoy dinner with my family and an hour or two to play with my children before tucking them in.

What advice would you give new graduates planning a career your field?
Be open minded about the methods and processes you explore. Don't take for granted that the way our industry traditionally does something is the best way. ●

Boston Student Wins Poster Competition at the ISPE Annual Meeting

by Rick Pierro and Dave Novak

More than 2000 attendees were witness to the Annual awards event held in Scottsdale, Arizona during the ISPE Annual Meeting held in early November 2005.

Bhawna Gupta, a graduate student at Northeastern University and a Member of the ISPE Boston Area Student Chapter, won the graduate level in ISPE's International Student Poster Competition.

For the ISPE Boston Area Chapter, Bhawna's win was the culmination of a personal goal set by Bhawna last year, during the local Chapter Poster Competition.

"It is this drive and goal setting by our Student Members that inspires us to pursue more Student Chapters within our region," stated Mike Denault, Vice President of the ISPE Boston Area Chapter.

Rick Pierro, ISPE Boston Area Chapter Board Member and Student Development Chair stated, "Our Chapter's goal is to increase student involvement in ISPE both in local and International activities and it was decided by the judges and confirmed by the board that we send three deserving student winners to compete nationally at the ISPE Annual Meeting."

And what is the Poster Competition? It's a high-pressure event where each student presents a five to 10 minute verbal summary of their research, using a detailed poster to illustrate very advanced and complex information for the judges. The judges add to the tension by quickly firing questions at the delegates to see how well they know and how well they can communicate the subject matter.

ISPE Chairman Gert Moelgaard with Bhawna Gupta.

Not only did Bhawna graciously help fulfill her goal of winning... but the Boston Area Chapter received the Chapter Excellence Award for Student Development, an award given to only one of the 16 North American Chapters each year.

Again, we must congratulate our student poster representatives Bhawna Gupta, Dennis Callahan, and Tamer Elbayoumi, whose hard work and preparation allowed them to compete at the international level. The ISPE Boston Area Chapter Members were impressed with their professionalism throughout the competition and conference. Thank you again for representing our Chapter so well. We urge you to stay involved with ISPE and local and national activities.

You are the focus and the future, and will help us in our Chapter's and International's goal to "Engineer Pharmaceutical Innovation." ●

Industry News in Brief

by Janet Tice

***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.*

Alnylam Halts AMD Drug Development, Proceeds with iRNA Technology

Citing increased competition, Alnylam Pharmaceuticals has suspended development of a treatment for Age-related Macular Degeneration (AMD), a leading cause of blindness in the elderly. In January, Pfizer and Eyetech Pharmaceuticals launched their AMD drug Macugen; and in July, Genentech announced highly favorable phase 3 data for the AMD drug Lucentis, which it is co-developing with Novartis AG.

On a brighter note, Alnylam has applied to the FDA to start human testing of an experimental drug to treat respiratory syncytial virus, a common disease that can cause pneumonia in infants and the elderly. If approved, the trial would be the first by the three-year-old firm and among the first-ever trials based on RNA interference technology. If the application is approved, Alnylam expects to begin testing the drug by the end of the year.

(Source: The Boston Globe, 21 September and Stephen Heuser, The Boston Globe, 11 November 2005).

Shire to Hire 50 at Former TKT Location

Shire Pharmaceuticals Group has said it plans to hire 50 employees at the former headquarters of Transkaryotic Therapies in Cambridge which it purchased in July. The expansion is intended to prepare the company for the anticipated launch next year of a drug to treat the rare genetic disease Hunter syndrome. David Pendergast, General Manager of the Cambridge operation, said fewer than 20 people were laid off when Shire integrated support functions with the former TKT. The Cambridge division has about 400 employees, roughly the same as when TKT accepted a $1.6 million takeover offer from Shire in April. Some of the new jobs were posted in the spring, before the acquisition was completed, but hadn't yet been filled. "The message here is a continued commitment to genetic diseases," Prendergast said.

(Source: Jeffrey Krasner, The Boston Globe, 7 September 2005).

Cubist Files with FDA to Expand Use of Antibiotic

Lexington-based Cubist Pharmaceuticals has won an expedited review of its application to market the Cubicin antibiotic, already approved for treatment of skin infections caused by heart and blood infections. This means the FDA will rule in six months, instead of the standard 12, on Cubicin's effectiveness in complicated infections of the blood and the heart's inner lining and valves.

Cubicin works on certain infections caused by Staphylococcus aureus regardless of whether the bacterium has developed drug resistance, allowing doctors to treat the disease without running lab tests. Cubist's application to enter the market, worth about $1 billion annually was helped by a study of 236 patients with dangerous staph infections that resist treatment by other antibiotics.

(Source: The Boston Globe, 7 September and 22 November 2005).

Genzyme Invests $210 Million in Massachusetts Expansion

Riding a wave of acquisitions and upbeat financial news, Genzyme Corp. recently announced a November start for construction on its largest research facility to be located in Framingham. The building is part of the company's $210 million manufacturing and research expansion, which also is adding new labs in Waltham and two bioreactors at its flagship protein-manufacturing facility in Allston.

The Framingham lab, scheduled to open in 2007, will initially be home to about 200 scientists now scattered across Genzyme's sprawling campus in Framingham and could eventually house more than 300. Their focus will be early-phase research on genetic diseases, cancer, kidney disease, and other areas key to Genzyme's long term business strategy. The new lab is expected to serve the company's Massachusetts lab space needs through 2010.

Based on its current market value of $18 billion, Genzyme is the largest biotech company in Massachusetts and is second only to $19.7 billion medical-device maker Boston Scientific in the life sciences sector. The state's biotech leaders have hailed Genzyme's news as a validation of Massachusetts' argument that that the state's relatively high development and housing costs are more than offset by the area's extensive biotech and medical expertise in terms of its ability to attract and retain leading life science companies.

(Source: Stephen Heuser, The Boston Globe, 5 October 2005).

Wyeth Hires Vaccine Pioneer

In a coup for drug maker Wyeth, Emilio Emini, a pioneer in HIV vaccines, is joining the company to head vaccine research and development. Dr. Emini comes to Wyeth from the International AIDS Vaccine Initiative, where he was senior vice president for vaccine development. Before joining IAVI in 2004, Dr. Emini worked for two decades at Merck & Co., where he led work on AIDS vaccines, the development of Crixivan, a protease inhibitor that helped doctors treat AIDS as a chronic illness, and oversaw development of vaccines for shingles, cancer-causing viruses, and diarrheal disease.

Wyeth is one of the few US drug makers still active in the vaccine business. It sells Prevnar, a vaccine for pneumococcal disease, and Meningitec, a bacterial meningitis vaccine, and is working on new generations of those vaccines as well as new ones against Alzheimer's disease, HIV infection, and sexually transmitted diseases.

(Source: Scott Hensley, The Wall Street Journal, 2 November 2005).

Millenium to Cut 100 Jobs and Focus on Cancer Drugs

Millenium Pharmaceuticals Inc. has said it will cut about 100 jobs, 8 percent of its workforce, and abandon work on some treatments for inflammatory conditions to focus on cancer drugs. The company also will move out of some office space near Kendall Square.

Industry News in Brief

Continued.

The move marks the latest retrenchment by Millenium, once seen as Cambridge's most promising drug-discovery company, and the culmination of a strategic review that Chief Executive Deborah Dunsire began in June when she replaced longtime chief executive Mark Levin. Dunsire said the moves were necessary to get products now in clinical trials on the market, while keeping in place financial targets for next year. "These moves put us in a strong position to achieve [financial] targets through organic growth so we don't have to go out and strike a big partnership to achieve the goal," she said.

Millenium still aims to bring to market products to treat inflammatory diseases such as rheumatoid arthritis and multiple sclerosis that are now in clinical trials, but will wind down discovery efforts in those areas. The company will end up with 300 drug-discovery scientists, compared to 760 several years ago.

Millenium had about 1,500 employees at the end of 2004 and about 1,450 in July when Dunsire disclosed her first major initiative to sell additional rights to Schering-Plough for the heart drug Integrillin. That resulted in the loss of 200 jobs, mainly in Integrillin's sales force, though the majority of the affected employees were offered positions with Schering-Plough.

(Source: Ross Kerber, The Boston Globe, 27 October 2005).

Biopure, Biogen Execs Resign Abruptly

September saw the abrupt resignations of two high-level life sciences executives, Michael Gilman, executive vice president in charge of research at Biogen Idec Inc. and Carl Rausch, co-founder and chief technology officer at Biopure Inc.

As chief executive and chairman of Biopure from 1984 to 2002, Carl Rausch became one of the best known biotech execs in Massachusetts. Biopure had targeted oxygen therapeutics, specifically the development of a blood substitute called Hemapure. Although the military was initially interested in Hemapure for use on the battlefield, the FDA withheld its final approval. The company is currently pursuing the use of Hemapure as a treatment for heart attack patients who suffer from cardiac ischemia.

Although Biopure stock once sold as high as $300 per share, it recently stood at $1.50, reflecting the difficulties the company has had bringing product to market. To add to its financial woes, Biopure has been the target of a long-running Securities and Exchange Commission investigation which recently culminated in a civil suit against the company and several of its current and former execs, though Rausch is not among them.

Challenges also have befallen Biogen Idec (see related article below). In February, the company halted sales of Tysabri, its drug for multiple sclerosis after receiving news that several patients taking the drug had developed a rare brain disorder. Though no direct connection has been proven, the company has had to spend precious time and

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Regulatory and Legislative Highlights

by Janet Tice

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 May Scrap Plan to Require Longer Psychiatric Drug Studies

The FDA will likely scrap a plan to require drug makers to submit longer-term studies on how well proposed psychiatric drugs work as a condition of approval, following a unanimous vote against the idea by a panel of outside medical experts. The FDA had convened the panel to discuss requiring longer-term premarket efficacy data on drugs used to treat bipolar disorder, schizophrenia, and a range of other psychiatric illnesses.

Advisory panel members were unanimous in their view that the current system of allowing drug companies to conduct long-term efficacy studies *after* the drugs are put on the market was better than the FDA proposal. In order to have a drug approved, companies typically submit studies that compare patients on a drug to those on a placebo for six to 12 weeks. The studies are designed to show whether a drug is safe and effective at treating psychiatric disorders in the acute, or short-term, phase of the illness. Longer-term safety data also is submitted prior to approval, but the long-term safety studies are not designed to assess efficacy.

The FDA said the issue is that many patients need to be on medication long-term. Though long-term efficacy studies eventually do get done, there is little initial guidance for clinicians on how to use drugs for the first few years they are on the market.

(Source: Jennifer Corbett Dooren, The Wall Street Journal, 26 October 2005).

FDA Hits Quality Control at Guidant Pacemaker Plant

Guidant Corp. failed to ensure the quality of heart-implant devices during manufacturing and did not quickly warn physicians about software glitches that caused some pacemakers to fail, according to a 79-page document filed with the FDA by the manufacturer. The document described problems found by the Agency in an August inspection of the company's Minnesota manufacturing plant. According to the FDA findings, Guidant lacked an effective quality control system at all levels and its record-keeping was poor with little accountability for errors.

The August inspection was an outgrowth of the July Class 1 recall of certain Guidant pacemakers. The July recall was based on FDA conclusions that a seal within the devices could leak, allowing moisture to affect the electronic circuitry, which in turn could cause the devices to malfunction, leading to loss of consciousness, and possibly heart failure and death. In response to the FDA inspection, Guidant said it is reviewing safety procedures companywide and will change labeling on some devices to specify how many fail. It also stated that none of the FDA findings impact the "safety or effectiveness" of Guidant's products.

(Source: The Boston Globe, 28 October 2005 and FDA Web site, 21-22 July 2005).

Boston Research Labs Face New Safety Checks by City Officials

In a move that could constitute the most stringent municipal regulation of biological research in the nation if enacted, Boston city officials have proposed new safety rules governing research laboratories working with dangerous microbes in universities, hospitals, and biotech companies across the city. The proposed rules were developed by an eight-member lab safety panel convened by public health authorities and must be approved by the Boston Public Health Commission before they can take effect.

The proposed rules would require labs to receive safety permits from the city and mandate that neighborhood representatives sit on internal safety boards. Regular inspections of labs by internal reviewers and by a city inspector would also be required. Furthermore, facilities working with especially potent viruses and bacteria, including those that have been identified as potential tools for bioterrorists, would have to provide a list of those organisms, as well as an explanation of the research to city health authorities. Currently, only the federal government has access to such sensitive information.

The proposal represents a significant expansion of lab regulation. It comes 10 months after public disclosure that three Boston University scientists had fallen ill while working with tularemia, a lethal bacterium. City health authorities have acknowledged that it is a direct response to the tularemia exposures, as well as concerns from neighbors about the high-security Biosafety Level 4 lab that BU wants to build on its South End medical campus.

(Source: The Boston Globe, 15 November 2005).

Fears of Post-Vioxx "Overcaution" by FDA Appear Unfounded

Drug company officials, Wall Street analysts, and others have predicted that FDA would slow approval of new therapies after safety problems forced Vioxx off the market last year. But recent votes by federal advisory groups – whose actions are typically heeded by the FDA – suggest that those worries are misplaced. For instance, after two days of testimony in September, advisors recommended that the FDA approve three of the four cancer drugs up for consideration.

The drug industry pays especially close attention to advisory panels that assess cancer drugs because such products have the greatest revenue potential – a total of $11.2 billion in 2004. Plus, it is a segment of the market that is especially crowded – with 400 cancer drugs in the pipeline – and also is littered with failures.

Merck & Co.'s decision to pull the painkiller Vioxx triggered congressional hearings and a flurry of proposed bills designed to improve drug safety. Many who track the pharmaceutical industry worried a newly cautious FDA would delay drug approvals. Though the recent

Regulatory and Legislative Highlights

Continued.

positive actions bode well for the industry, the true impact of Vioxx on the approval process may not be known until the end of the year when the FDA grades itself on deadline performance.
(Source: Diedtra Henderson, The Boston Globe, 21 September 2005).

FDA Acts on Applications for Drug Approvals

Actions recently taken by the FDA include the following:

- The FDA recently granted approval to Pfizer to expand use of the drug Aromasin, an aromatase inhibitor for treatment of early stage breast cancer. The drug was first approved in 1999 to treat advanced breast cancer in postmenopausal women whose tumors had stopped responding to tamoxifen. Like tamoxifen, aromatase inhibitors are designed to block estrogen in postmenopausal women diagnosed with estrogen-sensitive tumors.
  (Source: Jennifer Corbett Dooren, The Wall Street Journal, 6 October 2005).
- In September, the FDA approved the Johnson & Johnson drug Remicade for treatment of ulcerative colitis, an inflammatory bowel disorder. The intravenous drug had already been approved for treating other diseases, including rheumatoid arthritis and Crohn's disease, and currently generates $2.1 billion in annual revenue for J&J.
  (Source: Daniel Rosenberg, The Wall Street Journal, 26 September 2005).
- In a setback for Celgene Corp., the FDA has said it needs more time to review the company's application for Revlimid, a drug designed to treat a serious blood disorder that can lead to cancer. An outside panel of medical experts had recently voted to recommend the Agency grant approval for the drug.
  (Source: Jennifer Corbett Dooren, The Wall Street Journal, 4 October 2005).

FDA Chief Resigns – Cancer Official Named as Acting Head

Lester Crawford, confirmed just two months previous to run the FDA, abruptly resigned on 23 September. The FDA offered no explanation, but people familiar with the matter said it was connected with stockholdings he may have failed to disclose. The investments of an FDA commissioner would be a particularly sensitive issue because of the Agency's broad influence over about 20 percent of the US economy. Plus, conflict-of-interest issues at the FDA are under a special spotlight because of a series of drug safety problems that arose last year, leading to questions about whether the Agency is tough enough on the industry.

The White House reacted to the resignation by immediately appointing Andrew von Eschenbach, the Director of the National Cancer Institute, as acting Head of the Agency. Dr. von Eschenbach, a cancer-survivor and high-profile surgeon, has been backed by patient groups and seen as a strong advocate of rapid progress toward better treatments for cancer. In fact, only two days after his appointment as acting head, he said he would like to examine whether the drug-review process needs changes to "streamline and accelerate" the approval of promising new therapies.
(Source: Anna Wilde Mathews, Sarah Lueck and John D. McKinnon, The Wall Street Journal, 24 and 26 September 2005).

Baxter Drug Pumps Seized by Federal Officials

FDA investigators and US marshals took the unusual step in October of seizing 6,850 Baxter International Inc. drug-infusion pumps from company warehouses after federal regulators concluded the company has taken too long to fix production and design problems. 6,000 of the confiscated units were Colleague drug pumps that were earlier withdrawn from future sales after being implicated in three patients' deaths and six serious injuries over the past two years. The remaining units, pulled from future sales in July, were Syndeo PCA syringe pumps used by patients to self-administer pain medication.

With regard to the Colleague infusion pumps, the FDA had said in July that the pumps had electrical, software, and basic design flaws that could affect all models on the market. The Syndeo units had not been implicated in any deaths or serious injuries, though patients had been notified that the units could stop infusing pain medication and sound an alarm. Baxter said it is working with the FDA and has a corrective action plan in place, but it declined to discuss the FDA's con-

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October Product Show – An Exhibitor's Perspective

by Bob Perry

From my perspective, the 14th Annual Product Show was a great success. I understand Dave Novak introduced Massachusetts Lt. Governor Kerry Healey who spoke on the "Future of Biotechnology in Massachusetts." The Lt. Governor talked about how great this area is for our industry because of the pool of talented workers and the existence of excellent universities to supply future talent. In answering a question from the floor, she acknowledged that extensive "red tape" exists in the Commonwealth, but she promised to work to help simplify the process. My understanding of the keynote address is second hand because I did not attend the address myself. You see, I was an exhibitor at this year's product show and was late setting up our exhibit!

As a service supplier to the biotech/pharma markets, my company exhibits at several product shows each year. I have to admit, booth duty at most product shows is not one of the highlights of my career. The Boston Product Show is the exception to this rule. This is in small part because I've lived in the Boston area most of my life so I know a lot of the people at the Boston Product Show. The main reason I enjoy the Boston Product Show is it is consistently the best product show I attend or exhibit at.

Over the years, I've attended technical seminars and workshops at the Boston Product Show. The quality of these seminars is excellent, as exhibited by the standing room only crowds of previous years. Feedback on this year's Talking Shop discussions from attendees that I spoke with was very favorable. We are fortunate to have so much talent in our local association.

In establishing our annual marketing budget, the ISPE Boston Product Show is always given top priority. From a vendor's perspective, the technical interaction, the social interaction, the vendor networking, and the quality of leads generated is excellent. If you are contemplating exhibiting at next year's Product show I encourage you to do so. Don't wait too long as space is limited and always sells out.

2005 ISPE Boston Area Chapter Product Show Floor (Photo courtesy of Peter Teague, Boston Scientific).

If you've never attended the ISPE Boston Product Show I encourage you to do so. You will find it to be the best four to five hours you invest in your career each year. Where else can you get top quality technical seminars/workshops, several vendors for each of your needs, and great food/drink under one roof and not have to miss a whole day's work? Your "problem" is an opportunity for many of the exhibitors. Ask your question or state your problem to an exhibitor or fellow attendee. You'll be surprised how much good advice you will get. Did I mention that the food is absolutely fantastic! I hope to see you at the 15th Annual Product Show. ●

Regulatory and Legislative Highlights

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cern with the pace of corrective actions.
(Source: Thomas M. Burton, The Wall Street Journal, 14 October 2005).

State Senate Plan Would Boost Investment in Sciences

Senate leaders, worried that Massachusetts is lagging in science and technology, recently announced plans for a $50 million life sciences program and a state office charged with bringing high-speed Internet access throughout the state. The initiatives are included in a $500 million economic development package currently under consideration in the Senate. They stem from a growing concern that Massachusetts needs to work harder to keep pace with states that have invested more aggressively in the sciences and with Asian countries that place a greater emphasis on math and science in their schools.

The initiative includes a life sciences center similar to the Massachusetts Office of Business Development, which gives grants, loans, and other financing to companies looking to build in the state. Other key components include a $35 million investment in an $80 million facility proposed for UMass-Lowell and $10 million toward a smaller, similar facility at UMass-Dartmouth where university researchers and private companies would work together toward commercializing a variety of technologies in the areas of nanotechnology and biotechnology.

The plan also includes funding for a study to determine how to make broadband or wireless Internet available from Pittsfield east and a new Wireless and Broadband Affairs office. Other cities, notably Philadelphia and San Francisco, are already working toward citywide wireless networks, but no states have yet done so. Along with the Internet and life sciences center initiatives, the senate plan would allocate new funding for math and science education in the areas of teacher training and student internships at engineering and other high-tech companies.
(Source: Scott Helman, The Boston Globe, 2 November 2005). ●

Industry News in Brief

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resources re-establishing the drug's safety while losing the revenue it would otherwise generate. It recently announced the layoffs of 650 of its 4000 employees and the sale of its Tysabri plant in Oceanside, California in a cost-cutting measure. Though Gilman has not been directly implicated in the drug's potential imperfections, much of the commercialization of Tysabri occurred "on his watch" and he was a high-visibility executive when the bad news was delivered.

(Source: Ross Kerber, The Boston Globe, 7 September 2005 and Dyke Hendrickson, Mass High Tech, 19-25 September 2005).

Biogen Idec Profits Down, Prospects Up

Biogen Idec Inc. announced in October that its third-quarter profits dropped 26 percent compared to the previous year. Extraordinary charges that put a drag on earnings included write-downs related to the 2003 merger between Biogen and Idec, expenses due to layoffs begun in September 2005, and losses expected from the sale of a California manufacturing plant.

On a brighter note, the company announced in November that it had won priority review by the FDA for its application to return multiple sclerosis drug Tysabri to market. The priority designation means the Agency should rule on the application by late March 2006. Tysabri was voluntarily withdrawn from the market in February 2005 by Biogen Idec and its partner, Elan Corp. of Ireland, after a patient taking the drug died of a rare brain disease. In its application, the company submitted data from a stand-alone trial of Tysabri and a trial of Tysabri taken in combination with Avonex, its other MS drug.

In a second favorable development, the company said its cancer drug Rituxan showed positive results in treating patients with rheumatoid arthritis. The patients in the trial either did not tolerate or did not respond well to existing treatments for the autoimmune disease characterized by swollen, painful, and deformed joints. The findings were included in the company's application to the FDA seeking approval to sell the drug for the additional condition. The FDA has granted priority review to the application and is expected to announce its decision in early 2006. If the application is approved, it could dramatically increase sales of the drug, co-marketed in the US with Genentech.

(Source: Jeffrey Krasner, The Boston Globe, 27 October 2005 and The Boston Globe, 17 and 21 November 2005).

Novartis Targets Vaccine Market with Buyout Bid for Chiron

Flu vaccine manufacturer Chiron Corp. announced in November that its Board of Directors accepted a $5.1 billion takeover offer from Swiss drug giant Novartis AG, which already owns 42 percent of the company. Chiron touched off a public health crisis in the US last year when it failed to deliver half of the nation's expected stockpile of flu vaccine due to contamination issues at its UK plant. Novartis has vowed to "turn around" the Chiron vaccine business with investments in research and manufacturing designed to increase quality and capacity.

Analysts said Novartis is buying Chiron for two major reasons. It wants to protect a sizeable investment and the once-sleepy vaccine market is heating up due to global concerns about a bird-flu pandemic. As prevention becomes a bigger part of healthcare, Novartis expects the global market for all vaccines to double to more than $20 billion from $9.6 billion last year. While influenza is Chiron's biggest vaccine product, the company also makes inoculations for meningitis and polio, among others.

The deal must still be approved by regulators and a majority of the stockholders of the outstanding shares not already owned by Novartis. Chiron chief exec Howard Pien said he expects the deal to close in the first half of 2006.

(Source: The Boston Globe and David P. Hamilton, The Wall Street Journal, both 1 November 2005).

Interest in Inhalation Treatments leads to $63 million Deal for Syntonix

2005 has been a banner year for Syntonix Inc., a small Waltham-based company with a staff of 30. The company finalized a partnership with Boehringer Ingelheim that could result in a yield of $63 million and closed on a multimillion dollar collaboration with Serono SA. Syntonix is developing biopharmaceuticals that enable treatment options for patients with chronic diseases such as anemia, hemophilia, and mul-

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What Some of our Members Have Been Doing Lately

An Update by the Membership Services Committee

by Jim Grunwald, Chair, ISPE Boston Area Chapter Member Services Committee

The ISPE Boston Area Chapter Membership Services Committee has had an active program year this year with a number of new initiatives designed to try and provide a meaningful experience to the Members of the Chapter. Two items that we would like you to know more about are:

- "The Advocates Program"
- Our Committee Level Volunteers

Advocates

This is a new initiative launched this past fall by the Membership Services Committee with the support of the Board to foster better communications with our end user companies, their ISPE Members, and future members.

This program, referred to as "The Advocates Program" seeks to identify those persons within operating companies that can help us on a number of levels.

We ask our advocates to act as the "point person" within their firm to help make sure those members and nonmembers within the firm are aware of our upcoming programs, the benefits of membership, and to be our feedback mechanism ensure that we are adding value within our local Chapter.

The "Advocate" receives the benefit of being able to have members of his or her staff attend a program of interest as a guest of the Board as a sort of "test drive" of the Society. The hope being that we will continually bring in new members and keep long standing members engaged.

The "Advocate" is invited to communicate directly with the Board as a guest at Board Meetings and our yearly Strategic Planning Session. The intent here is to get direct input into programs and activities that would address needs within the client company.

The Board is pleased to announce that the following people have joined the Advocates Program!:

Alan MacDonald, Therion Biologics
David Brown and Henry Brush (Co-Advocates), Alkermes
Neil Bergeron, Lonza Biologics
David MacKay, Wyeth

Volunteers

Our Committee Level Volunteers are responsible for working with Committee Chairs to plan and execute our educational, special and social programs. When you consider the number of events that have come to comprise any given program year it should be no surprise that our organization requires a large contingent of talented and dedicated individuals to manage the workload and continually improve our Chapter.

This group tackles tasks as diverse as finding speakers for a particular program to lining up a Bus to transport an ISPE group to a Ski/Snowboard Outing.

The Board of Directors of the ISPE Boston Area Chapter thanks the following individuals for their contribution to the success of our Chapter over the past year:

2005 Product Show

Kimberley Baxter, Practical Applications Inc.
Jim Berry, Camp Dresser & McKee, Inc.
Jay Comire, Whiting-Turner Contracting Co.
Tim Crowley, Sentrol
Gene Dennen, UltraFiltronics
Brian Hagopian, Fluid Solutions
John Ouellette, Integra Companies
Peter Petrillo, Millennium Facilities Resources
Tony Urciuoli, GE Infrastructure & Water Technologies

Communications

Patti Charek, Linbeck
Sylvia Corr, SLAM Collaborative
Dave Knox, Arcadis
Christine Lindberg, Wyeth BioPharma
Sean Lyons, EBI Consulting
Pietro Perrone, Millipore Corp.
Janet Tice, GMP Piping Inc.

Educational Program Committee

Leena Asplund, Steris
Henry Brush, Alkermes
Erik Caldwell, Northeast Water Services
Mike Denault, Denault Associates
Ana Echaniz, BioMetics Inc.
Niall Johnson, Millennium Pharmaceuticals
H. Steve Kennedy, Parsons
Daniel Lavin, Parsons
David Novak, A/Z Corp.
Peter Petrillo, Millennium Facilities Resources Inc.
Dan Rufo, Massachusetts Biologic Laboratories
Mark Sitcoske, High Purity New England
Tony Urciuoli, GE Water System
Jim Verhulst, Innovative Process Solutions
Mary Wojtyk, Biogen Idec

Membership Services

Steven Cheung, M+W Zander
Tim Crowley, Sentrol
Tara Galvin, Labrepco
Jim Grunwald, SPEC Process Engineering & Construction
Amanda Hyland, Commodore Builders
Alan MacDonald, Therion Biologics
Bob Urbanowski, Automatech

Social Program

Bob Bilodeau, Sentrol
Sylvia Corr, SLAM Collaborative
Gene Dennen, Ultrafiltronics
Tara Galvin, Labrepco
Amanda Hyland, Commodore Builders
Doyle Johnson, Massachusetts Biologic Laboratories
Kathy Zirpola, Steris

Student Chapters

Daniel Lavin, Parsons
Carolyn Lee-Parsons, Northeastern University
Robert Mitchell, SPEC Process Engineering & Construction
Rick Pierro, Superior Controls

We look forward to the balance of the program year and encourage all of our members to consider getting involved at the Committee or Advocate level. This will continue to push our dynamic organization forward, please feel free to contact **ispe@camihq.com** if you are interested in learning more about Advocate or Volunteer opportunities. ●

Industry News in Brief

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tiple sclerosis. The goal of its technology is to develop longer-acting biopharmaceuticals that may be inhaled or injected less frequently than current medications.

Relating to the Serono deal, Syntonix technologies may enable the development of an "interferon-beta therapy" for MS that can be administered by inhalation. Serono currently markets Rebif, a high-dose, high-frequency interferon beta-1a therapy for relapsing forms of MS that must be administered three times a week via injection. In the Boehringer Ingelheim deal, Syntonix will work with the German company to optimize certain therapeutic peptides for inhalation.

"There has been increasing interest in delivering drugs through inhalation rather than frequent injection," said John Ripple, Chief Executive of the six-year-old company. He said he expects to land one more major deal before the end of 2005 and expects to close on another round of funding in early 2006, adding to the $50 million the company raised in its first two rounds.

(Source: Dyke Hendrickson, Mass High Tech, 31 October 31 - 6 November 2005). ●

New Members

Anthony J. Ammendolia, Tech Team Leader/Sr. System, Bristol-Myers Squibb
David A. Campanella, Project Manager, Millipore
David Cohen, Northeast District Sales Manager, Despatch Industries
Tim Cowher, NE Sales Manager, Flow Sciences
Kenneth Cristofori, Senior Electrical Designer, Integrated Design Group
Frank DAgostino, Toxikon Corporation
Jennifer Doherty, The Chisholm Corp.
Vicki L. Fagan, Metrology Doc. Coord., Avecia Biotechnology
David W. Ferguson, Sales Manager, SF Medical
Tom Frazar, DePuy
Tara A. Galvin, Boston Area Representative, Labrepco Inc.
Elizabeth Gardner, Purification Associate II, EMD Pharmaceuticals
Michael F. Garvey, Senior Technician, ImmunoGen Inc.
Kevin A. Gregory, Principal, Integrated Design Group Inc.
Elizabeth Hart, Process Development Engineer, Alkermes
Patrick Haughney, Consulting Engineer, Millipore Corp.
Dave Huffman, R&D Team Leader, Spraying Systems Co.
Paul Joyce, Senior Project Engineer, AstraZeneca
William J. Mack, Director Business Devel, Chapman Construction Design
Edward Marsh, Fusion Concepts, Inc.
David McCarthy, Regional Manager, Lym-Tech Scientific
Mark Moody, Director of Manufacturing Operations, Merrimack Pharmaceuticals
James R. Murray, Software Engineering Manager, Foster-Miller, Inc.
Stephen ORourke, President, Applied Project Management
Michael J. Putnam, Marketing Manager, MARKEM
John Reever, Manager, RJS Associates
William K. Russo, AutomaTech NE
Fran Selvaggio, Tour Andover Controls Corp.
Kathleen Sheehan, QA Manager, Sepracor, Inc.
Oleg Shinkazm, Processing Engineer, Insco Group
Saxon Smith, Senior Consultant, Decision Mgmt International, Inc.

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November MBL Tour

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been produced from a given lot of raw material.

The utilities areas of the building were well thought out and spacious. I am sure many facilities people on the tour were envious of those who will get to run the systems that we were shown. The building management system incorporates mobile workstations that can be rolled to where they are needed and plugged in for commissioning or troubleshooting.

The tour wrapped up with food and an excellent opportunity to network with other attendees and talk with the MBL staff. ●

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New Members

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May Sun, Portfolio Strategy Manager, Millipore Corp.
Richard Tetreault, Electrical Engineer, Bristol-Myers Squibb Medical Imaging
Paul S. Tierney, Jr., Pres/GM, Northeast Engineering Inc.
Andrew Timofeev, Wyeth
Kristen Trapani, Alkermes Inc.
Geoffrey A. Von Holton, Validation Engineer, Valicare-Bosch Packaging
Laura L. Ward, Manufacturing Manager, ImmunoGen Inc.

New Faculty Members

John J. Fitzmaurice, Dir. Information Tech, University of Massachusetts Medical School
Erika M. Moxham, Project Manager IT, University of Massachusetts Medical School

New Student Members

Megan E. Bentley, Student, Tufts University
Caitlin A. Blacker, Student, University of Massachusetts
Christopher R. Broderick, Student, University of Massachusetts
Stephen J. Connaughton, Student, University of New Hampshire
Shay Hershkovitz, University of Massachusetts
Antrangig Kalaydjian, Student, University of Massachusetts
Prerana S. Katti, Student, University of Mass Amherst
Colleen A. Kelley, Student, University of Massachusetts
Jonathan M. Koppelman, Student, University of Massachusetts
Jason M. Lajoie, Student, University of Massachusetts
Foteini Makrydaki, Student, Tufts University
Steven R. Mazzarelli, Student, University of Massachusetts
Michael T. Mills, Student, University of New Hampshire
Felipe V. Moitinho, Student, University of Massachusetts
Leya A. Neilson, Student, University of New Hampshire
Michael R. O'Conner, Student, University of New Hampshire
Jeremy P. Sauer, University of Mass Amherst
Nalma L. Sharaf, Student, University of Massachusetts
Xzangping Shen, Student, University of New Hampshire
Vibha Sundaram, Student, University of New Hampshire
Jameson B. Wood, Pharmacy Tech, University of Massachusetts