



Boston Area Chapter

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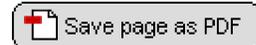


NEWSLETTER

April 2009, Volume XIX, No. 2

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President's Message: New Chapter Initiatives Help Members Avoid the "Doom and Gloom"

Dear ISPE Boston Area Chapter ISPE Members,

These are certainly challenging times with the economy in such a tailspin. Consolidations continue on a much larger scale with \$128 Billion in transactions as Wyeth merges with Pfizer and Merck agrees to buy Schering-Plough. The value of biotechnology is shown by the price Roche was willing to pay for Genentech - valued in the deal at a P/E of nearly 30 compared to the more pedestrian P/E of Pfizer (12) and Merck (7). In fact, more than one-third of the global total of all M&A deals in 2009 are in healthcare.

This high degree of uncertainty and change was reflected in the atmosphere at the ISPE Tampa conference. Large companies tend to freeze their budgets and activities when mergers are occurring, and this includes travel and training. Much of the discussion in Tampa was about how the International Society will need to cut costs and push more activities down to the Chapter level. You see this reflected in our new Boston Area Chapter initiatives on training, marketing yourself and a local job board accessible via the Chapter Web site. We will also continue to try to offer lower cost programs that require less time commitment so that our Members can continue their career development as their companies wait to see what happens next.



Our "Marketing Yourself" event on April 9 is a first for the Chapter and geared especially to out-of-work members trying to learn how to put their best foot forward in their job search. On April 21 we will present "Business Partnering and Contract Manufacturing" at the Royal Sonesta in Cambridge, and our two-day training program on Biotechnology and Cleaning Validation will be at the Radisson Hotel in Boston on June 18-19. The latter is a new type of program for the Boston Area Chapter, involving two full days of training on either of the topics using ISPE-certified instructors. It is intended to orient newer employees to the basics of biotechnology. If the program proves to be successful (and we're virtually certain it will be), we plan to offer similar programs in the future.

We are also trying an experiment by having a local job board on the Chapter Web site called the Boston Area Career Exchange - it is intended to allow local companies to focus their recruitment efforts in our area. A side benefit is the Chapter realizes some of the revenue from the job posting fees. You can check this out for yourself at:

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http://www.ispeboston.org/boston_area_chapter_career_exchange.html.

The bottom line is you might be able to avoid some of the "Doom and Gloom" malaise by networking and improving your job skills at one of our events. We will do our part by trying to make them as interesting and entertaining as possible while providing good value for your money.

Sincerely,

Doyle Johnson

President, ISPE Boston Area Chapter

Upcoming Events: Mark Your Calendar!

Thursday, April 9, 2009

Marketing Yourself - MEMBERS ONLY INTERACTIVE WORKSHOP

Speakers:

Bob Steininger, Accelaron

Linda Trowbridge, Change Dynamics, Inc.

Bob Vear, Change Dynamics, Inc.

FW Webb, Bedford, MA

[CLICK HERE TO REGISTER ONLINE](#)

Tuesday, April 21, 2009

Business Partnering and Contract Manufacturing

Speakers:

Peter Latham, BioPharm Services US

Susan Dexter, BioPharm Services US

Royal Sonesta, Cambridge, Massachusetts

[CLICK HERE TO REGISTER ONLINE](#)

Thursday, June 18 - Friday, June 19, 2009

Two-Day Spring Classroom Training

Sessions:

Biotechnology Basics or

Cleaning Validation Principles

Radisson Hotel, Boston, Massachusetts

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Monday, August 17, 2009

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7th Annual Golf Tournament
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Wednesday, October 7, 2009

Annual Product Show
Gillette Stadium Clubhouse, Foxborough, Massachusetts

Boston Area Chapter Launches New Training Initiative

by Doyle Johnson, Massachusetts Biological Laboratories

The ISPE Boston Area Chapter has started a pilot program to promote educational programs in the Boston area which have traditionally been available only at International ISPE meetings. The advantages to Chapter Members are many. The programs are of consistent high quality, taught by faculty certified by ISPE and available locally so it is not necessary to travel anywhere or stay in a hotel to take them. We first tested this new concept at Shire, which is engaged in a rapid expansion of their manufacturing capabilities and needed a program such as this to train their employees on the principles of biotechnology. You can read their appraisal of this course in the article below.

We plan to offer this same two-day course with a different instructor on June 18-19 in Boston, in combination with a course on CIP Principles. These courses are intended for people with less experience in Biotechnology - for example, those who are new to the industry or who graduated from college only a few years ago. We can also set up a company-only program such as the one at Shire - just call the office at 781-647-4773 and let us know if you're interested.

Training at Shire Deemed a Success

by Patrick Kelley, Shire, Human Genetic Therapies

On December 10th, 2008, Jeff Odom from ISPE facilitated an onsite training session of Biotechnology Basics for Shire HGT in Cambridge, MA. The training consisted of multiple 90-minute sessions geared for manufacturing and other technical operation employees. The training would not have been a success without the coordination of Mike Denault of the Boston Area Chapter. Mike was helpful in identifying the multiple modules that were presented and customizing the training to fit the audience.

The morning kicked off with an introduction to the biotechnology industry which helped set the scene for the rest of the day, especially for those newer to the industry. By mid-morning Jeff was engaging us with information about the science of biotechnology and then after lunch introduced bioprocess basics. The afternoon ended with an overview of the biotech industry today, focusing on current statistics and metrics.

Participants evaluated Jeff as very knowledgeable and interactive. He did a great job of being able to speak to all levels of employees whether they had just started in the industry or have been in the industry for years. Overall, the customized program conducted by ISPE was a success for Shire HGT and we are looking forward to scheduling more training sessions this year!

"Career Exchange" Website - A New Resource for Chapter Members

The Boston Area Chapter is proud to announce a new and exciting resource - a Career Exchange Web site providing Members with access to current job openings in the life sciences industry. As an added benefit, job openings are accessible *only* by Members for the first 15 days of posting. The Career Exchange is a great tool for circulating your resume, accessing multiple, relevant job opportunities at once and comparing job openings. Furthermore, it offers several features that distinguish it from generic job boards:

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- a highly targeted focus on employment opportunities in a specific sector, location, or demographic;
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- access to industry-specific jobs and top-quality candidates often not found on Monster, CareerBuilder, HotJobs or similar generic sites.

Whether you're a job seeker or employer, the Chapter invites you to visit the site today at:
http://www.ispeboston.org/boston_area_chapter_career_exchange.html



Career Exchange | ISPE Boston Area Chapter - Microsoft Internet Explorer

Address: http://www.ispeboston.org/boston_area_chapter_career_exchange.html

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- Boston Area Career Exchange**

Become a Member

ISPE Boston Area Career Exchange

Looking for an exciting new career opportunity interested in reaching qualified candidates? New to the industry and want to get your feet wet?

The Boston Area Career Exchange is available to ensure a day to better serve the needs of job seekers and employers.

Job Seekers

Search job postings, post your resume, and access career-related articles and resources. ISPE members have a 15 day advance preview period for all job postings and may create custom job alerts.

[Job Seekers: Start Here](#)

Employers

Post your job openings on ISPE's Boston Area Career Exchange site and begin your search for qualified pharmaceutical science and manufacturing professionals.

[Employers: Start Here](#)

ASTM E2500 Standard Draws Crowd to Biogen Idec in February

by David Truex, Commissioning Agents, Inc.

On 17 February, 2009, members of the Boston Area Chapter traveled to Cambridge to attend an educational seminar hosted by Biogen Idec. This time the subject was the ASTM E2500 Standard and where it stands today. The program was developed especially for engineers, validation and quality personnel who have been in the biopharmaceutical workplace and wanted to learn more about the standard and how it will affect their company's validation procedures. Because of its location, or perhaps because of its topic, the seminar was extremely well-attended.

The speakers for the evening were Robert Chew, President of Commissioning Agents, Inc., and Robert Smith, CQV Manager

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for Parsons. Mr. Chew began by comparing the ASTM Standard to the draft FDA Process Validation Guidance, discussing how the documents are different yet very much the same. He explained that ASTM E2500 is a "consensus standard," defined that term and described the process used to develop a consensus standard. He pointed out that consensus standards are required to be used unless inconsistent with the law or impractical. Although ASTM E2500 was approved in August 2007, many companies are still studying implementation; those companies that have implemented the standard have done so partially.

Next he explained the status of the FDA Process Validation Guidance document. It has yet to be approved and was sent out for comment in November 2008. Many organizations have submitted comments, including ISPE. In comparing the standard to the guidance document, Mr. Chew showed the two are similar in many ways. Both focus on science-based process understanding and meeting process requirements. Both require that equipment and facilities be suitable for their intended use. Both require that the Quality function approve the qualification plan and report. Both call for a risk assessment effort that is flexible.

The second presenter for the evening, Robert Smith, was the COV manager for a project that tried to implement the standard and found that it is harder than expected. His biggest challenge was getting the project leaders to agree to use the standard in the first place. Once that was accomplished, his next challenge was to get people out of the mindset that the "old way" was better. Some of his successes included the use of Subject Matter Experts and the team approach to Commissioning and Validation. Once this was done, the onus fell on the team to get their equipment qualified.

Some of the "lessons learned" described by Mr. Smith included the importance of design review. In-depth reviews were needed to identify risks and develop mitigation plans. Those plans consisted of as-built inspections, performance testing and life-cycle reviews. One thing he emphasized that stands out in my mind is this: there were no report problems on new equipment, only existing equipment. Another lesson learned was that quality documentation does not make up for bad design or poor fabrication/installation.

Both presentations were very well received by the audience, who used the Q&A sessions to further clarify a few points. In all, the evening was a good chance to learn the future of commissioning and validation while meeting old friends and making new acquaintances during the networking reception.

Ski-Palooza: Ninth Annual Boston Area Chapter Ski Trip

by Tim Crowley, Sentrol, Inc. with photos by Chris Opolski and Sylvia Beaulieu



Larry Weiner and Phil de Vilmorin - ice-encrusted but still smiling!

On Friday, March 6th approximately 50 people from the ISPE Boston Area Chapter made the 2-hour trek to the Loon Mountain Ski Resort in Lincoln, NH for a day of skiing and boarding. Most of the skiers and boarders hopped on the bus at one of the three pick-up locations in the Boston area (Newton, Andover and Concord, NH). The first group of bleary-eyed combatants boarded the bus at 5:30am in Newton, while the final 10 people joined the trip in Concord, NH. A couple Boxes of Joe some lite Andover breakfast sweets fortified the travelers during the trip north up Rte 93. A number of skiers drove and joined up with the group at Loon by about 8:30am.

"Snowboarders and skiers alike, enjoyed the generous covering of snow and near spring like conditions until after lunchtime." Actually, that is an excerpt from the trip report of the 5th Annual Ski Outing which took place on March 5, 2004. This year's crew wasn't so lucky. Skiing in New England always a little bit of pot luck in March and that is just what this year's participants got. Freezing rain greeted skiers and boarders as they unloaded from the gondola at the top of Loon South Peak, 2,400 ft. summit, just past 9am. Trails like Angel Street and Flying Fox proved more challenging than expected because of the elements. Nonetheless, the clean, cold mountain air and good camaraderie more than made up for the less than ideal conditions.

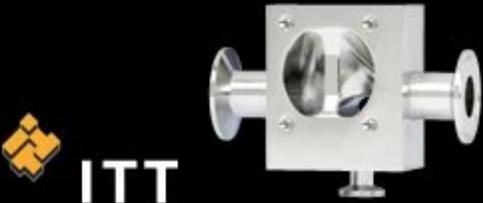


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ISPE Ski

As you might suspect, several of the participants didn't see the need to battle the hard, icy ski conditions and headed to the Pa Bunyan room to stake out a claim at 10am. When you think of who was leading the charge, think of the Battle of Thermopylae and Spartan King Leonidas leading 300 Spartans against the Persian "God King" Xerxes. Doyle was not to be denied. Thank you to sponsors Ultrafiltronics, A/Z Corporation, Sentrol, Integra Companies, GMP Piping, Signer Harris Architects, and Superi Controls for sponsoring an afternoon (and for some of us morning) of nourishment.



Members enjoy well-earned apres ski R&R.

At about 5:15pm the group boarded the bus for the ride back to the Boston area. Good conversation, a couple cans of cold tea and a little napping highlighted the journey home. A great time was had by all and discussions for procuring two buses for next year's trip are already underway. Thanks to Gene Dennen of UltraFiltronics for all his hard work in organizing this year's event

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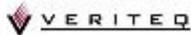
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Tech Talk: Use of GAMP, ISA-S88 and Integrated C&Q to Speed Plant Startups

by Jack Greene

(Note: For reference, a list of acronyms is found at the end of the article.)

Introduction

One of the most critical choices in the plant design phase is how to break up the plant systems and their controls into logical and manageable chunks. The better the breakout, the more flexible the plant will be and the easier it will be to manage the validation effort as it expands. Using an ISA-88/GAMP facility design strategy and an integrated commissioning and qualification (C&Q) approach can help reduce plant timelines by:

- defining clear validation boundaries up front to avoid costly over-validation;
- defining clear process train boundaries to reduce the impact of downstream changes and expansions;
- providing a framework to make informed choices as to whether a system should be custom designed or OEM designed; and
- reducing the duplication of work between the commissioning effort and validation.

Plant Controls Layout Using the ISA-S88 Model at the Process Train Level

The following rules of thumb can be used to divide the plant systems and their controls into logical and manageable groupings.

- Place utility systems that serve more than one process train onto a separate PLC and keep them separate from the process trains and their PLCs. This prevents changes in any given process train from affecting utilities that serve all trains.
- When the entire process train is custom designed, place all of the controls for the train on the same PLC. This allows interlocks among units to be passed within the logic of one PLC and not among multiple PLCs.
- When the process train is comprised of a number of OEM units, use either a DCS or S88 software batch engine to tie them together. In either case, ensure that there is a dedicated high-speed communication bus between each OEM PLC on a process train and the DCS or batch engine.
- Isolate the controls for validated and non-validated systems. This allows for clear boundaries and allows for the validation resources to be concentrated on the systems with the most GMP impact.

Custom vs. OEM Equipment

Another series of critical choices is whether equipment (and their controls) should be supplied by OEM vendors or custom designed. The following rules of thumb can be used when making this decision.

- Select an OEM vendor when the equipment and controls can be purchased completely off the shelf.
- Select an OEM vendor when a system is truly stand-alone (i.e. when there is very little interlocking with other plant systems).
- Select an OEM vendor when the OEM equipment is expected to be pre-optimized by the OEM and will not need upgrades or receive complex PAT initiatives.

Where these rules do *not* apply, custom-designed equipment or OEM equipment with custom controls may be a better choice. Generally, OEM skidded systems are less expensive to purchase and implement than custom-designed systems. Additionally, OEM systems are less expensive to validate and tend to come with good canned validation packages. Thus, the result is often a "best of breed" approach, where the various units in a process train come from a number of different OEM vendors with different control systems. If the design assessment leads to this type of architecture, it is critically important that adequate integration resources be leveraged to ensure that the process train functions smoothly as an integrated unit via a DCS or batch engine.

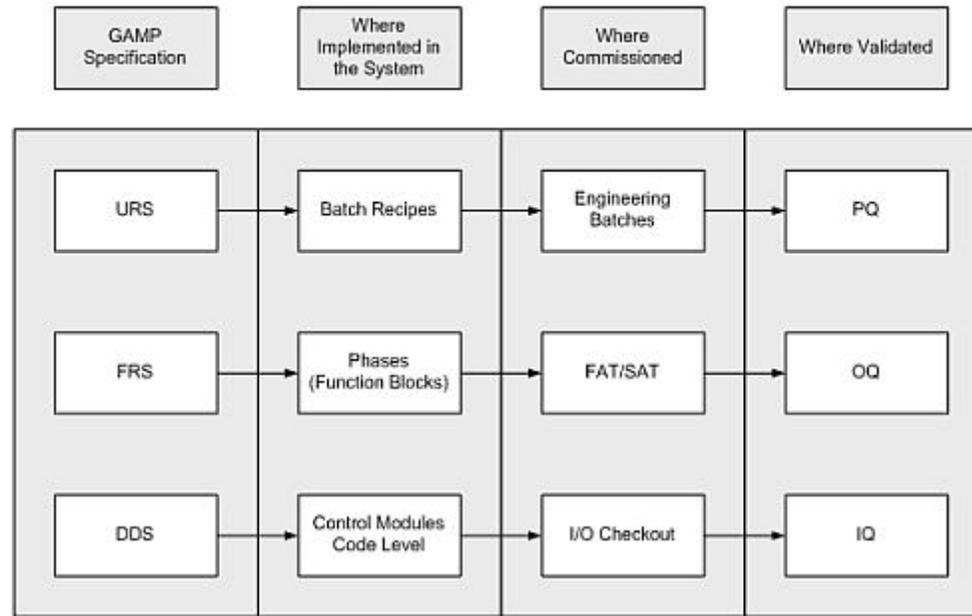
Standardized ISA-S88 Modular Design Reduces Costs and Time

A benefit of the S88 Control Module approach is that all devices of a given class operate in the same way, share the same PLC code subroutine and have a common HMI faceplate design. Standardizing custom control systems across a plant in this way saves time and reduces costs; and the more systems that use the standard library of control modules, the greater the benefit.

- The logic of each control module (including the alarm and fault logic) can be challenged offline to ensure that it performs as specified. This reduces the validation effort to I/O checkout and alarm set point review.
- An I/O checkout procedure can be developed for each control module class. This standardized approach dramatically simplifies the generation of the I/O checkout protocols.
- The standardized code and consistent HMI look and feel allows for rapid execution of the I/O checkout.

GAMP and ISA-S88

Pharmaceutical Engineering/Validation departments have embraced the GAMP design and validation model developed by ISPE. GAMP provides a framework for managing the life cycle of automated systems and directly maps to the S88 model and the traditional FAT/SAT commissioning models, as shown below.



In the URS, the top level requirements for a system are defined. These are implemented within the S88 Batch Recipes, commissioned during the engineering batches and validated in the PQ.

In the FRS, the equipment sequencing, faults and interlocks are defined. These are implemented in the S88 Phases, commissioned in simulation at FAT and on the equipment at SAT and validated at OQ.

In the DDS, the control modules, I/O alarms, I/O cabinets and field wiring are defined. These are implemented in the S88 Control Modules, commissioned as part of I/O checkout at the SAT and validated at IQ.

C&Q Strategies

Traditional C&Q strategies fall into two categories. In the first, validation is conducted when a plant is mechanically complete, but prior to process development. As the process development effort progresses, there will be an inevitable need for I/O and function block changes that will fall under change control (since validation has already been conducted). This adds significant overhead and time to the process development effort and leads to an "it's good enough" approach to commissioning.

In the second, validation is conducted *after* commissioning and process development is complete. This allows I/O and function block changes to take place before the onset of change control. But without a change management framework in place to track issues, changes and resolutions, and to update the design documents and ETOP's, these activities usually do not take place. Before validation can start up, an as-built specification/drawing set needs to be reverse engineered and the impact of the changes during commissioning needs to be assessed. If the changes are significant, it becomes difficult to leverage the commissioning effort towards validation. This results in a time-consuming and costly validation effort where all of the testing done under commissioning needs to be repeated and documented in a GMP fashion.

A newer approach gaining acceptance in the industry is to integrate the C&Q by focusing on defined efforts during the pre-commissioning work and leveraging these efforts to minimize the downstream work needed to complete the validation program. This approach requires that the FAT is executed under protocol. To avoid the need to write a lengthy and detailed test protocol, the current Phase FRS is printed and each function tested accordingly. During testing, as each function is challenged, the FRS is initialed and dated indicating that testing was performed.

Phase (Function Block) FRS

Control Module SDDS and HDDS

Software FAT
At Integrator
Capture Changes as part of the
FAT Change Management

Hardware FAT
At Panel Shop

Implement at Site

SAT Effort Requires Phase
(Function Block) changes
Capture Changes as part of the
FAT Change Management

SAT
I/O checkout
Capture Changes as part of the
SAT Change Management

SAT PID Tuning Effort Requires
I/O changes
Capture Changes as part of the
SAT Change Management

Process Development Start

PD Effort Requires Phase changes
Capture Changes as part of the
FAT Change Management

PD Effort Requires I/O changes
Capture Changes as part of the
SAT Change Management

Process Development End

Close Out FAT and SAT with Summary Reports. List all system changes and describe the retesting that has occurred. Merge in all redlines to the Design Specification and Drawing Set to create an "As-Built" set.

Validation Start - IQ and OQ heavily reference SFAT and SAT data and summary reports

Recommendations

The methods described have yielded smoother startups with improved time schedules. However, this has not been achieved without learning important lessons that form the basis for the following guidelines.

- Review the FRS level documentation for each Phase as it is developed. Holding off until all of them are complete makes review insurmountable.
- Pre-planned design reviews are critical to the success of the project. Too many design review meetings are preferred over too few. Waiting until FAT for a design review is way too late.
- Although Phases are less portable from project to project, having a full library jump starts the project.
- Take full advantage of FAT activity. While the FAT needs to be executed by an integrator, it is an opportunity for the engineering staff to see the system run and fault. This is a chance to test multiple simultaneous failures, recovery from process upset, and refine prompt and alarm text.
- Better results are obtained when the SAT checkout is executed by the plant operators and support personnel. It takes a little bit longer but is an unparalleled training opportunity.

Acronyms/Glossary

C&Q - Commissioning and Qualification

FRS - Functional Requirements Specifications

DDS - Detailed Design Specification

DCS - Distributed Control System

FAT - Factory Acceptance Test - Tests performed at equipment manufacturer or automation integrator shop that ensures the equipment or automation software meets the design intent prior to shipment.

GAMP - Good Automated Manufacturing Practices

I/O - Input/Output

ISA-S88 - A publication of the International Society of Automation that describes common terminology and structure for Batch Manufacturing.

OEM - Original Equipment Manufacturer - Company that designs and builds equipment.

PLC - Programmable Logic Control

SAT - Site Acceptance Test - Tests performed after installation of equipment or automation software at a site to ensure that it works properly

URS - User Requirements Specification

##

Jack Greene is an independent contractor specializing in the design, commissioning and validation of Plant Wide and Enterprise Wide Solutions for GMP environments. Jack's experience includes work at Altus, Alkermes, Genzyme and Serono. He has worked with a variety of IT, Manufacturing and Laboratory systems including PLC/DCS/SCADA Solutions, BAS/BMS Systems LIMS/Chromatography Management Systems, and IT infrastructure systems. You may reach Jack at jack.greene1@gmail.com

Industry News In Brief

by Patti Charek, Linbeck

Merck to Acquire Schering-Plough in \$41 Billion Deal

Merck & Co. and Schering-Plough Corp. have announced a definitive merger agreement under which Merck and Schering-Plough will combine, under the name Merck, in a stock and cash transaction. Merck Chairman, President and Chief Executive Officer Richard T. Clark will lead the combined company.

Based on the closing price of Merck stock on March 6, 2009, the consideration to be received by Schering-Plough shareholders is valued at \$23.61 per share, or \$41.1 billion in the aggregate. Upon closing of the transaction, Merck shareholders are expected to own approximately 68 percent of the combined company, and Schering-Plough shareholders are expected to own approximately 32 percent.

"We are creating a strong, global healthcare leader built for sustainable growth and success," said Mr. Clark. "The combined company will benefit from a formidable research and development pipeline, a significantly broader portfolio of medicines and an expanded presence in key international markets, particularly in high-growth emerging markets. The efficiencies we gain will allow us to invest in strategic opportunities, while creating meaningful value for shareholders."

"We look forward to joining forces with an outstanding partner we know well and that shares our commitment to patients, employees and the communities where we work and live. Through their talent and dedication, Schering-Plough employees have built an industry leading R&D engine and late-stage pipeline that is complementary to our own. We are confident that, together, Merck and Schering-Plough will make a meaningful difference in the future of global healthcare," Mr. Clark added.

Fred Hassan, chairman and chief executive officer of Schering-Plough, said, "Over the last six years, Schering-Plough colleagues have transformed our company into a strong competitor in the global pharmaceutical industry. We have built a strong, diverse business and a robust pipeline that offers hope to patients who are waiting for new medicines. I am proud of what we have accomplished. Our success is a testament to the hard work and dedication of our colleagues in every country. We are joining forces with Merck, our long-term partner in our cholesterol joint venture, to create a dynamic new leader in the pharmaceutical industry. By harnessing the strengths of both companies, the combined entity will be well-positioned to further deliver on our shared goal of discovering new therapies for patients to help them live healthier, happier lives."

"The talent and dedication of Schering-Plough scientists has helped to build an outstanding clinical development pipeline," said Peter S. Kim, Ph.D., Merck executive vice president, and president of Merck Research Laboratories. "Schering-Plough's considerable biologics expertise will complement Merck's novel proprietary biologics platform and aligns with our commitment to build a powerful biologics presence. The Schering-Plough and Merck pipelines are remarkably complementary and will greatly increase our ability to deliver important new medicines to patients. I believe the combined pipeline will be the best in the industry, by far." (Source: Schering-Plough Website, 9 March 2009)

Roche Agrees to Buy Genentech for \$47 Billion

The Swiss drug giant Roche Holding has agreed to buy out the shareholders of Genentech for \$95 a share, ending a takeover effort that began last summer. The new offer came a few days after Roche raised its bid to \$93 a share to buy the 44 percent of Genentech that it did not already own. At \$95 a share, the companies said the deal would be valued at \$46.8 billion. A special committee appointed by Genentech's board of directors approved the deal and recommend it to Genentech shareholders.

Charles Sanders, who led the Genentech committee, said: "We believe this is a fair offer for Genentech shareholders, and the committee is pleased to come to a successful conclusion of this process. We look forward to working with Roche to complete the transaction as expeditiously as possible." Roche's bidding for Genentech turned hostile in January after its offer of \$86.50 a share, down from the \$89 it first offered in July, was rejected. The Genentech committee had put the asking price at \$112 back in December.

Roche might have forced the deal through at a lower price. But Roche, based in Basel, did not want to stifle Genentech's culture or alienate key researchers. To that end, it said that research and early development would operate "as an independent center within Roche from Genentech's existing base in South San Francisco, retaining its talent and approach to

discovering and progressing new molecules."

Analysts said that Roche wanted to wrap up the deal before information is released next month from a clinical trial of Avastin, one of Genentech's cancer drugs. That trial, testing Avastin as a treatment for colon cancer after surgery to remove tumors, could potentially open a huge new market for the drug, which is now approved to treat cancer only at a later stage. If Avastin works in the trial, Genentech's shares have the potential to rise to \$100 or more, making the deal more costly for Roche. If the drug does not work, analysts say, Genentech's shares might fall below \$70. (Source: David Jolly, International Herald Tribune, 12 March, 2009)

Pfizer Acquiring Wyeth in \$68 Billion Deal

Number one drug maker Pfizer Inc. is buying number 12 Wyeth in a \$68 billion deal that will quickly boost Pfizer's revenue and profit and transform it into a more diversified company less reliant on its dwindling drug pipeline. Pfizer managed with one stroke to overshadow a full house of issues: a 90 percent drop in income, a hefty charge to end an investigation, a severe cut in its dividend, a shockingly low profit forecast for 2009, and 8,000 job cuts starting immediately. That's all on top of the colossal problem triggering this deal: the expected loss of \$13 billion a year in revenue for cholesterol fighter Lipitor starting in November 2011, when it gets generic competition.

By buying Wyeth, Pfizer will mutate from a maker of blockbuster pills to a one-stop shop for vaccines, biotech drugs, traditional pills, and nonprescription products for both people and animals. The cash-and-stock deal, one of the biggest in the history of the drug industry, is expected to close late in the third quarter or in the fourth quarter. It comes as Pfizer's 2007 fourth-quarter profit takes a brutal hit from a \$2.3 billion legal settlement over allegations it marketed pain reliever Bextra and possibly other products for indications that had not been approved.

Pfizer's goals include increasing sales in emerging markets, enhancing the ability to treat specific diseases, such as Alzheimer's, and becoming a top player in vaccines and biologics. The New York-based maker of the impotence pill Viagra and Detrol for overactive bladder said it will pay \$50.19 per share for Madison, NJ-based Wyeth, a 14.7 percent premium. (Source: Associated Press, The Boston Globe, 27 January, 2009)

GTC Wins Approval for Drug Produced using Genetically Modified Animals

Framingham biotech GTC Biotherapeutics became the first to win federal approval to manufacture a drug by using genetically modified animals, an approach that could eventually be used to produce many drugs using farm animals.

The FDA approved GTC's ATryn, an anticlotting drug made using genetically modified goats that live on a farm in Charlton. GTC engineered the herd to secrete a special therapeutic protein in their milk. "It's really a milestone event," said Eric Overstrom, chairman of biology and biotechnology at WPI, who collaborated with GTC on some of its early research using goats. "This adds to the toolbox for the pharmaceutical industry."

Though ATryn is likely to have limited marketing potential because it would serve a relatively small pool of patients, the drug's approval could clear the way to produce many more drugs with genetically modified animals, an approach nicknamed "pharming." European regulators approved the drug - and the novel production technique - in 2006.

In addition to goats, Overstrom said, drug companies could potentially use other animals, such as cows or rabbits, to produce drugs in their milk, blood, or even urine. Overstrom said animals could be particularly helpful in cultivating enzymes and other large molecules that are more difficult to produce using bacteria or individual cells.

Still, some activists are wary about the use of genetically engineered animals. The Center for Food Safety, a nonprofit group, complained that the animals could pose unforeseen health and environmental risks. "The creation of GE animals is a very slippery slope," Jaydee Hanson, the center's policy analyst on cloning and genetics, said in a statement. "All it takes is one mating between an escaped specimen and a natural animal to set off a chain of events that could lead to contamination or extinction."

Some investors are also uncertain how much GTC will benefit from its achievement. Thomas Newberry, GTC's vice president of corporate communications, acknowledged the drug's revenue potential is modest. And like many small biotech companies, Newberry said the firm only has a limited amount of cash, which could cause some investors to worry about its future. But he said GTC's technology could eventually produce billions of dollars in revenue. "It's still tough times for development-stage companies," Newberry said. "But the upper bounds for the company are virtually limitless." (Source: Todd Wallack, The Boston Globe, 7 February 2009)

Targanta to be Acquired for \$133M

Super-bug-focused biotech Targanta Therapeutics Corp. will be acquired by New Jersey's The Medicines Co. in a deal that could be worth about \$133million, according to The Medicines Co. The news comes a few weeks after Cambridge-based Targanta decided to cut 86 employees, or 75 percent of its staff, in response to a decision by the FDA not to approve oritavancin, a drug designed to treat complicated skin and skin structure infections (cSSSI). The sale agreement calls for Targanta shareholders to receive \$2 in cash for each common share tendered in up front cash, or \$42 million. Targanta shareholders could also be entitled to get further cash payments if the company achieves certain regulatory and commercial milestones within agreed upon time periods that could net the shareholders another \$91million. The boards of directors of both companies have given approval to the deal, and Targanta's board has recommended that its shareholders tender their shares into the tender offer, adopt the merger agreement and approve the merger.

Targanta's lead product, oritavancin, is a hospital-based antibiotic targeted at a wide range of gram-positive bacteria including methicillin-resistant staphylococcus aureus (MRSA) and other drug-resistant bugs. The FDA instructed Targanta to conduct an additional clinical study to demonstrate the drug's efficacy and safety. In November, Targanta reported a net loss of \$12.7 million for its third quarter. In 2007, it saw a net loss of \$63.4 million on zero revenue. (Source: Mass High Tech, 13 January 2009)

Biogen Idec Talking with MS Pill Maker

Biogen Idec is in talks to buy Acorda Therapeutics Inc. to gain an experimental pill for patients with multiple sclerosis. Acorda shares surged 19 percent when the company said its lead experimental drug, Fampridine, helped MS patients walk. Biogen, the world's largest maker of medicines for multiple sclerosis, is also talking about buying rights to market Fampridine. The pill may be cleared for US sale this year.

Biogen Idec is racing Merck KGaA and Novartis AG to market the first pill for multiple sclerosis, a disease currently managed by injected medicines that generate \$6 billion a year worldwide. Acorda, based in Hawthorne, NY, said its 2008 net loss doubled from the previous year and the company is trying to sell marketing rights to Fampridine to fund operations beyond 2010. "The next rational step is exploratory discussions with potential partners," said Acorda chief executive Ron Cohen. "That does not in any way preclude us from exploring other options."

Biogen's top-selling MS medication, Avonex, generated \$2.2 billion last year. Its fastest growing product is the MS drug Tysabri, which had 2008 sales of \$589 million. The company's oral MS drug, BG-12, is in final human tests. Biogen is also developing at least three other experimental treatments for MS, daclizumab, CDP323, and Lingo. (Source: Bloomberg News, The Boston Globe, 25 February 2009)

Massachusetts Life Sciences Center Names Winners of First Grants

The Massachusetts Life Sciences Center announced the six grant winners of the agency's first Cooperative Research Grant Program, which awards more than \$3.7 million to promising scientists, academic institutions and industry developers, whose work has commercialization potential. The winners will receive funds for the work which will be matched by industry partners in the field.

University of Massachusetts Lowell professor Rudolf Faust, along with postdoctoral and graduate students at UMass Lowell and Boston Scientific Corp., will receive a three-year grant of \$199,596 per year for their nanomanufacturing of a special polymer-based lead coating of pacemakers and defibrillators.

Harvard Medical School professor Judy Lieberman, along with the Immune Disease Institute and Epic Therapeutics Inc., will receive a three-year grant of \$250,000 per year for testing antiviral transmission effects that could be extended to HIV transmission between women and newborns.

Harvard University physics professor David Weitz, along with Harvard University School of Engineering and Applied Sciences and Raindance Technologies Inc., will receive a three-year grant of \$250,000 per year for development of individual cell data collector via a fluorescence-activated cell sorter.

Andrew Luster, chief of the division of rheumatology, allergy and immunology at Massachusetts General Hospital, as well as Idera Pharmaceuticals Inc., will receive a three-year grant of \$63,100 per year for determining the TLR7 and TLR9 molecules' inhibitor effect on human immune cells.

Richard Lee and Parth Patwari of Harvard Medical School, along with Brigham & Women's Hospital and Biomeasure Inc., will receive a three-year grant of \$250,000 per year for protein development that could lead to post-traumatic cartilage regeneration and osteoarthritis therapy.

Michael Czech and Gary Ostroff of UMass Medical School, along with RXi Pharmaceuticals Inc., will receive a three-year grant of \$249,593 per year to develop orally administered RNAi treatment. (Source: Mass High Tech, 16 December 2008)

Proteon Raises \$38 Million in Finance Round

Proteon Therapeutics Inc., a privately held Waltham biopharmaceutical company, said it has completed a \$38 million Series B equity financing led by MPM Capital, a firm with Boston offices that invests in life-sciences companies. Proteon said it has also entered an agreement with Novartis AG that grants the Swiss drug maker an exclusive option to acquire Proteon following the successful completion of a phase 2 clinical study of PRT-201, which dilates blood vessels to improve blood flow.

Including the initial acquisition payment plus potential additional regulatory milestone payments, the deal with Novartis could exceed \$550 million, Proteon said. In September, the company said that PRT-201 had received fast-track designation from the Food and Drug Administration. With yesterday's financing included, Proteon has raised \$72 million in equity financing to date. (Source: Chris Reidy, The Boston Globe, 6 March, 2009)

Altus Cuts Staff by 75 Percent, Drops Cystic Fibrosis Drug

Picking which horse to bet on, Altus Pharmaceuticals Inc. will focus on its recombinant human growth hormone candidate and will discontinue its Trizytek program activities, eliminating about 75 percent of its staff positions. Discontinuing the development of Trizytek will result in the transfer of certain Trizytek intellectual property rights to Cystic Fibrosis Foundation Therapeutics Inc. (CFFT), the nonprofit affiliate of the Cystic Fibrosis Foundation, according to Altus' 2001 agreement with CFFT.

The Waltham-based company will continue developing its ALTU-238 compound as a once-per-week treatment for adult and pediatric patients with growth hormone deficiency. Most of the job cuts will be in functions related to the Trizytek program, according to Altus officials, as well as certain general and administrative positions. Those include chief medical officer Burkhard Blank; chief financial officer Jonathan Lieber; and vice president, business development, John M. Sorvillo, all of whom will be leaving Altus. After the cuts, Altus will have approximately 35 employees. Altus said that the personnel cuts and program reduction should reduce operating expenses by approximately 65 percent and should give it enough cash to last until about the end of 2009.

CFFT has told Altus that its decision to discontinue the clinical development and planned regulatory filings for Trizytek puts Altus in breach of the 2001 agreement, and Altus expects that will terminate its exclusive sublicense to Trizytek in North America and that CFFT will get exclusive control of the Trizytek program and related IP rights in North America. Altus and CFFT are also in discussions over an agreement under which CFFT would obtain worldwide rights to Trizytek and assume funding responsibility for the ongoing Phase 3 long-term safety study for Trizytek. (Source: Mass High Tech, 26 January 2009)

Dynogen Pharmaceuticals Seeks Bankruptcy Protection

Waltham biotech Dynogen Pharmaceuticals has filed for Chapter 7 bankruptcy protection, likely leading to the company's liquidation. The economic downturn has made it difficult for early stage firms such as Dynogen to raise money to develop new drugs and cutting-edge technologies. In its bankruptcy filing, the company, which burned through at least \$67 million in venture capital and other funding, said it owed \$10.6 million to more than 100 creditors and only had about \$18,393 in assets. The company had been trying to develop drugs to treat irritable bowel syndrome, overactive bladder disorder, and nocturnal gastroesophageal reflux disease (often associated with heartburn). A year ago, Dynogen said it would merge with Apex Bioventures Acquisition Corp. of Hillsborough, CA but the companies called off the \$98 million deal two months later, citing "current market conditions." (Source: Todd Wallack, The Boston Globe, 25 February 2009)

Panacos Cuts Jobs, Weighs Possible Sale

Panacos Pharmaceuticals Inc., a Watertown biotech working to develop HIV treatments, said it is cutting more than half its workforce and is considering selling the company. Panacos said it will close its Gaithersburg, MD office and reduce its total workforce to four employees, down from 11. The layoffs include Jane Pritchett Henderson, chief financial officer, and Graham

P. Allaway, chief operating officer and cofounder.

In addition, Panacos said it hired Oppenheimer & Co. to advise the company on "strategic alternatives," including selling its HIV drug development programs or the entire company. Unless it strikes a deal soon, Panacos warned, it may not be able to continue to operate beyond the second quarter. (Source: Todd Wallack, The Boston Globe, 25 February 2009)

Innovative Spinal Technologies Closes

A once-promising Mansfield medical device company has apparently closed. Innovative Spinal Technologies Inc., which made spinal devices, has shut down its website and did not return calls seeking comment. A former board member, Bill Starling, said several founders told him the firm shut down last week. And Xconomy, a Boston business website that covers technology and life sciences companies, reported the company was forced to close after a deal collapsed to sell itself to Biomet Spine of Parsippany, NJ.

Innovative Spinal had raised \$75 million in funding and had more than 100 employees at its peak in 2007, before gradually trimming its staff, Xconomy said. It had 80 employees, according to the new 2008 New England Technology Directory. The company, originally spun off from the Texas Back Institute, had attracted a number of investors, including OrbiMed Advisors LLC, JP Morgan, and MPM Capital. (Source: Todd Wallack, The Boston Globe, 4 February 2009)

Sepracor to Shift Focus, Cut 530 Jobs

Marlborough drug manufacturer Sepracor Corp., shifting its focus and streamlining its operations in a slumping economy, said it would cut 530 jobs, roughly 20 percent of its workforce. The move, coming as Sepracor posted higher fourth-quarter profits, is intended to save about \$210 million, including \$20 million already shaved from its budget in the last three months of 2008. Sepracor said it would reduce its corporate staff by 180 positions and its field staff by 350, though it didn't specify how many jobs would be eliminated overall in Massachusetts. The company said it would also cut 410 contract sales employees.

In a statement, Adrian Adams, Sepracor president and chief executive, said the company had to adapt to "a challenging time for the country and the pharmaceutical industry" to remain competitive. The company's move represents a shift toward more reliance on its respiratory drug products (including Xopenex, Brovana, Omnaris, and Alvesco),

which are cheaper to promote, and less on its sleep drug, said Ian Sanderson, chief pharmaceutical analyst for the Cowen and Co. research firm in Boston. Sanderson said the timing "makes great strategic sense" because Sepracor's insomnia drug, Lunesta, will be facing increased competition this year as generic versions of Ambien CR, its chief rival, come onto the market. (Source: Robert Weisman, The Boston Globe, 29 January 2009)

Vertex Founder Joshua Boger Stepping Down

Vertex Pharmaceuticals Inc. chief executive Joshua Boger, the Harvard University-trained chemist who has long been one of the biotechnology industry's best known executives, is stepping down after 20 years. The Cambridge biotech said that Boger, who founded Vertex in 1989 when the industry was still relatively young, plans to retire in May as the company edges closer to gaining approval for potentially significant treatments for hepatitis C and cystic fibrosis. Vertex doesn't currently have any drugs on the market. In introducing his successor, Matthew Emmens, Boger said a new leader is needed to take Vertex "to the next level" - a full-fledged commercial drug company.

Emmens is a Vertex board member who has experience running more mature pharmaceutical companies. He previously worked as chief executive of Shire PLC, served as president of Merck KGaA's global pharmaceuticals business and served in various positions at Merck & Co., where he worked with Boger in the late 1980s before Boger went on to found Vertex.

In a conference call with analysts yesterday, Emmens made it clear that Vertex is doing well and doesn't need major changes. "I'm not going to mess with success," he said. "There isn't anything broken here. To the contrary, we have an amazing pipeline" of potential new drugs. Vertex and Boger have long been in the public eye, even as a start-up. The company and the man were the stars of Barry Werth's 1995 business biography "The Billion Dollar Molecule," which chronicled the challenges of developing cutting-edge drugs. That so-called billion dollar molecule never materialized. But Vertex and Boger soldiered on, later working with a British drug company to develop a pill to treat HIV.

More recently, Vertex has been advancing a potential blockbuster treatment for hepatitis C called telaprevir. Last year, the company launched large-scale trials of the drug to prove that it is safe and effective, a key step toward gaining approval from the FDA to market the drug to patients. Wall Street analysts expect the drug to generate billions of dollars in annual revenue

when it hits the market in the next few years. Based largely on the hopes for telaprevir, Vertex has a stock market value of more than \$5 billion, making it one of the largest biotech companies in the state.

The company has grown to more than 1,300 employees, including 1,000 in Cambridge.

In addition, Vertex is also working on other experimental drugs, including one to treat cystic fibrosis, a rare debilitating disease, that has shown promising results in midstage clinical trials. The work was underwritten by funding from the Cystic Fibrosis Foundation. Boger said Vertex hopes to market the cystic fibrosis drug within the next three years.

Boger has become one of the key faces of the biotechnology industry. He is chairman of the Biotechnology Industry Organization, the industry's largest trade group. And he worked with Massachusetts Governor Deval Patrick and other local political leaders to promote the state's biotech business. He also serves on the board of the Massachusetts Life Sciences Center, the quasi-public organization charged with overseeing the state's new \$1 billion life sciences initiative. (Source: Todd Wallack, The Boston Globe, 6 February 2009)

Massachusetts Life Science Innovation Stats Dipped in 2007

The Massachusetts medical devices pipeline shrank noticeably in 2007, sparking what could be a trend for the sector. The number of 510(k) submissions to the FDA was the second lowest since 1996, according to the recently released 2008 Index of the Massachusetts Innovation Economy. The Massachusetts Technology Collaborative produces the index, which is used to gauge the progress of innovation in various tech sectors of Massachusetts against other benchmark states, such as California, Illinois and Minnesota.

Looking just at medical devices, Massachusetts companies had only 241 510(k) submissions, which are applications necessary for marketing a medical device that poses a moderate risk to the user, such as condoms or inflatable blood pressure cuffs. The number, a drop from 264 in 2006, reflected a national decline in submissions. Although Massachusetts had fewer submissions than in 2006, its percentage share of the national total actually increased slightly between the two years from 15 to 16 percent, the highest it has been since 2003. "241 is still an impressive number for any state," said Thomas J. Sommer, president of the Massachusetts Medical Device Industry Council. Sommer attributes the low number of 510(k) submissions to normal yearly fluctuations and said it was not a sign of an impending downturn.

The index also revealed that the FDA granted no premarket approvals to Massachusetts companies in 2007. PMAs are approvals from the FDA that are required for any medical device that requires significant safety and effectiveness data before going to market. The national total was only 13 PMAs, a sharp drop from the 30 approvals in 2006. As the national economy tanked in 2008, California more than doubled its PMAs from 6 to 13, helping to bolster the national total from 13 to 20. In contrast, Massachusetts had only one PMA. "2008 looks just like 2007," said Beth Ashman, a MTC research manager who worked on the report. "I would characterize this as an early warning sign that the pipeline has slowed down." The research also showed that while 2008 saw a total increase in the number of biotechnology drugs in development from 2006, Massachusetts had a decrease from 82 in 2006 to 76 in 2008 during approximately the first half of each year. (Source: Lynette F. Cornell, Mass High Tech, 27 February 2009)

FDA Won't Sign Off on Genzyme Plan for Lumizyme Yet

Genzyme Corp. said it failed to win approval for Lumizyme, a version of its drug for Pompe disease made in larger batches. Genzyme must reach an agreement with the FDA for a post-approval study of the treatment, the Cambridge-based company said. The company also said it must respond to an FDA warning letter citing deficiencies in its manufacturing plant that would produce the larger batches of the drug.

Genzyme sells Myozyme for children and infants with Pompe disease, which leads to a buildup of sugar in the body that can harm the heart, liver, muscles, and nervous system. The company said it has asked regulators to approve Myozyme in 2,000-liter containers under the name Lumizyme for adults in addition to the 160 liters now allowed. Genzyme said the warning letter was "unexpected" because it had responded Oct. 31 with a plan to address regulators' requests and was on schedule to finish its corrective actions by March 31.

"We have made an enormous effort for more than two years to make this product broadly available in the US, so we are obviously surprised and disappointed by this further delay," said Genzyme chairman and chief executive Henri Termeer. "We are confident we will be able to resolve all remaining issues with the FDA within three to six months." (Source: Bloomberg News, The Boston Globe, 3 March 2009)

Genzyme on the Hunt for New Products

Genzyme Corp. may spend about \$600 million this year to acquire products that treat chronic diseases, said chief executive Henri Termeer. Genzyme will seek opportunities to purchase "personalized drugs, highly specialized medicines where you can easily explain their value," Termeer said. Acquisitions made by the Cambridge-based biotechnology company will focus on individual products already tested in humans, Termeer said. He prefers buying products rather than entire companies because he wants to invest in "the value of maintaining the team" that got the new therapies started. "When you buy a program, the heart of the company is still there," Termeer said. (Source: Bloomberg News, The Boston Globe, 24 February 2009)

Exact Sciences Works a \$24 Million Partnership with Genzyme

Marlborough-based cancer diagnostics company Exact Sciences Corp. has made Genzyme Corp. a strategic partner in a deal worth \$24.5 million. Under the terms of the deal, Genzyme will acquire intellectual property rights to some of Exact's prenatal and reproductive health technologies, and three million shares of Exact's common stock. Exact will receive \$24.5 million in cash; it already has received \$16.65 million, and Genzyme will pay an additional \$1.85 million over the next 18 months, contingent upon "the non-occurrence of certain events." Genzyme purchased the shares of Exact's common stock for an aggregate purchase price of \$6 million.

However, Exact will retain exclusive worldwide rights to its colorectal cancer screening and stool-based DNA testing intellectual property. Exact's intention is to use this relationship to assist it to increase its oncology diagnostics business. Genzyme will be sharing its extensive development and regulatory know how to help Exact introduce its next-generation platform for colorectal cancer screening. Additionally, Genzyme and Exact have amended an existing license, signed in March 1999, to provide Exact with the additional rights necessary to distribute a FDA-approved kit for the stool-based detection of disease and colorectal cancer screening.

Exact also announced it believes that its cash resources should last into 2011. Its board rejected an earlier buyout proposal from Sequenom Inc., a genetic analysis product maker based in San Diego. (Source: Marc Songini, Mass High Tech, 28 January, 2009)

Regulatory & Legislative Highlights

by Deepen Joshi, Sepracor, Inc.

Executive Order Removes Barriers to Human Stem Cell Research

On March 9, in conjunction with the issuance of a new Presidential memo on scientific integrity, President Obama signed a Presidential Executive Order removing barriers to responsible scientific research involving human stem cells. This Executive Order revokes that signed by President Bush on June 20, 2007 and the Bush Presidential statement of August 9, 2001 that limited federal funding of research involving human embryonic stem cells.

The previous Administration allowed the NIH to fund human embryonic stem cell research on cell lines created before an arbitrary date, August 9, 2001, but prohibited research on cell lines created after that date. The Executive Order signed by President Obama lifts this restriction.

Under the Obama Executive Order, the Director of NIH is instructed to develop guidelines for the support and conduct of responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law. Doing this will involve gathering the necessary scientific data and published best practices. NIH will then post draft guidelines for public comment, will carefully review all the public responses and will issue final guidance within 120 days of the signing of the Executive Order.

Research involving human embryonic stem cells and human non-embryonic stem cells has the potential to lead to better understanding and treatment of many disabling diseases and conditions. Advances over the past decade in this promising scientific field have been encouraging, leading to broad agreement in the scientific community that the full range of promising stem cell research should be supported by Federal funds. The purpose of the Executive Order is to remove the limitations on scientific inquiry in this area, to expand NIH support for the exploration of human stem cell research, and in so doing to enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind.

(Source: <http://www.whitehouse.gov/>)

Bill Backs Copies of Biotech Drugs

A bipartisan group in Congress wants to give the FDA power to approve copies of biotech drugs. Representative Henry Waxman, a California Democrat and chairman of the Energy and Commerce Committee, and Georgia Republican Nathan Deal introduced legislation to create a pathway for the approval of copies of biotechnology-based medical treatments. There is currently no regulatory process for approving such copies in the US, leaving the drugs' makers insulated from the generic competition the traditional drug industry faces.

President Obama called recently for the creation of a regulatory pathway as part of a plan to reduce overall healthcare costs. "I believe this bill will lead to healthy competition and long-term savings for patients and payers and will preserve innovation to the biotech marketplace," Waxman said in a statement.

The debate over an approval process for biotech copies has dragged on for years, with both the biotechnology and generic drug industries at loggerheads over how much competition-free marketing the original drugs should get. The biotechnology industry has called for up to 14 years of exclusivity for their drugs before a copy could be introduced. But the bill instead mirrors the current system for chemical compounds, which allows for five years of market exclusivity for new drugs and up to three years additional exclusivity for modifications. (Source: Associated Press, The Boston Globe, 12 March, 2009)

President Obama Announces Key FDA Appointments

President Obama has announced the appointments of Dr. Margaret Hamburg as Commissioner of the Food and Drug Administration, and Dr. Joshua Sharfstein as the Principal Deputy Commissioner.

Dr. Hamburg is a nationally and internationally recognized leader in public health and medicine, and an authority on global health, public health systems, infectious disease, bioterrorism and emergency preparedness. She served as the Nuclear Threat Initiative's founding Vice President for the Biological Program. Before joining NTI, she was the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. Prior to this, she served for six years as the Commissioner of Health for the City of New York and as the Assistant Director of the National Institute of Allergy and Infectious Diseases of the National Institutes of Health.

Dr. Joshua M. Sharfstein is Commissioner of Health for the City of Baltimore. He also serves as chair of the board of four affiliated nonprofit agencies. He has been recognized as a national leader for his efforts to protect children from unsafe jewelry and over-the-counter medication, and ensuring Americans with disabilities have access to prescription drugs. He is a member of the Board on Population Health and Public Health Practice of the Institute of Medicine. (Source: <http://www.whitehouse.gov/>)

FDA Launches Program to Improve the Safety of Drugs Produced Outside the US

The FDA has announced the launch of a voluntary pilot program that would help promote the safety of drugs and active drug ingredients produced outside the US. The FDA plans to select 100 applicants to participate in the Secure Supply Chain pilot program.

The goal of the pilot is to allow FDA to determine the practicality of developing a secure supply chain program. Such a program would assist the agency in its efforts to prevent the importation of drugs that do not comply with applicable FDA requirements by allowing the agency to focus its resources on foreign-produced drugs that fall outside the program and that may not be compliant. It will also expedite the entry of products meeting the pilot's criteria into the United States.

Each applicant may designate up to five drugs for selection in the pilot program. To qualify, applicants will need to meet the pilot's criteria, including a requirement that they maintain control over the drugs from the time of manufacture through entry into the United States. A secure supply chain will help mitigate risks such as contamination and counterfeiting. (Source: FDA Website, 14 January, 2009)

FDA Panel Backs Lilly Blood-Thinner

Eli Lilly and Daiichi Sankyo won the backing of a US panel to introduce the first rival to the blood-thinner Plavix, the world's second-biggest drug. FDA advisors voted 9 to 0 that prasugrel should be approved to reduce the risk of blood clots in patients with heart problems who undergo procedures to keep their arteries open. The FDA usually follows the recommendations of its

panels, though it isn't required to do so.

Prasugrel, to be marketed as Effient, is critical to Lilly's plans to replace revenue when its top-selling antipsychotic, Zyprexa, loses patent protection in 2011. Analysts say prasugrel, if approved, may take up to a fifth of market share from Plavix, which generated \$8.1 billion in 2007 sales for makers Bristol-Myers Squibb and Sanofi-Aventis. (Source: The Boston Globe, 4 February, 2009)

City of Woburn Sets New Rules for Biotech

As Woburn strives to become a Massachusetts leader in biotechnology research, the city is also attempting to regulate the expanding industry locally so it may protect residents from potential dangers. The City Council agreed last week to adopt the Planning Board's recommendations to create new local laws prohibiting the most hazardous types of biotech research in Woburn and to change zoning regulations to differentiate between biological testing and all other types of research. The Council also agreed to reinstitute the dormant Biomedical Oversight Committee.

The proposed new regulations will prohibit the most hazardous types of research from being done in the city. As part of a national safety protocol for laboratory workers, every research lab is ranked on a biosafety-level scale based on the dangers of the materials being tested. Biosafety Level-1 is akin to a laboratory at a high school or vocational school. BSL-2 is common at most hospitals. BSL-3 and BSL-4 involve the most dangerous testing on potentially harmful or lethal agents.

Pete Abair, director of economic development for the Massachusetts Biotechnology Council, said biotech companies seeking lower rents and shorter commutes for their employees are expanding north and west out of Cambridge along major highways and public transportation routes. Woburn has more than 30 such companies, trailing Cambridge and Waltham as a center of Massachusetts biotech activity. Abair, whose group encourages communities to keep oversight of the industry and calm residents' fears, said biotech will continue to grow and Woburn should balance any proposed municipal regulation against the benefits the industry provides. (Source: The Boston Globe, March 5, 2009)

FDA Takes New Regulatory Action Against Ranbaxy

The FDA has announced that a facility owned by India-based Ranbaxy Laboratories falsified data and test results in approved and pending drug applications. The facility, Paonta Sahib, has been under an FDA Import Alert since September 2008. To date, the FDA has no evidence that these drugs do not meet their quality specifications and has not identified any health risks associated with currently marketed Ranbaxy products.

The affected applications are for drugs that fall into three categories: Approved drugs made at the Paonta Sahib site for the US market; drugs pending approval at the FDA that are not yet marketed; and certain drugs manufactured in the United States that relied on data from the Paonta Sahib facility.

On Sept. 16, 2008 the FDA issued two warning letters and instituted an Import Alert barring the entry of all finished drug products and active pharmaceutical ingredients from Ranbaxy's Dewas, Paonta Sahib and Batamandi Unit facilities due to violations of US cGMP regulations. That action barred the commercial importation of 30 different generic drugs into the US and remains in effect. (Source: FDA Website, 25 February, 2009)

Cardinal Health Signs Amended Consent Decree with FDA

The FDA has announced that California device manufacturer Cardinal Health 303, formerly known as Alaris Medical Systems, and three of its top executives have signed an amended consent decree to correct violations of cGMP requirements in the company's infusion pumps. Infusion pumps are devices intended for controlled delivery of intravenous solutions and medications to patients.

Under the terms of the amended consent decree, Cardinal 303 agrees to comply with the cGMP requirements and Quality System regulations in the designing, manufacturing, processing, packing, repacking, labeling, holding or distributing of its infusion pumps. Cardinal 303 also must retain an independent expert consultant to inspect all of its infusion pump facilities and recall procedures, and certify to the FDA that corrections have been made. The amended consent decree also authorizes the FDA, in the event of future violations, to order Cardinal 303 to cease manufacturing and distributing, to recall products, and to take other actions. The defendants may be required to pay damages of \$15,000 per day if they fail to comply with any provisions of the decree, plus an additional \$15,000 for each violation, up to \$15 million per year. (Source: FDA Website, 19 February, 2009)

FDA Issues Public Health Advisory Concerning Genentech's Raptiva

The FDA has issued a public health advisory concerning three confirmed and one possible report of progressive multifocal leukoencephalopathy (PML), a rare brain infection, in patients using the psoriasis drug Raptiva (efalizumab). Three of those patients have died. All four patients were treated with the drug for more than three years. None of the patients were receiving other treatments that suppress the immune system.

PML is caused by a virus that affects the central nervous system. PML usually occurs in people whose immune systems have been severely weakened. It leads to an irreversible decline in neurologic function and death. Symptoms may include unusual weakness, loss of coordination, changes in vision, difficulty speaking and personality changes. There is no known effective prevention or treatment.

Psoriasis is a chronic disease, for which a number of effective therapeutic options are available, including four other approved biologic agents, ultraviolet light therapy, and the drugs cyclosporine, acitretin, and methotrexate. Generally, treatment for psoriasis patients involves a rotation of therapies.

The FDA strongly recommends that health care professionals carefully monitor patients on Raptiva, as well as those who have discontinued the drug, for any signs or symptoms of neurologic disease, and that they periodically reassess the benefits of continued treatment. (Source: FDA Website, 19 February, 2009)

FDA Approves Takeda's Uloric for Gout Management

The FDA has approved Uloric (febuxostat) for the management of gout, a painful form of arthritis. Uloric works by reducing levels of uric acid, a waste product that is produced during digestion or ordinary metabolism. If uric acid levels in the blood are too high, crystals may form in the big toe, foot, ankle, or knees. Formation of these crystals can cause an attack of sudden burning pain, stiffness and swelling known as gout.

Although a causal relationship was not established, there was also a numerically higher rate of cardiovascular deaths, non-fatal heart attacks and non-fatal strokes in patients treated with Uloric than treated with allopurinol. The number of cardiovascular events was small in the clinical trials and the higher rate seen with Uloric may have occurred by chance. As a condition of approval, Takeda will be required to conduct a study to further assess the drug's cardiovascular safety.

An FDA Arthritis Advisory Committee met to discuss the safety and efficacy of Uloric. While the committee was concerned about the possibility of increased cardiovascular risk with Uloric, they concluded that the numerically higher rate of cardiovascular events may have occurred by chance but recommended that more data be collected after Uloric is approved. (Source: FDA Website, 13 February, 2009)

FDA and International Consortium Release First Data on Genetic Basis of Adverse Drug Events

The first data offering health care professionals a better look into the genetic basis of certain types of adverse drug events has been released by the FDA and the International Serious Adverse Event Consortium (SAEC). The SAEC is a nonprofit partnership of pharmaceutical companies, the Wellcome Trust and academic institutions focused on research relating to the genetics of drug-induced serious adverse events.

The data are focused on the genetics associated with drug-induced serious skin rashes, such as Stevens-Johnson syndrome and toxic epidermal necrolysis, and helps better predict an individual's risk of developing these reactions. Both skin conditions appear as allergic-like skin reactions associated with blistering and peeling, and are considered life-threatening. Medications causing these serious allergic reactions should be discontinued; and if such signs and symptoms are not quickly recognized, these reactions can be fatal.

The samples from the initial serious skin rash cases and matched controls were collected by GlaxoSmithKline plc, London, UK and donated to the consortium for this research. By pooling these samples, the SAEC has identified numerous genetic associations that may contribute to an individual's risk of developing serious drug-induced skin reactions. The data was compiled and analyzed just 16 months after the consortium was launched. (Source: FDA Website, 10 February, 2009)

FDA Posts Quarterly Reports of Potential Drug Safety Issues

The FDA has posted two new quarterly reports listing the drugs that are under evaluation for potential safety issues. The latest reports cover the second quarter (April-June) and the third quarter (July-September) of 2008. In addition, the FDA is

updating an earlier report on the first quarter (January-March 2008).

This posting is the latest in a series of quarterly reports describing new safety information or potential signals of serious risks based on a review of reports submitted to FDA's Adverse Event Reporting System (AERS). The AERS database contains millions of reports of adverse events submitted to FDA by drug manufacturers, health care professionals and patients. The FDA Amendments Act of 2007 directed the FDA to conduct regular, bi-weekly, screening of the AERS database and to provide new drug safety information to the public on a quarterly basis.

The FDA has not concluded that the drugs listed actually have the reported risks and has not identified a causal relationship between the drug and the listed risk. Drug products are only on the list because FDA has identified a potential safety issue. The reports are available at: http://www.fda.gov/cder/aers/potential_signals/default.htm (Source: FDA Website, 6 February, 2009)

FDA Approves First Ablation Catheters for Atrial Fibrillation

The FDA has approved the first ablation catheters for the treatment of atrial fibrillation (uncoordinated contractions of the upper heart chambers), one of the most common types of arrhythmias, affecting more than two million Americans. Atrial fibrillation is usually treated with drugs and, in certain severe cases, with open heart surgery. Catheter ablation should be used only after drug treatment has failed to adequately control the symptoms of the condition.

While atrial fibrillation is a major risk factor related to stroke, there is no conclusive evidence that links the treatment of symptoms by ablation to a reduction in stroke. Therefore, the FDA agrees with the American College of Cardiology, the American Heart Association and the European Society of Cardiology, which recommend that patients at risk for stroke continue to take blood-thinning medications after ablation procedures for atrial fibrillation.

As a condition of approval, manufacturer BioSense Webster of Diamond Bar, California must establish a physician training program and conduct postmarket studies to collect data on these devices' long-term safety and effectiveness (including incidence of stroke, mortality, cardiac arrest, major bleeding, and pulmonary vein stenosis), and the effect of physicians' experience in operating the device on procedural safety. (Source: FDA Website, 6 February, 2009)

FDA Issues Final Guidance on Regulating Genetically Engineered Animals

The FDA has issued a final guidance for industry on the regulation of genetically engineered (GE) animals under the new animal drug provisions of the Federal Food, Drug and Cosmetic Act (FFDCA). The guidance, titled "The Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs," clarifies the FDA's statutory and regulatory authority, and provides recommendations to producers of GE animals to help them meet their obligations and responsibilities under the law.

Genetic engineering generally refers to the use of recombinant DNA (rDNA) techniques to introduce new characteristics or traits into an organism. When scientists splice together pieces of DNA and introduce a spliced DNA segment into an organism to give the organism new properties, it is called rDNA technology. The spliced piece of DNA is called the rDNA construct. A GE animal is one that contains an rDNA construct intended to give the animal new characteristics or traits.

The FFDCA defines "articles (other than food) intended to affect the structure or any function of the body of man or other animals" as drugs. An rDNA construct that is in a GE animal and is intended to affect the animal's structure or function meets the definition of an animal drug, whether the animal is intended for food or used to produce another substance. Developers of these animals must demonstrate that the construct and any new products expressed from the inserted construct are safe for the health of the GE animal and, if they are food animals, for food consumption. (Source: FDA Website, 15 January, 2009)

New Members

Mr. David S. Allen, PE, *Principal*, Allen Consulting, LLC

Stephen Allen, Tarpon

Walt Bassett, *Director of R&D*, Millipore Corporation

Laurie A. Di Chiara, *Senior Validation Engineer*, NNE Pharmaplan US Inc
Mr. Michael M. Enos, *Process Engineer*, Hart Design Group
James Felton, *Project Manager*, Lantheus Medical Imaging
Mr. Joseph M. George, *Senior Manager*, Ariad
Mr. David M. Gray, *Product Manager*, Mettler-Toledo Thornton, Inc.
Mr. Craig E. Hill, Sr., *Senior Manager, Facilities Operations*, Momenta Pharmaceuticals
Teresa James, *Business Application Mgr*, Covidien
Dr. Paul F. Killian, *Research Chemist*, Millipore Corporation
Jeff E. Martin, *Project QA Manager*, Decco Process Solutions
Charles E. McCall, Jr., *Design Engineer*, Organogenesis, Inc.
Mr. David J. Perrotta, *Process Engineer*, NNE Pharmaplan
Mr. Nicholas S. Renner, *Student*, Tufts University
Ms. Mia E. Richards, *Marketing Manager*, Technical Safety Services Inc
Steven Robak, *Project Executive*, J. Calnan & Associates Inc
Mr. Craig Rothman, *Process Engineer*, Genzyme Corporation
Christine M. Rutledge, *Student*, Villanova University
Dr. Brian Shoemaker, *Principal Consultant*, ShoeBar Associates
Mr. Robert W. Smith, *Senior Consultant*, Invensys Process Systems
Ms. Jaclyn K. Somadelis, *Student*, University of Massachusetts Amherst
Robert C. Spang, Jr., *Distribution Manager*, Pepperl + Fuchs
Mr. Peter C. St. John, *Student*, Tufts University

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