Boston Area Chapter
ENGINEERING
PHARMACEUTICAL
INNOVATION

www.ispeboston.org

NEWSLETTER

September 2010, Volume XX, No. 5





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## President's Message: Welcome to the 2010/11 Program Year of the Boston Area Chapter

Dear Friends,

Welcome to the 2010/11 Program Year of the Boston Area Chapter of ISPE. With the new season comes the installation of our new Board of Directors and the beginning of regular Committee Planning Meetings! This is the time of year when our course for the year is set and our collective Team comes together and plans for success.

This year we have a number of important programs and initiatives to offer to our membership. It is the goal of the Board of Directors, Committee Chairs and our incredible Volunteers to deliver the best programming and networking opportunities possible to you, our Members.

While we complete our Strategic Planning, the results of which will take us through to next July, we are also hard at work providing upcoming educational and social programs. We will start the season by offering three diverse events in September, an Educational Program on the 16th which will focus on Process Optimization, a Young Professionals social event featuring a Boston Harbor Cruise on the 17th and finally a Young Professionals vs. Grizzled Veterans Softball Challenge, at the Teddy Ebersol Field on the Esplanade, on the 21st. (This is a first-ever event for ISPE and we thank the Young Professionals for agreeing to spotting the Vets a three-run advantage. Perhaps a fantasy softball league will spring up this winter to keep us engaged until our next major tilt!)

Immediately following the recovery of the Grizzled Veterans from their pulled hamstrings and the healing of bruised egos for the Young Professionals, we are fortunate to have our 19th Annual Product Show ready for you on October 6th at the Gillette Stadium Clubhouse in nearby Foxboro. If you are a regular attendee then you know the drill - you can't miss this day! If you have never attended, you well should. The event is open to all, free-of-charge, and presents an incredible opportunity to be part of the best regional event in the industry.

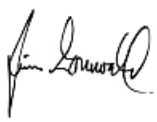
The Product Show Educational Programs are top-notch, starting with a GAMP® Seminar in the morning and stretching into the early evening. There's something for everyone, with educational tracks designed for both Young Professionals and Industry Veterans.

The Product Show Keynote Address has been moved to 3:30pm this year to give everyone an opportunity to hear Dr. Sylvie Gregoire, President of Shire Human Genetic Therapies, introduce Shire and its culture and describe the reasons Shire elected to stay local with its current and future expansion plans. Dr. Gregoire will also review the critical decisions that led Shire to adopt a disposables approach in their new production plant. A question and answer period will follow her address and will feature a group of Shire leaders. With Shire as a leading global biopharmaceutical with a major commitment to the local area, we are very fortunate to have Dr. Gregoire as our Keynote. Our sincere thanks to Dr. Gregoire and all those at Shire who have supported the planning of this event so enthusiastically.

In closing I would like to thank you all for the once-in-a-career privilege that comes with leading your Chapter this year. It is my intention to be accessible to all Members in the hope that we can continue to build on the incredible strength and diversity of our Chapter. Please call me or drop me an email if you have an idea or request at ispe@camihq.com

I look forward to a year of great dialog and many successful programs and events.

Thank you,



Jim Grunwald

## Raise Your Visibility, Further Your Career & Share Your Knowledge - Publish a Tech Article in the Chapter eNewsletter

Whether you are involved in research, pilot production, scale-up or manufacturing - or provide products or services to the industry - your specialized knowledge and experience make you a valuable source of information for members. Plus writing a technical article is a great way to raise your visibility and further your career - in addition to appearing in the eNewsletter, tech articles are archived on the Chapter's website where they remain permanently accessible by a worldwide audience.

Articles should be written for technical professionals in the pharmaceutical, biotech or medical device industries and should meet the following simple requirements:

- articles should be 2000 words or less
- charts, graphs, photos, etc. are encouraged
- information should be technical & non-promotional
- generic descriptors should be used in place of product trade names

The Chapter will assist by providing light editing to correct any spelling and/or grammatical errors (authors will be consulted if more extensive editing is required) and reserves the right to accept or reject articles for publication.

Publishing a technical article in the Chapter eNewsletter will showcase your expertise, allow you to share your knowledge with your peers and help to strengthen the Chapter. So don't delay - email your article to ispe@camihq.com. (Please review your company's policy concerning publication and obtain any necessary approvals prior to submitting your article.)

## Upcoming Chapter Events - Mark Your Calendar

Thursday, September 16, 2010
"Optimize What? A Panel Discussion on Process Optimization in the Biopharmaceutical World"

In classical chemical engineering terms, a process is a set of unit operations arranged, controlled, and operated in a particular way, to produce a product. The product must meet certain specifications, such as a certain production rate, product quality, and cost. Thus process optimization is the discipline of adjusting a process so as to optimize some specified set of parameters while keeping all others within their constraints.

Enter the regulated environment of bio-pharmaceutical manufacturing. Product quality, safety, potency, purity are sacrosanct, yet you are being asked to "optimize". The processes require additional support utilities such as media prep, buffer prep, CIP, SIP, and water systems which must be operated in perfect harmony with the underlying process. Often times the support utilities are more complex that the process itself.

Add to this the notion of concurrent multi-product operation and scheduling, and you have yourself a challenging problem to "optimize". Join our distinguished panel who will discuss the issues surrounding process optimization; how do you do it, and what are the issues?

The panel will consist of:

James Blackwell, PhD, Senior Consultant, BioProcess Technology Consultants, Inc
Joseph Kauten, Senior Scientist, Manufacturing Science and Technology, Lonza
John (Jack) Prior, ScD, Senior Director of BioProcess Engineering, Genzyme
James Dean Vogel, PE, Principal, BioProcess Facilities Services
Larry Weiner, Director of Manufacturing Engineering & Validation at Biogen Idec

Moderater, Dick Priester, Principal of Strategic Facility Planning LLC

Royal Sonesta, Cambridge, MA
5:30 pm Reception; 6:30 pm Panel Discussion

**Walk-in Registrations are being accepted onsite!**

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**Friday, September 17, 2010**
**Young Professionals Boat Cruise**

Boston Belle Charters
Marina Bay, Quincy, MA
7:15 pm to 10:30 pm

**Walk-in Registrations are being accepted onsite!**

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**Tuesday, September 21, 2010**
**Softball Game - Young Professionals Vs. Seasoned Professionals**

The Challenge: This September Tuesday the 21st, the 'Young Professionals' challenge the 'Seasoned Veterans' to a game of Softball.

The Stakes: The unfortunate team that does NOT prevail will be the wait staff during post-game dinner for the winning team. So, its' time to ransack that old cabinet, grab your glove and bring your guts to join your comrades in an epic battle for glory!

Be there to support your squad as the battle rages pitting old guard vs. newbie, done-that vs. rookie, young-at-work vs. young-at-heart and finally... good vs. evil (well maybe not that one). Also don't worry, both skilled and unskilled players should feel free to play or simply attend if softball is more like speaking Wookie to you.

Teddy Ebersol Field, Boston, MA

**Register today at www.ispeboston.org/events**

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**Wednesday, October 6, 2010**
**Annual Product Show**

Attend the Chapter's flagship event and learn about the current and future state of Biopharm. Its FREE to Attend!

Keynote Address-Hear from Sylvie Gregoire, President of Shire HGT

Source new products-View new technology and innovations from over 270 exhibitors, 30 are new

Improve your knowledge-Attend any of the eight Broad Based Educational sessions

Develop new resources-Connect with 2000 biopharmaceutical professionals

Gillette Stadium, Foxborough, Massachusetts

**Register today at www.ispeboston.org/events**

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**Wednesday, October 6, 2010**
**GAMP Forum**

Join us at Gillette Stadium for the ISPE Boston GAMP Forum. This is your chance to see presentations on hot topics, and be updated on the GAMP world of activities. Meet other local and regional people from Quality, Technical and Compliance fields to share ideas and experiences that benefit your company and our industry.

Topics for this year include:

• Review the latest FDA Inspection Initiative related to CFR 21 Part 11, as the agency reviews the industry's interpretation and implementation of the Final Guidance issued in 2003.

• Discover how ISO 9001 standards, the foundation of the ICH Quality Systems, are being re-introduced to life sciences and how your cGMP Quality System can benefit.

• Learn how to select and utilize practical tools available to you for performing risk analysis in your day to day implementation of Quality Risk Management.

• Hear about the latest best practices being discussed within the GAMP Special Interest Groups with opportunities to participate and collaborate with industry colleagues.

Pre-registration for this special GAMP Forum, being held in conjunction with the Annual Product Show, is manditory for attendance. Registration for GAMP automatically registers you as an attendee for the Product Show.

Gillette Stadium, Foxborough, Massachusetts

**Register today at www.ispeboston.org/events**

## Join the Excitement: Visit Product Show XIX at Gillette Stadium on October 6th

*by Brian Hagopian, Mar Cor Purification*

This year the 19th Annual ISPE Boston Area Chapter Product Show will be held on Wednesday, October 6th. at Gillette Stadium in Foxboro. It is going to be the biggest and best Product Show ever, loaded with more products and educational content than ever before. If you've attended prior shows here, you already know what a great venue it is. If you have not been to Gillette before - you really have to make a point of visiting the show. Why?

- Free admission and free parking for all attendees
- Over 270 exhibitors setting a new record for the event

An expansive view of Gillette Stadium forms a spectacular backdrop for the Annual Product Show

More than 50 new exhibitors you've never seen here before
- Five career center tables from companies looking to add staff
- Keynote Address by Dr. Sylvie Gregoire, President of Shire HGT, on the biotech industry and Shire's plans for growth in Massachusetts
- Six industry-specific educational programs (see related article) held in Gillette's luxury club level boxes
- Information-packed morning GAMP® session (see related article)
- Free hot and cold food, bottled water and non-alcoholic beverages throughout the dayStudent Chapter and Young Professionals gathering - meet the industry's future leaders
- Valuable raffle prizes given away throughout the day and first-ever silent auction
- Stadium tours

There is no other single place where members of the local life sciences community can mingle and meet the ISPE Boston Area Chapter board of directors, past presidents and advisory committee members (many of whom are local industry leaders) - all while viewing new and exciting products and services offered by the exhibitor community. The Product Show committee has worked diligently to bring products of interest to companies needing products in a fun, exciting, and hospitable location.

Over 270 exhibitors and 1800+ attendees are expected to participate this year

Since its beginnings at HoJo's in Cambridge, the Product Show has evolved into much more than a vendor and product-based event and has truly become a one-of-a-kind extravaganza. We've heard from so many exhibitors that this Show surpasses other local events and is THE ONE SHOW that everyone should attend. In fact, the Product Show has received such acclaim that it won an award from ISPE International as the best special event in all of the Americas.

The Clubhouse bar provides a convenient area for networking with colleagues

Gillette Stadium provides a unique venue that holds a special place in the hearts of New England Patriot fans. Excitement and anticipation are high this year as the Patriots contend to add another championship banner to the rafters. We've taken advantage of some of Gillette's unique offerings including stadium tours (a 40-minute guided tour of the press box, visitor's locker room, and the stadium field) and a raffle for gift certificates to the pro shop and area restaurants. As a special bonus, attendees will be able to enjoy Gillette's outdoor "red seats" during the Show (an area normally reserved for season ticket holders) and possibly even one of Gillette's luxury club boxes. This year, with the expansion at Patriot Place, Gillette is a better venue than ever, also featuring a newly opened Renaissance Hotel.

This year we have another excellent lineup of speakers for our Keynote Address and Educational Program. The morning GAMP®session will be rich in content and carries a modest sign up fee, primarily to defray the cost of lunch being furnished to session attendees. Visit our website www.ispeboston.org for a complete roster of programs and speakers and to register to attend these sessions. Last year, participation at the Keynote Address and Educational Program reached record levels, with over 750 attendees taking advantage of scheduled events, so be sure to save your spot by pre-registering online.

The show runs from 12noon until 7:30pm - so you can get your work done early and still have plenty of time to attend and participate. (The morning GAMP® session begins at 8:30am, prior to the Show.) We guarantee you will find the Show rich in content. Plan to arrive early to beat rush hour and take advantage of the many opportunities offered. We promise you a rewarding day well worth the short trip from your workplace. Gillette Stadium is only a 35-minute ride from

## Previous Issues



## Newsletter Archive

Delicious buffet offerings keep attendees well-fed throughout the day

Kendall Square (we timed it!), Boston, and a bit longer from Worcester, so it's really closer than you think.

And remember, the show, including the Keynote Address and Educational Program (except GAMP®), is FREE (free parking, too), with complimentary food and non-alcoholic beverages served throughout the day, a cash bar and a complimentary lunch for exhibitors. The food at Gillette is top-shelf all the way - just ask anyone who has ever attended. You won't go home hungry!

The Product Show generates the funds needed to operate the Boston Area Chapter, so your attendance not only provides you with valuable and pertinent information but helps attract the exhibitors whose participation ensures the Chapter's continued success. Because of the funds raised by this event, the Chapter is able to sponsor top flight educational programs, social events, facility tours, workshops, student chapters, communities of practice, and much more throughout the year.

Please register at our Web site (www.ispeboston.com) and help support the Boston Chapter by attending this event. It will be a smart decision that you will not regret, we promise!

## Keynote Speaker Dr. Sylvie Gregoire of Shire HGT to Address Attendees

*by Laurie Masiello, Masy Systems, Inc.*

The ISPE Boston Area Chapter is thrilled to announce that Dr. Sylvie Gregoire, President of Shire HGT, will be the keynote speaker at this year's Product Show at Gillette Stadium on October 6th. Dr. Gregoire has over 20 years of pharmaceutical and biotechnology experience. She has held senior positions at IDM Pharma in California, GlycoFi in New Hampshire, Biogen in the US and France, and Merck in the US and abroad. Dr. Gregoire joined Shire in September 2007 and is President of Shire Human Genetic Therapies. As one of the world's leading specialty biopharmaceutical companies, Shire is focused on a single purpose: to enable people with life-altering conditions to lead better lives.

Dr. Gregoire's keynote address will begin at 3:30pm. She will introduce the audience to Shire and its culture and will touch on some of the reasons why Shire elected to stay local with its current and future expansion plans. She will also describe the critical decisions that led Shire to a disposables approach in their new production plant, including timing, automation and validation. A question and answer period follows Dr. Gregoire's address and will feature a group of Shire leaders.

The ISPE Annual Product Show has been held at Gillette Stadium for the past five years, and has been a flagship event for the Boston Area Chapter for the past nineteen years. In addition to the Keynote Address, the Product Show offers a full day of activities including educational sessions, almost 300 vendor exhibits (vendor booths sold out again this year) and the opportunity to network with the 2000 or so local life sciences professionals expected to attend this year.

Register for the Product Show today to attend Dr. Gregoire's keynote address and other scheduled sessions - as always, admission, parking and food are free.

## Attend the Product Show Educational Program & Learn from Industry Leaders

*by Brian Hagopian, Mar Cor Purification*

This year's Product Show at Gillette Stadium offers eight opportunities to learn from local industry leaders. The morning session starts out with a GAMP® forum from 8:30am to 12:30pm (see following article for details) where attendees will receive up-to-date industry information and enjoy Gillette's excellent lunch buffet. You must pre-register to attend the GAMP session; there is a nominal fee to cover the cost of lunch.

Attentive audiences and sold-out presentations are the norm for the educational programs

The six afternoon sessions will run about an hour apiece, affording speakers more time to dive into their respective subject matter while still leaving ample time for questions and answers afterwards. Three sessions run concurrently; the first group from 1:30pm to 2:45pm and the second group from 5:00pm to 6:15pm.

The Product Show is proud to feature two speakers from the University of Massachusetts this year. Dr. Carl Lawton from UMass Lowell will cover the basics of biotech in his talk entitled "Biotech 101." Back by popular demand, this introductory session attracted a record turnout at last year's event. Dr. William Thomas from UMass Medical in Worcester will take the next step in his discussion covering Biotech R&D and Scale-up.

The production-oriented sessions feature two accomplished speakers. Dr. Michael Drues from Vascular Sciences will be speaking on "Combination Products and Convergence," while Gregory Zarbis-Papistoitsis from Percivia will cover "Streamlining Monoclonal Antibody Purification Processes."

The focus shifts to facilities with Charles Pappalardo from Charles

River speaking on "Innovative Energy Management and Maintenance of GLP facilities" followed by a panel discussion on "Sustainable Building Designs in Practice" featuring Francis Boucher from National Grid, Paul Lukitsch from Millipore, Dan Wall from RDK Engineers, and Steve Zilonis from Aricogen, Dresser-Rand.


Seminars and panel discussions cater to a wide range of interests and experience levels

And if that's not enough to get you to the show, hold on. We're thrilled to have Dr. Sylvie Gregoire, President of Shire Human Genetic Therapies as our Keynote Speaker (see related article).

There's only one way to guarantee your attendance and that's to pre-register. Follow this link http://www.ispeboston.org/ProductShow/index.html to be sure you don't miss out - most sessions were standing-room only last year. We look forward to seeing you on October 6th!

## Product Show Schedule of Events

AGENDA
19th Annual Product Show and Educational Seminars
Wednesday, October 6, 2010

| | | | |
|---|---|---|---|
| **8:30 – 12:30** | **GAMP Forum**<br>Speakers:<br>**Theresa McCarthy**, Past Chair of the American Society of Quality Boston Section<br>**Kristin S. Murray**, Pfizer<br>**Randy Perez, PhD**, Novartis Pharmaceuticals<br>**Stephen Reich**, Pfizer Global Quality | | |
| **1:00 pm** | **Announcements and Door Prize Drawing #1** | | |
| **1:30 – 2:45** | **Combination Products and Convergence: An overview of clinical benefits, regulatory issues and manufacturing challenges**<br>Speaker:<br>**Dr. Michael Drues**, Vascular Sciences | **Biotech 101 and Leveraging New Technology**<br>Speaker:<br>**Dr. Carl Lawton**, Massachusetts BioManufacturing Center and UMass Lowell | **Innovative Energy Management & Maintenance of GLP Lab Facilities**<br>Speaker:<br>**Charles Pappalardo**, Charles River |
| **3:15 pm** | **Announcements and Door Prize Drawing #2** | | |
| **3:30 – 4:30** | ***Keynote Address: Shire HGT--An Overview of the Company, Production Platform, and What's Ahead for the Future***<br>***by Dr. Sylvie Grégoire, President, Shire Human Genetic Therapies*** | | |
| **5:00 – 6:15** | ***Towards a Single Use Downstream Process for the Purification of Monoclonal Antibodies***<br>Speaker:<br>**Michael Kuczewski**, PERCIVIA LLC | ***Biotech R&D: Monoclonal Antibody Discovery, Testing, and Development***<br>Speaker:<br>**William D. Thomas, Jr. PhD**, MassBiologics of UMass Medical School | ***Sustainability in Practice – A Panel Discussion***<br>Panelists:<br>**Francis Boucher**, National Grid<br>**Paul Lukitsch**, Millipore Corporation<br>**Dan Wall**, RDK Engineers<br>**Steve Zilonis**, Aircogen, Dresser-Rand Company |
| **6:15 – 7:15** | **Student and Young Professional Networking Social – Location: R15** | | |

| | |
|---|---|
| | |
| **6:30 pm** | **Announcements and Door Prize Drawing #3** |
| **7:30 – 9:00** | **Open Networking Reception** |

## GAMP® Forum Brings Together Experts and Local Practitioners at Gillette

*by Greg Ruklic*

The GAMP forums are sponsored regionally around the world by the ISPE Good Automated Manufacturing Practice (GAMP) Community of Practice to bring together experts and local practitioners from the life sciences industries for learning and networking opportunities in creating and managing the life cycle of critical computer systems.

Begin your day at Gillette with the half-day GAMP Forum - before the Product Show begins

Each year, ISPE assembles a program of speakers to present current hot topics and facilitate question and answer sessions. Once again, this year we are fortunate to be able to conduct our regional forum in association with the Boston Area Chapter Product Show on Wednesday, October 6th from 8:30am to 12:30pm at Gillette Stadium. The forum is a great opportunity to update your knowledge and share experiences with your colleagues and peers in Engineering, Quality, Compliance, IT, Operations and other disciplines that must work together to achieve efficient approaches and reliable operation of systems while meeting regulatory requirements.

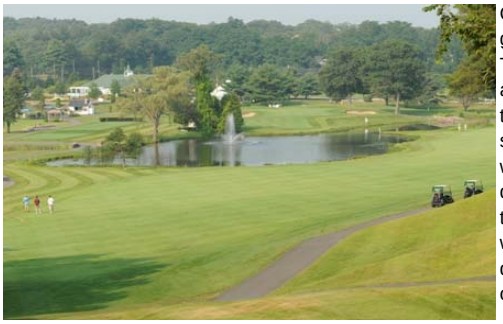
This year's half-day forum features:

- Update and Q&A on Special Interest Groups such as MES, JETT (equipment), Laboratory Systems, Risk Management, R&D Systems, and more. Learn how your peers are collaborating and developing/replicating best practices.
- Presentation and discussion on Quality Risk Management (QRM) Tool Selection: Getting to Right the First Time. A tutorial on utilizing appropriate tool sets for success.
- ISO 9001:2008 and 21 CFR 210, 211 '"Working Together for Quality." ISO 9001 and cGMPs can be brought together to augment compliance initiatives. Another "back to the future" approach where melding of mature and new initiatives can be used to enhance your existing cGMP quality system.
- The FDA Part 11 Inspection Initiative. Learn how the FDA is coming to your door with a specific assignment to determine how well companies have implemented and remain compliant with CFR 21 Part 11 (electronic records and signatures).

We hope you will join us for an informative experience. Register online at www.ispeboston.org/events before September 29th to guarantee attendance. Members $40; non-members $65; students $5. Registration fee includes lunch; payment is by credit card or check. See you at Gillette!

## Boston Area Chapter Scores with 8th Annual Golf Outing

*by Christopher Opolski, Alexion Pharmaceuticals*



Overlooking the course at Ferncroft Country Club

On August 16th, the Boston Area Chapter hosted our annual golf tournament at the Ferncroft Country Club in Middleton, MA. This is the third year that Ferncroft was the site of our event and once again they did a wonderful job. A full field of 36 teams competed on this beautifully maintained course. A few sprinkles in the morning cleared to a mostly cloudy, dry day with low humidity and moderate temperatures; quite a departure from last year's tournament which had seen 95„aF temperatures, high humidity and a cloudless day. The day wasn't just about the golf! Some of the special "extras" of the day included a Dewar's tasting hole and cigars to help golfers on the hole-in-one contest hole.

At the end of play, everyone enjoyed a cocktail reception in the club house. During the reception, 27 contestants that previously sunk a 10' putt during play had a chance to win $10,000 if they first sunk a 30' putt and then a final 50-footer. Unfortunately, a valiant effort by Jason Becker just missed falling in the hole. Congratulations to all of the day's winners.

First place winners, sponsored by Robert W. Sullivan, (l to r)
Brian Hagopian, Matt Chardovoyne,
Tony Preteroti & Paul Sullivan

Second place winners, sponsored by Erland Construction,
(l to r) Bob Liptrot, Bill Piombino, Bob Lewis & Chuck Vaciliou

Third place winners, sponsored by Shilay Associates, (l to r)
Tony Schena, Jason Becker, Tom Schiller & Granger Toper

The winning teams:

| First Place (61) | Second Place (62) | Third Place (63) |
|---|---|---|
| Robert W. Sullivan | Erland Construction | Shilay Associates |
| Paul Sullivan | Bob Lewis | Granger Toper |
| Matt Chardovoyne | Bill Piombino | Tom Schiller |
| Tony Preteroti | Chuck Vaciliou | Jason Becker |
| Brian Hagopian | Bob Liptrot | Tony Schena |

And the individual winners:

| | Men | Women |
|---|---|---|
| Longest Drive | Justin Edwards | Pat Nugent |
| Closest to Pin | Tony Pretoroti (2' 2") | N/A |
| Straightest Drive | Jarrod Dore | Sylvia Beaulieu |

Many, many thanks to our Golf Outing sponsors: Decco, Robert W. Sullivan, Cotter Brothers, Structure Tone, DPS Bio, GxP Automation, New England Controls, Superior Controls, Interstate Electrical Services, North Shore Mechanical Contractors, The Richmond Group, Erland Construction, SciTech Builders, TRG Builders, Arion Water, Aztec Technologies, Shilay Associates, Water Consulting Specialists, AES Clean Technology, ValSource, and RDK Engineers, all of whom helped to make this event another big success for the Chapter.

A special thanks to tournament co-chair Michelle Greaney, P&IDC, whose tireless and enthusiastic support helped make this event a huge success. Additionally, thanks to Daniel Rufo, Christopher Hoell, John Ramirez, and Brian Hagopian for volunteering their support during the event.

## Boston Area ISPE Student Members Shine in Annual Poster Contest

*by Rick Pierro, Superior Controls*

It was Friday evening on May 21st at 6:00pm and most Boston students were out relaxing and enjoying the evening. At Northeastern University's Curry Student Center however, the scene was far more tense. Five ISPE Student Members and graduate students displayed their colorful posters and nervously prepared themselves for their 10-minute presentation, to be followed by rapid fire technical questions about their research from four ISPE veterans and judges. The yearly Boston Area ISPE Student Poster Contest was in session!

Proud Poster Contest Winners (from l to r)
Sheba Goklany and Fulden Buyukozturk.

The judges, each with a stern demeanor and critical eye, included Henry Brush, Mike Denault, Kevin Lynch and Rick Pierro. They were amazed and impressed by the high quality of all five presentations and in the excitement one judge even asked the students if he could invest in their new venture. That particular judge had to be reminded that this was only a student poster contest.

As the evening went by, points were noted, scores were tallied, the judges huddled, and finally two brilliant Northeastern graduate students were pronounced winners. Sheba Goklany ("Transcriptional regulation of terpenoid indole alkaloid biosynthesis in methyl jasmonate-induced C. roseus hairy root cultures") and Fulden Buyukozturk ("Impact of emulsion-based drug delivery systems on intestinal permeability and drug release kinetics") proudly took to the stage, had their photos taken and were pronounced the 2010 Boston Area ISPE Student Poster Contest winners.

Both Sheba and Fulden will represent the Boston Area Chapter at the International ISPE Poster Contest held in conjunction with the ISPE Annual Meeting in early November in Orlando, Florida. In one of the many contributions the Chapter makes toward student development, their travel expenses will be covered in full by the Chapter. Although the competition from around the country will be stiff - 11 other Chapters will send their best - our Boston Area winners can certainly handle it.

Special thanks go to the Northeastern University ISPE Student Chapter for hosting the Poster Contest again this year and to all the students and judges who participated.

## Boston Area Young Professionals Reconvene after Summer Break

*by Josh Strauss, Commissioning Agents, Inc.*

The Boston Area Chapter's Young Professionals (YP) Committee recently held our first meeting following summer recess and has already begun to build on the success of last year's events. Based on the positive feedback we have received from young professionals in the pharmaceutical industry, our goal will be to offer more educational and social events that will spur further career development and networking opportunities for Chapter members. The committee now numbers nine members, with several new faces added. This will help us offer even more services and events than last year. The current members include:

MJ Bruce - Capaccio Environmental Engineering
Jared Marshall - Genzyme Corporation
Rob DeCoste - Commissioning Agents
Keyur Doshi - Acceleron Pharmaceuticals
AJ McMahon - Sentinel Process Systems
Aarash Navabi - Genzyme Corporation
Dan Ramsey - Commissioning Agents
Josh Strauss - Commissioning Agents
Jillian Willard - Genzyme Corporation

In the works for fall 2010 are a Boston Harbor cruise Friday, September 17th, 7:30-10:30pm. The cruise departs from Boston Belle Charters, Marina Bay, 333 Victory Road, Quincy. Tickets are on sale for $30 for members and $35 for non-members. This will be an excellent event to attend for networking with other young professionals in the industry while enjoying Boston's beautiful skyline. More importantly, the Young Professionals have challenged their senior (yet young at heart) ISPE counterparts to a softball game on Tuesday, September 21st, 7-9pm at the Teddy Ebersol Redsox Field on the Esplanade in Boston. If you have any questions about either event, please contact Rob DeCoste at ispeyp@gmail.com or sign up online at www.ispeboston.org/events.

One of the core activities of the YP Committee is student outreach. Last spring we visited Worcester Polytechnic Institute

to gauge student interest in forming an ISPE Student Chapter. Based on the positive student reaction, we are on track to have a new Chapter operating at WPI in September. Other student outreach activities include visiting existing Student Chapters on campus to investigate how a group such as ours can best support students' career and networking interests and providing practical information to students such as resume writing, acing the interview and general information about the industry.

Part of our student outreach activity emphasizes networking with industry representatives. Educational events are planned for November, January, and March (watch for further announcements). The topics we plan to cover include project management, networking control devices for pumps/valves, and a hands-on event to dissect valves and pumps. We are planning at least three membership drives to coincide with these educational events. Also, come find us at the Product Show October 6th at Gillette Stadium.

The Young Professionals are always in need of volunteers and we welcome anyone interested in helping new professionals transition to industry. The ISPE Boston Area Young Professionals has a new email address: ispeyp@gmail.com. If you have any questions, comments or editorial remarks, we would love to hear from you.

## Tech Talk: Single-Use Technology - Achieving Smooth Transitions into Your Operations

*By Adam Goldstein and Pietro Perrone, P. E.*

This article provides guidelines for the assessment of single-use technology and recommends plans for a smooth and speedy integration of single-use technology into your operation. We present an implementation model to switch from stainless steel tanks to bioprocess containers (BPC). While the article focuses on BPC, the techniques can be applied to other single-use components or assemblies.

### What are the benefits?

The benefits are simple - switching from stainless steel tanks to BPCs increases efficiency and flexibility while decreasing capital costs. Achievement of these benefits depends on a strong analysis for your particular situation and a well executed implementation program. Conducting the right activities at the appropriate time is critical for success. The project plan should be all encompassing from the beginning and minimize surprises throughout.

### Get started with an effective follow through

A comprehensive implementation process is a key factor in achieving these benefits. For this process to be effective, input from several company functions are required. This can be assured if the project includes the following elements:

1. Define a multifunctional team with a project manager knowledgeable in BPCs.
2. Develop a project plan covering all affected areas in the company's operations.
3. Decide on vendors that can best support your initiative.
4. Plan for and conduct testing to qualify the switch in the operation.

It is important to assign a project manager to head the BPC implementation team. The project manager should have sufficient knowledge about BPCs to work with the implementation team to define the scope of the project, the needs of the company, and the processes/applications where BPC implementation is most beneficial.

### The mechanics of getting it done right the first time

When defining the scope of the project, it is necessary to examine the specific needs of the company. Though BPCs allow for cost savings by eliminating steam-in-place and clean-in-place operations, the investment needed to switch to BPCs may not make it feasible for every stainless steel tank to be replaced. It is important to involve as many area managers as necessary, along with quality and validation representatives, to determine which applications would most benefit from BPC implementation.

Once process applications have been earmarked for BPC implementation, the project team decides which BPC sizes and volumes will be used based on production needs. Taking into account available space in a facility is key to deciding upon BPC sizes. Regardless of the cost savings benefits that might come from implementation, if there is no available space in a facility to support a certain-sized BPC, then implementation is not possible. Furthermore, if the BPC is to be used in multiple areas and rolled or carried around, it is necessary to consider the feasibility of doing this with the proposed size and volume BPC. Finally, when determining BPC volumes it is important to overestimate the maximum fill volume as overfilling BPCs is not recommended.

After production needs have been agreed upon, the implementation team's focus should shift towards determining specific bag requirements. Not all BPCs are created the same and as such a list of bag requirements specific to the proposed process should be formulated so that it can be presented to vendors. Among the requirements that need to be examined are the usage and tubing specifications that the BPC will be introduced into. For example, when looking at the process in which BPCs would be utilized, usage requirements would include filling strategy and whether the BPC is compatible with the proposed method of filling. Other usage requirements that must be studied prior to implementation are filtration requirements (i.e. whether the filters used in the process are compatible with the BPC) and whether a certain BPC will be used for a single application or multiple ones.

Since BPCs are usually introduced into a process rather than as stand alone entities, it is just as important to make sure that tubing requirements are also in line with the proposed operation. Tubing should be compatible with the flow rates, pressure, connections, and inlet/outlet configuration that will be present in the process as well as being the right length in order to be accessible. Tubing also needs to be compatible with the chemical and mechanical properties of the process as well as the temperatures, leachable standards, and biocompatibility of the process.

### Deciding on vendors

Once the implementation team decides on their needs and specific BPC requirements it is time to bring those requirements to vendors to supply the team with the product. It is important to evaluate enough vendors to identity at least

two that meet the implementation team needs. Having dual-sourced BPCs will buffer against vendor supply issues affecting the process. Another thing to consider when choosing vendors is the responsiveness and knowledge base of their staff. If you have to hold a vendor's hand during the purchase process, do not expect much help from them if anything goes wrong. Furthermore the chosen vendor should have the quickest turnaround time for engineering changes and should operate with corporate standards similar to those at your own company. Engineering change turnarounds between two and three weeks should prevent the implementation process from being dragged out due to vendor inadequacy. In addition, qualified local support from the vendor can mean the difference between a process being run on time or not.

Another consideration that must be made when evaluating vendors is the flexibility in BPC tote design. The ability for the vendor to add wheels or a temperature control jacket to a BPC tote to fit your facility needs is an important factor in the selection. While this flexibility can be considered anywhere in the vendor selection process, Figure 1 (see later section of article) identifies an optimum location in the timeline to do this evaluation.

Furthermore, if the BPC will be placed into a regulated process, it is important to evaluate the availability of validation and extractable testing data and endotoxin and particulate (EP) testing provided by the vendor. Qualification and validation testing can put a serious dent in your budget to the point where a vendor's willingness to provide that testing may make or break the decision to go forward with BPC implementation in your facility. Also, along with the above BPC testing, a vendor should be evaluated on their availability of appropriate USP and EP testing on all components.

Ultimately, though it is important to evaluate a vendor on the basis of many different conditions, the most important consideration should be placed on the quality of film and overall product provided by the vendor along with the functionality of the design in terms of your process.

### Testing is a major factor

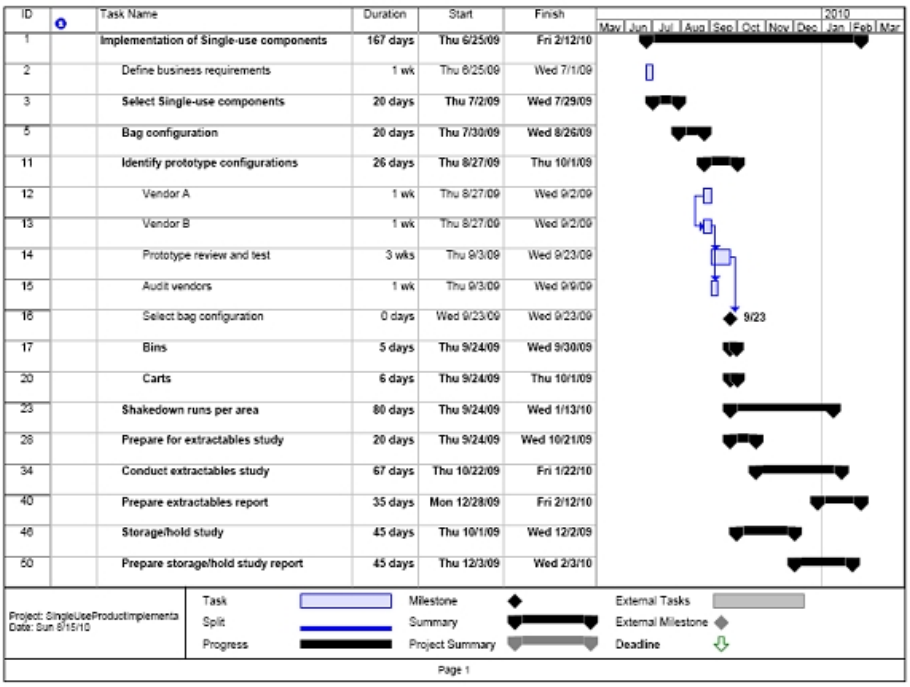
Once the primary and secondary vendors are selected, it is time to conduct the necessary testing in order to implement your new BPC into your process stream. While most vendors conduct contact layer testing for their specific containers, it is important that either your company or a contracted testing lab performs testing specific to the storage conditions, solutions and hold times that exist in your process. It is important that test conditions mirror the actual conditions that the BPC will encounter since temperature, the aggressiveness of the solution, and the organic content of the solution all affect the performance of the BPC and ultimately the proposed process into which it is being implemented. Since plastics can release soluble or insoluble materials into products, it is also necessary to conduct a technical assessment to identify the sources and amounts of these extractable chemicals.

An extractable testing program should be initiated to estimate the quantity of chemicals that can potentially leach from plastics into process streams by using model test solutions that bracket the process solutions. This bracketed approach generates a worst-case estimate for the maximum amount of extractables that could be concentrated within the product and evaluates the risk associated with the worst-case extractability findings. Other factors that must be controlled are maximizing the surface-to-volume ratio of the test container-solution combination and storing the containers for the actual time that will be used in production.

### Bringing it all together

By developing a strong team and following a structured implementation timeline (like the one seen in Figure 1), disposable bioprocess containers can be effectively and efficiently implemented into a facility's operation with minimal surprises and disruptions.

Fig.1 MS Project Example - Showing Key Implementation Tasks




While disposable bioprocess containers offer many advantages over their stainless steel counterparts, these cost savings vary in terms of the production process and scale in which it is being implemented into. Ultimately it is necessary to develop a strong implementation team capable of evaluating which applications work best for BPC integration and follow a

regimented implementation plan.

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This article builds on earlier articles "Single-Use Technology - Flexible technology that gives the user choices"1 and "Method for Implementing Disposables into a Bioprocess Facility"2. Also it is recommended that the reader visit the ISPE Disposables Community of Practice (COP) and the Implementation of Disposables COP for detailed communications among members about how Single-Use equipment is impacting their work.

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Adam Goldstein is currently the technical lead for the Clinical Purification Operations at Genentech. In his past roles, Adam developed new novel chromatographic and downstream capture processes. Several of the processes were cutting edge, pushing the vendors' envelope and challenging new ways to scale chromatography equipment. He is the author/inventor for several patents utilizing downstream processing techniques and has been a downstream lead for five significant biotech start ups including Genentech, Amgen, Biogen, Baxter, GenVec facilities. Currently, he is Co-Chair of the ISPE Disposables Community of Practice and an IBC Scientific Advisor. Adam earned his BS in immunology from Old Dominion University, Norfolk, VA; holds a biochemical regulatory engineering certificate, cGMP practices, from the University of Maryland; and a Masters in biomedical sciences/molecular biology from Hood College, Frederick, MD.

Pietro Perrone, P.E. is a Systems Engineer at EMD Millipore (EMD Millipore is a division of Merck KGaA, Darmstadt, Germany) where he oversees the design of single-use assemblies and associated components for the biopharmaceutical industry. Pietro is a Professional Engineer registered in Massachusetts with a degree in chemical engineering from Tufts University and 20-plus years of purification/separation technology experience in process development/optimization, equipment scale-up, and project management. He recently earned a Certificate in Nanotechnology from the University of Massachusetts, Lowell and is presently enrolled in its Biomedical Engineering and Biotechnology Program. Pietro is an active member of the ISPE Disposables Community of Practice and is on the board of directors of the Boston Area Chapter of ISPE. He is active in the Ichthyologists (Boston Section of American Institute of Chemical Engineers) and is a member of the American Chemical Society.

## Industry News In Brief

*by Patti Charek*

### Management Change and New Direction at GTC Biotherapeutics

William Heiden, the new president and CEO of the Framingham biotech GTC Biotherapeutics, admits that the last couple of years for the company have been a struggle. The company lost $27.9 million last year and another $7.7 million in the first quarter of 2010. But Heiden has a plan to put the company, which uses genetically enhanced goats to produce pharmaceutical drugs, on a growth trajectory within the next 12 to 18 months. The first step in that process began in mid-June when the GTC board of directors named Heiden the company's new president and CEO. He most recently served as president and CEO of Elixir Pharmaceuticals in Cambridge.

Also during the shakeup, the GTC board fired its top two executives along with 50 other employees. At the same time, the company received $7 million in debt financing from its majority shareholder, the French biotech company LFB Biotechnologies.

Heiden's goal is to transition GTC from a drug-development company into a drug-selling company. The company already has one drug, called ATryn, on the market that is approved for sales in the US and Europe. The drug, which is purified from the milk of genetically enhanced goats, is used to treat patients who have a protein deficiency in their blood that prevents clotting. GTC is working with Lundbeck Inc., a Danish company with US offices in Chicago, to market the drug to physicians.

A second goal is to continue to develop Factor VIIA, a drug developed with LFP to treat the blood disorder hemophilia. Heiden said he expects that drug to begin clinical testing in humans before the end of the year. Then, Heiden hopes to work with LFB on developing additional drugs that can be made using the transgenic process.

Heiden is hoping a renewed focus on cost-cutting measures and developing profitable drugs will allow the company to grow in the coming years. According to an SEC filing, the company will net $8 and $9 million in annual savings from the reduction in staff. The company will still have about 60 employees at its Framingham headquarters and a farm in Charlton where the goats are housed and the drugs are made. (Source: Brandon Butler, Worcester Business Journal, 8 July 2010)

### RXi Gets NIH Grant

Worcester's RXi Pharmaceuticals has won a $600,000 grant from the National Institutes of Health for pre-clinical development of RNAi therapeutics. The Advanced Technology Small Business Innovation Research grant from the National Institute of Allergy and Infectious Diseases will provide $300,000 per year in 2010 and 2011. The company can also apply for a second phase of funding that could provide up to $1 million per year for three years after the first phase is

completed. RXi's primary focus is developing treatments for skin and eye disorders, and it also does work in oncology and spinal cord delivery of therapies. (Source: Livia Gershon, Worcester Business Journal, 13 July 2010)

### Sanofi-Aventis and Regulus Therapeutics Form Strategic Alliance on microRNA

Regulus Therapeutics and Sanofi-Aventis have announced that they have entered into a global, strategic alliance to discover, develop, and commercialize microRNA therapeutics. The alliance represents the largest microRNA partnership formed to date, valued at potentially over $750 million, and includes a $25 million upfront fee, a $10 million future equity investment subject to mutual agreement on company valuation, and annual research support for three years with the option to extend two additional years. The alliance will initially focus on the therapeutic area of fibrosis.

Regulus and Sanofi-Aventis will collaborate on up to four microRNA targets, including Regulus' lead fibrosis program targeting microRNA-21. sanofi-aventis also receives an option for a broader technology alliance that provides Regulus certain rights to participate in development and commercialization of resulting products. If exercised, this three-year option is worth an additional $50 million to Regulus. Alnylam Pharmaceuticals and Isis Pharmaceuticals formed Regulus in 2007, with each company currently owning approximately 50% of the preferred stock.

microRNAs are small RNA molecules, typically 20 to 25 nucleotides in length, that do not encode proteins but instead regulate gene expression. Nearly 700 microRNAs have been identified in the human genome, and more than one-third of all human genes are believed to be regulated by microRNAs. As a single microRNA can regulate entire networks of genes, these new molecules are considered the master regulators of the genome. microRNAs have been shown to play an integral role in numerous biological processes including the immune response, cell-cycle control, metabolism, viral replication, stem cell differentiation and human development.

Most microRNAs are conserved across multiple species indicating the evolutionary importance of these molecules as modulators of critical biological pathways. Indeed, microRNA expression or function has been shown to be significantly altered in many disease states, including cancer, heart failure and viral infections. Targeting microRNAs with anti-miRs, antisense oligonucleotide inhibitors of microRNAs, or miR-mimics, double-stranded oligonucleotides to replace microRNA function, opens the possibility of a novel class of therapeutics and a unique approach to treating disease by modulating entire biological pathways. (Source: Regulus Therapeutics Website, 22 June, 2010)

### Alnylam Obtains Approvals for Phase I Study

Alnylam Pharmaceuticals, a leading RNAi therapeutics company, announced that its applications for ALN-TTR01 have been given clearance by Portuguese, Swedish, and British regulatory authorities to begin clinical testing. The trial will begin enrolling patients shortly in a blinded, randomized, placebo-controlled, multicenter Phase I study.

ALN-TTR01 is a systemically delivered RNAi therapeutic being developed for the treatment of transthyretin (TTR)-mediated amyloidosis (ATTR), including familial amyloidotic polyneuropathy (FAP) and familial amyloidotic cardiomyopathy (FAC).

ALN-TTR01 is being advanced to clinical development using stable nucleic acid-lipid particles (SNALP) delivery technology developed in collaboration with Tekmira Pharmaceuticals Corporation.

ATTR is a hereditary, systemic disease caused by a mutation in the transthyretin (TTR) gene. TTR protein is produced primarily in the liver and is normally a carrier for thyroid hormones and retinol binding proteins. The mutation causes abnormal amyloid proteins to accumulate in and damage body organs and tissue such as the peripheral nerves and heart, resulting in intractable peripheral sensory neuropathy, autonomic neuropathy, and cardiomyopathy.

In its severest form, ATTR represents a tremendous unmet medical need with significant morbidity and mortality as an orphan disease; combined, FAP (familial amyloidotic polyneuropathy) and FAC (familial amyloidotic cardiomyopathy) affect approximately 50,000 people worldwide. ATTR patients with FAP have a mean life expectancy of five to 15 years from symptom onset and the only treatment option is liver transplantation; as a result there is a significant need for novel therapeutics to treat patients who have a mutation in the TTR gene.

RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of a major new class of medicines, known as RNAi therapeutics, is on the horizon. Small interfering RNAs (siRNAs), the molecules that mediate RNAi and comprise Alnylam's RNAi therapeutic platform, target the cause of diseases by potently silencing specific mRNAs, thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way. (Source: Alnylam Website, 29 June 2010)

### Biogen Idec Names George Scangos Chief Executive Officer

Biogen Idec announced that George A. Scangos, Ph.D., has been appointed Chief Executive Officer, effective July 15. Dr. Scangos will also be named to the Board of Directors. Dr. Scangos brings nearly 25 years of experience in the biotechnology and pharmaceutical industries. He joins Biogen Idec from Exelixis, Inc. where he has served as President and CEO since 1996. Under Dr. Scangos' leadership, Exelixis has built and advanced a pipeline of 14 clinical compounds and forged numerous strategic partnerships.

Previously, Dr. Scangos spent 10 years at Bayer Corporation. He joined the company as a staff scientist, served as Senior Vice President of Research and Development, and most recently served as President of Bayer Biotechnology, where he was responsible for research, business development, process development, manufacturing, engineering, and quality assurance of Bayer's biological products. Before joining Bayer in 1987, Dr. Scangos was a Professor of Biology at Johns Hopkins University for six years. Dr. Scangos holds a B.A. in Biology from Cornell University and a Ph.D. in Microbiology from the University of Massachusetts.

Upon his appointment, Dr. Scangos stated, "As I approach day one, I see some clear priorities for the company. We have significant opportunities to advance the commercial business by driving the performance of AVONEX, TYSABRI and RITUXAN, preparing our organization and the marketplace for the potential launch of five significant new products over a three year period, and strengthening existing partnerships and forging new alliances. Another priority is advancing our promising pipeline which includes hiring a passionate and talented new head of R&D. I also plan to instill a sense of

urgency in every aspect of the business to ensure that we execute at the highest levels and capitalize on our growth opportunities. We have a lot ahead of us, and I'm eager to get started." (Source: Biogen Idec Website, 30 June, 2010)

### Shire Purchases Strategic Site in Massachusetts

Shire plc recently announced its purchase of the Lexington Technology Park campus in Lexington, MA. The purchase signifies an investment in the growth of its Human Genetic Therapies (HGT) business, which focuses on the discovery, development, and manufacturing of treatments for rare genetic diseases.

Shire had previously leased three buildings on the 96 acre campus, and owns the parcel of land on the site where its new 200,000 square foot manufacturing plant is located. The purchase agreement is for the remaining land, including the three existing buildings comprising 280,000 square feet. Through the acquisition, Shire gains ownership of an additional 570,000 square feet of expansion potential available under the current permit, including 170,000 square feet already under construction. The purchase is value enhancing compared to the current lease agreement and has no material earnings impact. The $165 million cash purchase price will be settled during Q2 2010.

"We are delighted to increase our presence in Massachusetts, which is one of the world's foremost centers for the biomedical and biopharmaceutical industry," said Sylvie Grégoire, President of Shire Human Genetic Therapies. "Shire currently employs 1,000 people in the Commonwealth. This strategic purchase will allow our company greater flexibility as we grow, and enable us to remain focused on the research, development and manufacture of therapies for those suffering from rare diseases." (Source: Shire Website, 30 June 2010)

### Lilly Halts Development of Drug for Alzheimer's Disease in Phase III Clinical Trials

Eli Lilly and Company will halt development of semagacestat, a gamma secretase inhibitor being studied as a potential treatment for Alzheimer's disease, because preliminary results from two ongoing long-term Phase III studies showed it did not slow disease progression and was associated with worsening of clinical measures of cognition and the ability to perform activities of daily living.

The company's decision does not affect the ongoing clinical trials of solanezumab, Lilly's other compound in Phase III trials as a potential Alzheimer's treatment. While both drugs focus on amyloid-beta proteins, which are believed to play a critical role in Alzheimer's disease, they have different mechanisms of action. Lilly also has two other compounds in earlier stages of clinical development; those studies are not affected by the announcement.

In two pivotal Phase III trials, semagacestat was compared with placebo in more than 2,600 patients with mild-to-moderate Alzheimer's disease. Lilly has now reviewed data from a pre-planned interim analysis of semagacestat studies. This interim analysis showed that, as expected, cognition and the ability to complete activities of daily living of placebo-treated patients worsened. However, by these same measures, patients treated with semagacestat worsened to a statistically significantly greater degree than those treated with placebo. In addition, data showed semagacestat is associated with an increased risk of skin cancer compared with those who received placebo.

Lilly's clinical team will continue to gather and evaluate data from these studies, and will publish the results for the benefit of future Alzheimer's research. Although dosing with semagacestat is being stopped, Lilly plans to continue collecting safety data, including cognitive scores, for at least six months through regularly scheduled follow-up visits with study physicians and modifications of the existing Phase III protocols. These additional follow-up visits will help to answer a number of important questions, including whether the differences between patients who received semagacestat and those who received placebo will continue after semagacestat has been discontinued.

"We are clearly disappointed by the results we are announcing today. However, Lilly's innovation strategy, based on advancing a pipeline of nearly 70 molecules currently in clinical development, does not rest on the success or failure of any single compound," said John C. Lechleiter Ph.D., Lilly's chairman and chief executive officer. "Pharmaceutical research always carries risk, as these results show. But it offers as well the potential for tremendous reward for millions of patients who await new medicines. Despite this and other recent setbacks, Eli Lilly and Company remains financially strong and is even more determined to prevail in our quest to provide new treatments for Alzheimer's and other serious diseases." (Source: Eli Lilly Website, 17 August 2010)

### Biogen Idec and Knopp Neurosciences in Agreement for Late-Stage ALS Drug

Biogen Idec and Knopp Neurosciences, a privately held, Pittsburgh-based biopharmaceutical company, have announced they have entered into an exclusive, worldwide license agreement under which Biogen Idec will develop and commercialize KNS-760704 (dexpramipexole) for the treatment of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, and potentially other indications.

KNS-760704 is a novel oral neuroprotective therapy under development. In a Phase 2 study of ALS patients conducted by Knopp, the compound achieved its primary endpoint evaluating safety and tolerability and showed favorable dose-related effects in preserving motor function and extending survival. KNS-760704 has received orphan drug designation from the FDA and the European Commission for the treatment of patients with ALS, as well as Fast Track designation from the FDA. Biogen Idec expects to initiate a Phase 3 program of the compound in the first half of 2011.

Under the terms of the agreement, Biogen Idec will lead the development of KNS-760704 for ALS and its potential commercialization in global markets, with Knopp providing development support and conducting certain US commercialization activities under the direction of Biogen Idec. As part of the transaction, Biogen Idec will purchase $60 million of Knopp stock, provide an up-front payment of $20 million and additional payments of up to $265 million based on the achievement of development, regulatory, and sales milestones. Biogen Idec will also pay tiered, double-digit royalties to Knopp on worldwide sales.

ALS is a universally and rapidly fatal neurodegenerative disorder characterized by progressive muscle weakness and wasting. ALS affects adults in the prime of life and creates a substantial burden for caregivers. US prevalence is approximately 20,000 and the global incidence is approximately two per 100,000. Only one drug has been approved for the treatment of ALS. Life expectancy after symptom onset is usually three to five years. (Source: Biogen Idec Website, 18 August 2010)

### Roche Backs New Method for Drug Delivery to Cells

The Swiss pharmaceutical giant Roche is throwing its weight behind an experimental technology that could be used to treat a number of diseases. The company has agreed to pay $25 million now and up to $1.1 billion later to Cambridge-based Aileron Therapeutics for developing a new type of drug technology called "stapled peptides."

Aileron, which holds patent rights from Harvard and the Dana-Farber Cancer Institute, hopes to start clinical trials next year. It is testing a stabilized form of peptides, a small protein, to deliver medicine inside cells for a variety of medical conditions, including Roche's priorities like treatments for cancer and inflammation.

The synthetic peptides, developed by a Harvard chemical biologist, have been described as a type of magic bullet that can deliver particularly potent doses of drugs at the cellular level. They are stabilized in a helical shape that stays active longer in the body. Joseph A. Yanchik III, the chief executive of Aileron, said they have been successfully tested in animals. He said the company started preliminary talks with the FDA in June; the FDA must approve an investigatory new drug application before human testing can begin.

Dr. Jean-Jacques Garaud, Roche's global head of pharmaceutical research and early development, said stapled peptides could open new horizons in medicines. "One of the challenges the industry is facing is not to identify new targets, but to be able to reach the target that we would like to reach with the right therapeutic benefit, particularly inside the cell," he said in a phone interview. He emphasized, however, that they are years from proving it will work in patients. "Obviously no one knows yet, but it is worth exploring as a tool," Dr. Garaud said.

Roche and Aileron said they would focus on five target diseases. Citing proprietary reasons, they would not identify the diseases but said they fall among Roche's priorities of cancer, viruses, inflammation, metabolism and the central nervous system. Aileron's lead research aims at cancer.

Dr. Garaud said Roche's chief executive has approved the deal with Aileron. Officials with both companies said Aileron would receive the full $1.1 billion only if its products succeeded in all five therapeutic areas. Most of the money would be paid after reaching certain milestones and in royalty rights.

Existing peptide products, without the stapling, include Forteo from Eli Lilly for osteoporosis and Byetta from Amylin and Lilly for Type 2 diabetes. So far the peptides must be injected; they do not come in pill form. Roche, based in Basel, is the world's largest biotech company and bought Genentech last year. Aileron, founded in 2005, has about 40 employees. (Source: Duff Wilson, New York Times, 24 August 2010)

### Merck Will Close Lab in Kendall Square, Cut 16,000 Jobs Globally

Pharmaceutical giant Merck & Co., running counter to other drug makers' moves to expand operations in the Boston area, said it will shut a five-year-old Cambridge research lab as part of a global cutback that will reduce the company's worldwide payroll by 16,000 jobs, about 15 percent. Merck would not specify how many jobs will be eliminated at its Kendall Square operation, which was developing cancer drugs. The lab had about 100 employees early last year, when it was run by its former owner, drug maker Schering-Plough Corp. An unspecified number of workers will move to another Merck lab in Boston's Longwood Medical Area, which also does cancer-drug research, a Merck spokesman said.

The Cambridge site is the only US research center scheduled to be closed as part of Merck's global consolidation, which also will include the shuttering of seven research-and-development sites across Europe and in Canada over the next two years. Merck's decision comes as other global pharmaceutical companies, most recently Sanofi-Aventis AG of France and Eli Lilly & Co. of Indianapolis, are boosting their presence in the Boston area to capitalize on its academic labs and biotech start-ups.

"We'll still have a presence in Boston," said Ron Rogers, a spokesman at Merck's headquarters in Whitehouse Station, N.J. "It's an important presence. This announcement doesn't change that." Rogers would not disclose how many people Merck employs at its Boston research lab, which is near Harvard Medical School and many of the city's Harvard-affiliated teaching hospitals. The lab had about 250 employees in March 2009, the company said at that time.

Merck's consolidation, which began in the fourth quarter of last year, follows its $41.1 billion acquisition of fellow New Jersey drug maker Schering-Plough, which opened the Cambridge lab at the beginning of 2006 and doubled it in size about six months later. Merck's goal is to save $3.5 billion annually by 2012. Toward that end, the company already has eliminated about 11,000 jobs. "There will be some head count reduction from Cambridge, and some people will move over to our Boston facility," Rogers said.

Even as Merck prepares to scale back local operations, Sanofi-Aventis is leasing space in Cambridge, where it plans to open a headquarters for its new cancer division. The $65 million expansion is expected to create 300 jobs.

Other drug makers with Boston research centers in the Boston area include Novartis AG of Switzerland; Shire PLC, AstraZeneca PLC, and GlaxoSmithKline of Britain; Takeda Pharmaceutical Co. and Dainippon Sumitomo Pharma Co. of Japan; and US pharmaceutical colossus Pfizer Inc. of New York. Lilly said it was grabbing a foothold in the area by purchasing Alnara Pharmaceuticals Inc. Merck KGaA, a German drug and chemicals company unrelated to Merck & Co., in March said it plans to move the headquarters of its US chemicals business to Billerica after its acquisition of life sciences toolmaker Millipore Corp. With that buyout, Germany's Merck will have 1,676 employees in Massachusetts and New Hampshire. (Source: Robert Weisman, Boston Globe, 9 July 2010)

### Sanofi-Aventis Bringing Jobs to Massachusetts

One of the world's largest drug makers, Sanofi-Aventis SA, is planning a $65 million expansion in Cambridge that will create about 300 jobs, making it the latest foreign pharmaceutical giant to invest in Massachusetts. The Paris-based drug maker is in the process of leasing space in Cambridgeport, where it will establish a joint headquarters for a new cancer division. "We believe that Cambridge is really the heart of oncology today," Hanspeter Spek, president of Sanofi-Aventis's global operations, told financial analysts and investors in a conference call earlier this year.

Sanofi-Aventis is the latest foreign drug maker expanding its operations in Massachusetts. Industry executives say the

companies are drawn to the intense concentration of medical and life sciences activities in the area, including top-flight research universities, respected hospitals, and a cluster of biotech companies.

The company's investment is particularly important because it comes at a time when many other businesses are reluctant to expand because of the weak economy. And pharmaceutical research, manufacturing, and management jobs tend to pay well and pump new money into the economy, benefiting ancillary businesses such as suppliers, law firms, and nearby hotels and restaurants. Sanofi-Aventis predicted the new jobs would pay an average of more than $100,000 per year.

Sanofi-Aventis has nearly 400 workers in Massachusetts, including 160 in Cambridge, largely through its 2008 acquisition of Acambis, a vaccine maker based in England. It also owns a small manufacturing facility in Canton. The new cancer operation in Cambridgeport will boost those numbers considerably. Sanofi-Aventis has posted dozens of jobs related to the new division headquarters on its website, including for laboratory research, clinical trials, and marketing. It has sublet 30,000 square feet of space elsewhere in Cambridge, but is now close to leasing 112,000 square feet at 640 Memorial Drive, an MIT-owned building aimed at life sciences companies, for the new division headquarters. The Cambridge location will share control of the cancer division with a Sanofi-Aventis office in Vitry, France. Company spokesman Jack Cox said the firm hopes to finalize a lease in the next few weeks.

To help support the expansion, Sanofi-Aventis also applied for $2.45 million in state tax credits from the Massachusetts Life Sciences Center, a quasi-public agency established by the state Legislature in 2006 and charged with implementing the $1 billion, 10-year life sciences initiative launched by Governor Deval Patrick in 2008, and plans to request another $6.5 million in aid over the next four years, according to the center.

Like other major pharmaceutical companies, Sanofi-Aventis is making a big bet on cancer drugs. In June it announced plans to buy San Diego biotechnology firm TargeGen Inc., which is developing a treatment for certain types of leukemia, lymphoma, and other blood disorders, for $75 million, plus up to $485 million in additional incentives. Last year it agreed to pay up to $500 million for BiPar Sciences, which is developing a new class of "tumor-selective drugs" to treat multiple types of cancer. BiPar is based outside San Francisco.

Sanofi-Aventis, which also has major operations in Pennsylvania, New Jersey, and elsewhere in the US, already has two blockbuster cancer drugs. Taxotere, a chemotherapy drug used to treat breast cancer, prostate cancer, and other types of cancers, generated $2.8 billion in sales last year. Eloxatin, used to treat colorectal cancer, reaped more than $1.2 billion for Sanofi-Aventis last year. Last month, the US FDA approved Sanofi-Aventis's Jevtana to be used in combination with another drug to treat metastatic hormone-refractory prostate cancer, and the company has an array of additional cancer drugs in its pipeline.

It has also been working with Massachusetts biotechnology firms to develop new drugs, including deals related to cancer research with Dyax Corp. in Cambridge, ImmunoGen Inc. in Waltham, and Merrimack Pharmaceuticals Inc. in Cambridge. (Source: Todd Wallack, Boston Globe, 8 July 2010)

### Plans for Further Expansion of Genzyme in Framingham

Genzyme is building a new $300 million manufacturing complex in Framingham. The biotech company is betting on the 50,000-square-foot plant, on track to open next year after the FDA completes its reviews, to help it overcome a production bottleneck created when Genzyme shut down manufacturing of two key drugs for treating rare genetic disorders after a series of highly publicized contamination problems arose at its marquee Allston plant. The new Framingham plant will initially produce Fabrazyme, followed by Cerezyme in 2012. Fabrazyme treats Fabry disease, an inherited disorder, while Cerezyme helps combat Gaucher disease, which can result in liver and neurological damage.

Genzyme's new manufacturing plant will be accompanied by a six-story, 185,000-square-foot quality control lab, slated to open in July 2011, company plans show. In addition, Genzyme's master plan, now under review by state environmental regulators, calls for another 400,000 square feet of research-related space in a section of the campus called the Science/Technology Development Block. These projects are slated for construction between 2015 and 2018. The biotech company also expects to develop another large block of manufacturing, office, and parking space as well, which could see another 360,000 square feet built starting in mid-decade. The planning, while still in its early stages, provides a good rough road map for Genzyme's future intentions in Framingham, said Henry Fitzgerald, vice president of facility operations at Genzyme.

Genzyme's expansion is being greeted enthusiastically by Framingham State College, which hopes to create an internship program for its students at the biotech company. There are already close ties with the company - Genzyme has a representative on a regional task force based at the college looking at ways to beef up training in the sciences and mathematics at local schools. A Genzyme employee is also president of the school's alumni association, while another sits on the college's board of trustees. "We are certainly hoping to expand our relationship," said Ellen Zimmerman, dean of academic affairs at Framingham State.

In a move that set the stage for the current expansion, the Massachusetts Life Sciences Center committed nearly $13 million to upgrade wastewater treatment facilities around Genzyme's Framingham campus. (Source: Scott Van Voorhis, Boston Globe, 11 July 2010)

## Regulatory & Legislative Highlights

*by Deepen Joshi*

### FDA Approves Rapid Test for Antibodies to Hepatitis C Virus

The FDA recently approved the first rapid blood test for antibodies to the hepatitis C virus (HCV) for individuals 15 years and older. The OraQuick HCV Rapid Antibody Test, manufactured by OraSure Technologies Inc. of Bethlehem, PA, is used to test individuals who are at risk for infection with HCV and people with signs or symptoms of hepatitis. OraQuick is not approved for HCV screening of the general population.

HCV is transmitted through exposure to infected blood, which, for example, can occur during intravenous drug use. The

virus can also be transferred from an infected mother to her child. Hepatitis C can lead to liver inflammation and dysfunction and, over time, to liver disease and liver cancer. OraQuick is a test strip and does not require an instrument for diagnosis. It takes about 20 minutes to obtain results from the test.

According to the Centers for Disease Control and Prevention, there are approximately 3.2 million people in the United States chronically infected with HCV and each year, about 17,000 people are newly infected. Chronic HCV infection is a leading reason for a liver transplants in the United States and HCV is associated with an estimated 12,000 deaths annually. Approximately 75 to 85 percent of people who become infected with the hepatitis C virus develop chronic infection. (Source: FDA Website, 25 June, 2010)

### FDA Approves First Generic Effexor Extended Release Capsules to Treat Major Depressive Disorder

On June 28, the FDA approved the first generic version of Effexor XR capsules (venlafaxine hydrochloride) to treat major depressive disorder. Venlafaxine hydrochloride extended-release capsules in 37.5 milligram, 75 milligram and 150 milligram strengths have been approved to be manufactured by TEVA Pharmaceuticals of North Wales, PA.

"The approval of this widely used antidepressant is another example of the FDA's efforts to increase access to safe and effective generic drugs," said Keith Webber, Ph.D., deputy director of the Office of Pharmaceutical Science in the FDA's Center for Drug Evaluation and Research. "Access to treatments for depression is important because depression can interfere with a person's daily life and routine, which can significantly affect relationships with family and friends."

The prescribing information (label) for the generic drug may differ from that of Effexor XR capsules because some uses of the drug and parts of the label are protected by patents and/or exclusivity held by the Effexor manufacturer, Wyeth Pharmaceuticals Inc.
Generic venlafaxine hydrochloride will have the same safety warnings as Effexor XR. The drug has a boxed warning indicating that antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, and young adults within the first few months of treatment. The warning also notes that depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions.(Source: FDA Website, 29 June, 2010)

### FDA Approves First Generic Version of Sanofi-Aventis' Lovenox

The FDA has approved the first generic version of Lovenox (enoxaparin sodium injection), an anti-coagulant drug used for multiple indications including prevention of deep vein thrombosis (DVT), a potentially deadly blood clotting condition. Approved for use in 1993, Lovenox is made from heparin, a blood-thinning drug whose active ingredient is a naturally-derived complex mixture of sugar molecules. Approval of generic enoxaparin sodium injection has been granted to Sandoz Inc. of Broomfield, CO.

For a generic drug to be approved by the FDA, the manufacturer must demonstrate it contains the same active ingredient as the brand-name drug. The process can be more complex for a natural product such as enoxaparin. "Before approving generic enoxaparin sodium injection, we expected, among other things, a series of sophisticated analytical tests and a study in healthy volunteers to assure that the drug would be as safe and effective as the brand name product," said Keith Webber, Ph.D., deputy director of the FDA's Office of Pharmaceutical Science.

Prior to the approval, the FDA received a citizen petition questioning the approval criteria for generic enoxaparin sodium injection. After carefully reviewing the petition, the agency determined that current scientific evidence, precedent, and FDA's legal authority establish a sound basis for the approval of generic enoxaparin sodium injection. A response to the petition was released by the agency today.

Use of enoxaparin can prevent DVT, a blood clot that forms in a vein deep in the body, especially in the lower leg or thigh. Preventing these blood clots can prevent a pulmonary embolism, which is a sudden, potentially fatal, blockage in a lung artery that can occur if the blood clot breaks free and travels through the bloodstream to the lungs. According to the National Heart, Lung, and Blood Institute, at least 100,000 cases of pulmonary embolism occur each year in the US. It is the third most common cause of death among hospitalized patients. This medicine is also used to prevent blood clots in patients confined to bed and also for patients experiencing chest pain and heart attacks.

The prescribing information for both Lovenox and its generic version includes a boxed warning that use of the drug in patients undergoing spinal/epidural anesthesia or spinal puncture increases the risk of spinal or epidural bleeding and bruising (hematoma), which may cause long-term or permanent paralysis. (Source: FDA Website, 23 June, 2010)

### Sanofi Sues FDA to Stop Sale of Generic Lovenox

Sanofi-Aventis SA, France's leading drug maker, has sued the FDA in a bid to make it withdraw its clearance of a lower-cost rival to the company's Lovenox blood thinner. Sanofi wants a judge to force the FDA to suspend its approval of the generic produced by Novartis AG's Sandoz unit with Momenta Pharmaceuticals' technology. Lovenox, an injection that helps prevent blood clots, was Sanofi's number two product last year, after the diabetes medicine Lantus.

Novartis and Momenta won US approval for a lower-cost copy of Lovenox on July 23rd, ending a five-year wait to challenge the $3.9 billion-a-year product. In its complaint, Sanofi said the generic is not clinically equivalent to Lovenox, and the FDA's decision may cause Sanofi irreparable harm.

The path for approval of the generic drug was cleared when Sanofi's patent was voided. In April 2009, the US Supreme Court left intact a lower court ruling that the patent was not enforceable because Sanofi had misled the US Patent and Trademark Office. The court rejected Sanofi's appeal, seeking reinstatement of the patent, which could have prevented competition until 2012. (Source: Bloomberg News, 28 July, 2010)

### FDA Approves Vaccines for the 2010-2011 Influenza Season

The FDA has announced that it has approved vaccines for the 2010-2011 influenza season in the US. Seasonal influenza vaccine protects against three strains of influenza, including the 2009 H1N1 influenza virus, which caused the 2009 pandemic. Last year, because the 2009 H1N1 virus emerged after production began on the seasonal vaccine, two separate vaccines were needed to protect against seasonal flu and the 2009 H1N1 pandemic flu virus, but this year, only

one vaccine is necessary.

According to the Centers for Disease Control and Prevention (CDC), between 5 percent and 20 percent of the US population develops influenza each year, leading to more than 200,000 hospitalizations from related complications and about 36,000 deaths. In addition to the important role that health care providers play in recommending influenza vaccination for their patients, influenza vaccination of health care personnel is important to protect themselves, their patients, their family, and the community from influenza. FDA urges health care organizations to encourage their members to get vaccinated.

The brand names and manufacturers for the upcoming season's vaccines are: Afluria, CSL Limited; Agriflu, Novartis Vaccines and Diagnostics; Fluarix, GlaxoSmithKline Biologicals; FluLaval, ID Biomedical Corporation; FluMist, MedImmune Vaccines; Fluvirin, Novartis Vaccines and Diagnostics; and Fluzone and Fluzone High-Dose, Sanofi Pasteur.

Each year, experts from FDA, World Health Organization, CDC, and other institutions study virus samples and patterns collected worldwide to identify strains likely to cause the most illness during the upcoming season. Based on that information and the recommendations of FDA's Vaccines and Related Biological Products Advisory Committee, manufacturers included the respective three strains in the 2010-2011 vaccines. The closer the match between the circulating strains and the strains in the vaccine, the better the protection against influenza disease. Vaccines for the 2010-2011 seasonal influenza contain the following strains:

• A/California/7/09 (H1N1)-like virus (pandemic (H1N1) 2009 influenza virus)
• A/Perth /16/2009 (H3N2)-like virus
• B/Brisbane/60/2008-like virus

There is always a possibility of a less than optimal match between the virus strains predicted to circulate and the virus strains that end up causing the most illness. However, even if the vaccine and the circulating strains are not an exact match, the vaccine may reduce the severity of the illness or may help prevent influenza-related complications.

The labeling for one vaccine, CSL Limited's Afluria, has undergone changes this season to inform health care providers about an increased incidence of fever and febrile seizure, which was seen in young children, mainly those younger than 5 years, following administration of the 2010 Southern Hemisphere formulation of CSL's influenza vaccine. The Southern Hemisphere influenza season occurs prior to that of the Northern Hemisphere.

CSL Limited will not be supplying the US with the 0.25 milliliter single-dose, prefilled syringes, which are used in very young children. The 0.5 milliliter single-dose, prefilled syringes and 5 milliliter multi-dose vials will be distributed. FDA is requiring CSL Limited to conduct a study of Afluria in children to obtain additional information regarding the febrile events that were seen in the Southern Hemisphere.

CDC has published recommendations for annual influenza vaccination to include all people aged 6 months and older. The expanded recommendation is to take effect in the 2010-2011 influenza season. The Advisory Committee on Immunization Practices (ACIP), which advises the CDC on vaccine issues, voted on the new recommendation during its February 24, 2010 meeting in Atlanta.

Prior recommendations for seasonal influenza vaccination focused on vaccination of persons at increased risk for complications from influenza including people with underlying health conditions, children 6 months through 18 years of age, and close contacts of high risk persons among others. (Source: FDA Website, 30 June, 2010)

### FDA Issues Reports on 510(k) Program and Use of Science in Decision-Making

The FDA has issued two comprehensive evaluations containing recommendations that address three key objectives of the agency's public health mission as it relates to medical devices - foster device innovation, create a more predictable regulatory environment, and enhance device safety.

The FDA's Center for Devices and Radiological Health assessment consists of two preliminary reports. One report focuses on ways to strengthen and clarify a premarket review process called the 510(k) program for medical devices that do not need to undergo a full premarket approval review. The other evaluates CDRH's use of science in decision-making, with an eye toward adapting to new scientific information, while maintaining regulatory predictability necessary for innovation. The two documents overlap in several places and cross-reference information. The documents can be found online.

In recent years, concerns have been raised both inside and outside of the FDA about whether the current 510(k) program achieves its goals of making safe and effective devices available to the public while fostering innovation. Concerns about the program have centered on whether it allows devices to enter the market without sufficient safety and effectiveness evidence and whether a lack of predictability, consistency, and transparency is hindering device development.

CDRH uses science to guide its regulation of medical devices across the total product lifecycle. At any stage of that lifecycle, new, unfamiliar or unexpected scientific information may arise that warrants a change in the FDA's thinking, expectations, and actions. CDRH is seeking to strike the right balance between the ability to adapt its approach as new science emerges and to provide predictable regulatory pathways.

"...it's important to remember that these recommendations are preliminary," said CDRH Director Jeffrey Shuren, M.D. "CDRH opened another public docket to receive additional comments on both reports. We will make a decision on which recommendations to adopt only after a thorough review of additional comments."

Selected recommendations and the key public health objectives addressed include:

#### Fostering Device Innovation

• The 510(k) report recommends major improvements to the regulatory pathway for lower-risk novel devices that cannot be cleared through 510(k) but which do not warrant the more rigorous premarket approval review applied to higher-risk devices. The report calls for major reforms in the implementation of this process - called the de novo classification

process.
• The science report recommends that CDRH make better use of scientific experts outside of the agency by developing a web-based network of external experts using social media technology. This network would help CDRH staff leverage outside knowledge without serving in an advisory capacity.

Enhancing Regulatory Predictability

• The 510(k) report recommends that CDRH develop a guidance document defining a subset of moderate-risk (Class II) devices, called Class IIb, for which clinical or manufacturing data typically would be necessary to support a substantial equivalence determination. This guidance document would help clarify what information submitters should include in their 510(k) submissions.
• The science report recommends use of a standardized "Notice to Industry" letter that would generally be issued as a "Level 1 - Immediately in Effect" guidance document to quickly communicate when CDRH has changed its premarket regulatory expectations due to scientific information that has emerged about a certain device type. CDRH currently communicates this kind of information through individual interactions during the review process, which can lead to delays.

Improving Patient Safety

• The 510(k) report recommends that CDRH consider revising regulations to explicitly require 510(k) submitters to provide a summary of all scientific information known or that the submitter should reasonably know regarding the safety and effectiveness of the device under review. This is not required now for 510(k) submissions and, as a result, relevant information may not be included in an initial submission. This summary would help CDRH review staff to more efficiently make decisions, and potentially avoid extensive follow-up inquiries and questions.
• The 510(k) report recommends that CDRH develop a guidance document that clarifies when a device should not be used as a predicate, such as when the device has been removed from the market because of safety concerns. The report also recommends that the center consider issuing a regulation that would clarify the circumstances under which the center would exercise its authority to rescind a 510(k) clearance to remove an unsafe device from the market and preclude its use as a predicate and also consider whether additional authority is needed.
• Both reports recommend that CDRH build upon public databases to include meaningful, up-to-date information that supports good decision making and promotes the safe use of devices. This could be accomplished by improving the current 510(k) database so that it includes summaries of FDA review decisions, current labeling and photos. In addition, the science report recommends that CDRH build upon the existing transparency website to provide more immediate information on how devices are regulated. (Source: FDA Website, 4 August, 2010)

FDA Warns GlaxoSmithKline Seizure Drug Lamictal Can Cause Aseptic Meningitis

The FDA has warned that the drug Lamictal (lamotrigine), approved to treat seizures and bipolar disorder, can cause aseptic meningitis, an inflammation of the protective membranes (meninges) that cover the brain and spinal cord not caused by bacterial infection. The agency is working with the drug's manufacturer, GlaxoSmithKline, to update the prescribing information and patient medication guide to include this risk.

Aseptic meningitis has a number of causes including, but not limited to, viruses, toxic agents, some vaccines, autoimmune diseases, and certain medications, including Lamictal. Symptoms can include headache, fever, chills, nausea, vomiting, stiff neck and sensitivity to light. Hospitalization may be required.

The FDA became aware of the association between Lamictal and aseptic meningitis through routine adverse event monitoring and communications with the drug's manufacturer. Since the drug's approval in December 1994 through November 2009, there were 40 cases of aseptic meningitis identified in patients taking Lamictal. The symptoms were reported to occur within one to 42 days after starting Lamictal. Thirty-five of the 40 patients required hospitalization. In most cases, symptoms ended after Lamictal was discontinued. In 15 cases, symptoms, often more severe, returned when patients restarted the drug. (Source: FDA Website, 12 August, 2010)

FDA Proposes Withdrawal of Low Blood Pressure Drug

The FDA has proposed to withdraw approval of the drug midodrine hydrochloride, used to treat the low blood pressure condition orthostatic hypotension, because required post-approval studies that verify the clinical benefit of the drug have not been done. Orthostatic hypotension is a condition in which patients are unable to maintain blood pressure in the upright position and, therefore, become dizzy or faint when they stand up.

The drug, marketed as ProAmatine by Shire Development Inc. and as a generic by others, was approved in 1996 under the FDA's accelerated approval regulations for drugs that treat serious or life-threatening diseases. That approval required that the manufacturer verify clinical benefit to patients through post-approval studies. To date, neither the original manufacturer nor any generic manufacturer has demonstrated the drug's clinical benefit, for example, by showing that use of the drug improved a patient's ability to perform life activities. Generic versions of the drug are made by Apotex Corp., Impax Laboratories Inc., Mylan Pharmaceuticals, Sandoz Inc., and Upsher-Smith Laboratories.

"We've worked continuously with the drug companies to obtain additional data showing the drug's clinical benefits to patients," said Norman Stockbridge, M.D., director of the Division of Cardiovascular and Renal Drugs in the FDA's Center for Drug Evaluation and Research (CDER). "Since the companies have not been able to provide evidence to confirm the drug's benefit, the FDA is pursuing a withdrawal of the product."

Under accelerated approval, a drug company may obtain approval of a drug used to treat a serious or life-threatening disease or condition based upon a surrogate endpoint. A surrogate endpoint is a clinical marker, such as a positive effect on blood pressure, believed to predict actual clinical benefits such as improved survival or decreased severity of the disease. Drug companies that obtain approval under this program are required to conduct additional clinical trials after approval to confirm the drug's benefit. If those trials fail to confirm clinical benefit to patients, or if the companies do not pursue the required confirmatory trials with due diligence, the FDA can withdraw approval of the drug using expedited procedures.

The agency is working with the drug manufacturers to develop an expanded-access program to allow patients who

currently receive the drug to continue to receive it. On a case-by-case basis, expanded-access programs allow the use of a drug outside of a clinical trial to treat patients with a serious or immediately life-threatening disease or a condition that has no comparable or satisfactory alternative treatment options. (Source: FDA Website, 16 August, 2010)

### Shire Elects to Withdraw ProAmatine from Market

According to the Shire PLC website, Shire acquired ProAmatine as a part of the acquisition of Roberts Pharma in 1999 and conducted and completed the post marketing trials that the FDA required. The FDA, however, viewed those trials as inconclusive and required that additional trials be conducted for ProAmatine to maintain its marketing authorization. As a result, Shire has elected to withdraw the product effective September 30, 2010 and notified the FDA in November 2009 and healthcare professionals earlier this year of this decision. Shire's withdrawal of the NDA was not related to any concerns regarding the safety of ProAmatine. (Shire PLC Website, 17 August, 2010)

### Murine Leukemia Virus Related Gene Sequences Found in CFS Patients

Researchers have found murine leukemia viruses (MLV) related gene sequences in blood samples collected from patients diagnosed with chronic fatigue syndrome (CFS) and some healthy blood donors, according to a study published online today by the scientific journal Proceedings of the National Academy of Sciences (PNAS). MLV is a type of retrovirus known to cause cancer in mice.

This study supports a previous investigation [Lombardi et al. Science October 23, 2009 326: 585] that showed XMRV, a genetic variant of MLV-like viruses, to be present in the blood of people with CFS. The study demonstrates a strong association between a diagnosis of CFS and the presence of MLV-like virus gene sequences in the blood. The study also showed that MLV-like viral gene sequences were detected in a small fraction of healthy blood donors. Although the statistical association with CFS is strong, this study does not prove that these retroviruses are the cause of CFS. Further studies are necessary to determine if XMRV or other MLV-related viruses can cause CFS.

A previous study, published in 2009, reported finding XMRV infections in a high percentage of CFS patients and a small percentage of healthy blood donors. However,
several other studies from the US (including a recent report from the Centers for Disease Control and Prevention), the UK and the Netherlands have found no evidence of XMRV or other MLV-like viruses in the blood of people with CFS.
(Source: FDA Website, 23 August, 2010)

## New Members

**Ms. Amy C. Bergeron,** *Senior Process Engineer,* Lantheus Medical Imaging

**Mr. Timothy J. Blaser,** *VP Operations,* Advanced MicroSensors

**Mr. Jordan R. Croteau,** *Automation Engineer,* Integrated Process Technologies

**Mr. Richard M. Desrosiers,** *System Specialist,* Hydro Service & Supplies

**Kim R. Doherty,** *Engineering PPE,* Genzyme Corp

**Mr. James L. Fisher,** *Facilities Supervisor,* Shire HGT

**Mr. Adam J. Foley,** *Project Manager,* Cotter Brothers Corporation

**Thomas Forster,** *,* Rockwell Automation

**Ms. Joyce Frisiello,** *Engineering Document Control Specialist II,* Acceleron Pharma

**Mr. Michael M. Giuliano,** High Purity New England

**Veronica Hunter,** Dyax Corp

**Mr. Tom Kelliher,** *Engineer,* Genzyme Facilities Biologics

**Joseph Lurie,** *Principal Quality Engineer,* Genzyme

**Ron Mac Donald,** *Corp Validation Manager,* Genzyme Corp

**Ms. Rachel Marshall,** *Mfg Sciences Engineer II,* Immunogen Inc

**Suesan Randlett,** *Manging Partner,* gammaSUPPLIES, LLC

**Mr. Philip R. Richards,** *Validation Engineer,* Genzyme Corporation

**Mr. Mark Schores,** *Account Executive*

**Mr. Brian M. Turley,** *Validation Engineer,* Valsource Inc

## Member Anniversaries

### 20+ Years of Membership

Mr. David C. Hardy

Mr. Thomas W. Moss, Applied Process Solutions, Inc

Mr. Hank Moes

Mr. Stephen R. Higham, PE, Genzyme Corp

Ms. Sandra Illich, Pfizer

Mr. Armen J. Nahabedian, Pfizer

Mr. Jonathan F. Stenbuck, Stenbuck Enterprises

Mr. Michael A. Boenitz, DUSA Pharmaceuticals Inc

Dr. Richard V. Levy, PDA

Mr. Donald M. Haiges, PE, WSP-Flack+Kurtz

Mr. Randolph A. Cotter, Sr., Cotter Brothers Corporation

Mr. Cesar B. Daou, PE, Daou Engineers Inc

Mr. Thomas R. Jerome

Mr. Robert W. Juffras, MS, Stryker Biotech

Mr. Frank J. Manning, VNE Corp

Mr. Alexander E. Smith, Jr., Parsons

Ms. Greta W. Davis, Lantheus Medical Imaging

Mr. John H. Evers, Lantheus Medical Imaging

Mr. David L. Hyde, Independent Contractor

Mr. George C. Enos, Hart Design Group

## 15 Year Anniversary

Mr. Alexander A. Felton

Mr. Daniel P. Lavin, Baxter

Mr. John S. Magyar, Parsons

## 10 Year Anniversary

Mr. Mark S. Caswell, Genzyme Corp

Ms. Katie Henchir, Biogen Idec

Mr. William R. Lee

Mr. Richard F. Reiland, CPI Controls Inc

## 5 Year Anniversary

Mr. Tim Cowher, Pharmaceutical Containment Technologies

Mr. Paul Joyce, AstraZeneca

Mr. Ed Kozloski, DPS

Mr. David R. Krantz, Shire HGT

Mr. Edward Marsh, Fusion Concepts, Inc.

Mr. Mark D. Moody, PhD, Merrimack Pharmaceuticals

Mr. John A. Morin, Overlook Industries, Inc.

Mr. Vishwesh D. Sankholkar, New England Controls Inc

Mr. Matt Stundtner, Genzyme Corp

Mr. Richard P. Tetreault, Sr., Lantheus Medical Imaging

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