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## Boston Area Chapter

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## NEWSLETTER

January 2012, Volume XXII No. 1

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### President's Message: A Look Back at 2011 - Building a Strong Foundation for 2012



Dear ISPE Boston Area Chapter Members

As the holiday season rolls in, it gives us time to reflect back on 2011 and all that's happened. Here at the Boston Area Chapter of ISPE, that means a lot. This year, our efforts were again recognized by the international ISPE organization at Annual Meeting where we took home both the "Chapter of the Year" award (for the third year in a row!) and the award for innovative educational programs.

Speaking of educational programs, our November program introduced the exciting field of Pharmacogenomics with Michael Drues' excellent presentation covering the personalization of medicine and how it will affect us all sooner than we think; and December brought a "standing room only" crowd to Genzyme in Cambridge for an enlightening discussion of Integrated Commissioning and Qualification by Jack Greene (see related articles).

And we have an excellent slate of programs on tap for 2012. We've listened to your input and put the programs in place that you've requested, including January (Automation), February (Project Management) and March (Water and Steam Systems, coupled with the introduction of the cutting edge ISPE baseline guide). Check out the Chapter's event calendar at <http://www.ispeboston.com/Events> to see the details. And hopefully you've noticed our programs are now being regularly held on the third Thursday of every month. So count on it and plan ahead for the programs you want to attend.

Please join me in welcoming our newest Student Chapter - Worcester Polytechnic Institute - another major accomplishment for 2011. Though not yet "official," the Chapter is well on its way toward recognition by ISPE. WPI's involvement with ISPE kicked off on December 1st when a group of 20 students toured the Abbott Bioresearch facility in Worcester. Many thanks to our hosts from Abbott - Joshua Froimson, Lorraine Mathis, and Michael Doucette - for the time they spent showing students their facility and giving them a taste

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of the practical side of what they've been learning (see related article). Welcome WPI!

We also re-introduced the Boston Area Chapter's Joel Goldenberg Memorial Scholarship Program during 2011. Joel, a past president of the Boston Area Chapter, would be proud to know that the Chapter awarded \$10,000 in his honor during the first year of the program. I am extremely proud to announce the winners for the fall application period:

Rebecca Cole (UNH)  
Ed Nickerson (Continuing Education)  
Matthew Schneiderhan (UConn)  
Jaimes Spring (WPI)

Congratulations to all! Applications for the next scholarship period are due between now and May 15th. Visit our website for details and an application.

While attending the ISPE Annual Meeting in Dallas, I made sure to meet the folks who head up the program for ISPE's new Certified Pharmaceutical Industry Professional™ credential, or CPIP. You may not know this, but this credential was suggested to ISPE by FDA officials. Because the initial eligibility requirements proved nearly impossible to meet, organizers had promised changes and I was pleased to learn that these promises have been kept. The entire application and eligibility process has been simplified, making the CPIP credential both rigorous and easier to obtain.

As a result, this spring we are forming our third CPIP study group to continue Boston's leadership position as this sought after credential gains traction. Personally, I'm planning to participate and I challenge you to do the same. Look for an announcement after the holidays and please plan to attend an informational meeting explaining the program, including the recent changes. Study group sessions will be starting in February and we will have you ready to take the exam in May. We promise!

Happy Holidays from the Boston Area Chapter!

Brian Hagopian  
President, ISPE Boston Area Chapter

### ISPE Membership Dues Reduced for Young Professionals

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Visit <http://www.ispe.org/young-professionals-membership> to see if you qualify for the new ISPE Young Professionals Membership, or contact the Chapter office at [office@ispeboston.org](mailto:office@ispeboston.org).

### Upcoming Chapter Events - Mark Your Calendar

**Thursday, January 12, 2012**  
**Annual New Year's Social**

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**Thursday, January 19, 2012**

**Automation - The Real Story Behind the Curtain**

**Biogen Idec, 14 Cambridge Center, Cambridge, MA 02142**

There has been much interest in the black box of automation. This program will give insight to the basics of automation found in the pharmaceutical industry, and the challenges that we face making the black box operate. Since critical automation of a pharmaceutical facility involves both HVAC and process control, the program will provide insight into both. Attendees will gain a basic understanding of HVAC theory of operation as well as a basic understanding of efficient design of process automation systems allowing them to appreciate and understand what it takes from all team members to provide automation systems that will produce quality and consistent product research and production.

**Register Today:** <http://www.ispeboston.org/events/registration.htm?eventID=162>

**Sneak Preview of Upcoming Events**

**Thursday, February 16, 2012**

Educational Program focusing on Project Management

**Thursday, March 15, 2012**

Educational Program focusing on Water and Steam

**Thursday, April 19, 2012**

Educational Program focusing on Engineering Documentation

**Thursday, May 10, 2012**

Educational Program focusing on Process Design Principles

**Pharmacogenomics: The Future of Clinical Trials, New Product Development and the Practice of Medicine**

*by John Sheridan, PMA Consultants, with photos by Joyce Chiu, CPIP, Honeywell Safety Products*

On Tuesday evening, November 15th, Michael Druess, Ph.D introduced pharmacogenomics at the Genzyme Science Center in Framingham after presenting the same topic at the Product Show the previous month at Gillette. Genzyme provided a smaller, more personal forum better suited to a spirited discussion on the future of medicine. After refreshments and networking in the lobby, the group moved into the "classroom" to

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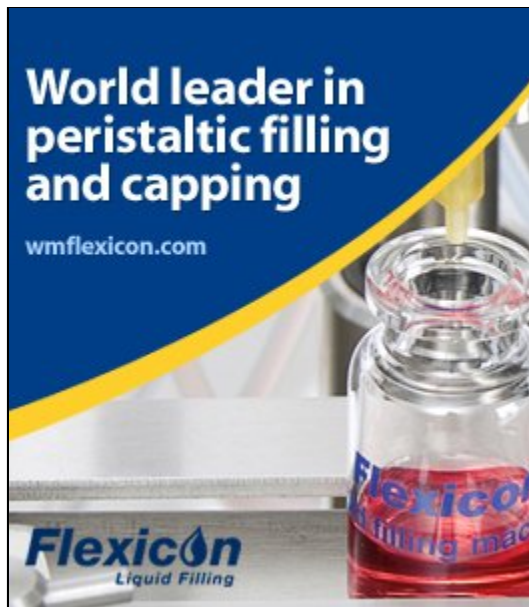
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Attendees enjoy a lively networking reception before the presentation

Before launching into his topic, Michael started with a brainteaser to get the mental "juices" flowing, and then just kept going for the following hour and a half. He started with how we got to this point and noted that pharmacogenomics (aka personalized medicine) is not really new since doctors have been practicing "personalized medicine" for centuries. So what's different now? Until today, we have been practicing medicine from a "phenotypical" perspective but in the future, we will be able to practice medicine from a "genotypical" perspective. To illustrate how this is becoming a reality, Michael described development of the "frost-resistant tomato." Instead of engineers looking at heaters to prevent tomatoes from freezing, researchers put the anti-freeze

protein (gene) from an arctic char (a popular food fish adapted to life in the frigid arctic waters) into a tomato and achieved the desired results genetically. This is reality, not science fiction!

The presentation continued with Michael explaining that the average efficacy for drugs (their ability to do what each product states on its label) is 20 to 40 percent - only slightly better than a placebo (which is typically 30 percent effective). A new drug to market does not need to be better than other drugs already existing and being sold; it just needs to be better than nothing (e.g. a placebo). To say the least, this opened the eyes of many attendees! Michael went on to comment that this low level of success would not be acceptable for automobiles starting or planes flying. He then likened the traditional approach to medicine to buying shoes at a store with only one size available and contrasted it with pharmacogenomics which provides a custom "shoe" built specifically for individual patients.

Michael explained that, moving forward, the question becomes: What is the FDA's role in personalized medicine since the FDA does not regulate the practice of medicine? It would appear that genetic tests and diagnostic tools would be a much better way to get the right drug to the right person at the right time. He then introduced the concept of pharmacogenomics as applied to medical devices - absolutely possible and with distinct advantages over what is being done currently. As an example, a real concern in the use of stents is the formation of deadly blood clots shortly after a stent is implanted. Currently, doctors cannot predict which patients are vulnerable to forming clots. However tests are available to identify people at risk, i.e. those who have genetic factors associated with early stent thrombosis.

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So how do we practice medicine more intelligently than we do today? Do we use companion diagnostic testing and genotyping during clinical evaluation before prescribing a drug? Using Plavix (a drug that functions like an anticoagulant) as an example, Michael continued. Many patients cannot metabolize the drug so the question is: Why wait for a patient to swallow the drug to see if it is going to work?

Regarding clinical trials with their long timeline, if personalized medicine is going to impact medicine sooner, it may need to utilize "platform technology," that is, new technology that could potentially be used for many applications, both existing and in ways that haven't been dreamed of yet. For example, currently variability is managed at the trial's back end by using statistics; the new paradigm would be to manage variability at the front end using

inclusion/exclusion criteria which would increase the probability of the trial's success. Then the ethical question becomes: Who pays for genetic testing before a trial vs. after? Another ethical question: If we are able to identify people with genes that respond to placebos, can we exclude them from the trial so that we require fewer patients and thus make the trial more efficient? Do we use placebos in medical device trials (i.e. sham procedures) to measure efficacy? Is this ethical?

Product development is costly and time consuming. In the past, most drugs came from discovery (e.g. the Amazon jungle), not invention. In the future, the new drug development paradigm can be changed to an engineer and chemist fabricating a molecule in silico (i.e. on a computer or via computer simulation). Another personalized approach to medicine could be using high tech compounding. Instead of just manufacturing millions of pills in a factory somewhere, pharmacogenomics is the engineering equivalent to stereo lithography. Michael used examples currently available in the consumer marketplace to further illustrate the concept: Coca-Cola Freestyle, custom-blended ice cream flavors and personalized orthotics - all created on the spot to satisfy the customer's requirements and delivered by a vending machine.

By this point, our heads were spinning with all the new concepts and possibilities. Michael suggested the idea of a "poly-pill" as a combination therapy - not a combination product (after all, the FDA doesn't get involved if a patient takes five pills). This could make a reality of a combination of drugs and biologics prescribed and produced right in a doctor's office (high tech vending), customizing the medication to the patient's specific needs.

Michael finished with some food for thought:

- Companion diagnostic - narrows market for drug but may enable higher margin?
- Clinical trial duration can be long if testing the whole population - more efficient if database of existing information is used to find applicable genetic types.

...and words of wisdom:

- If we don't have evidence that does not mean it didn't happen.
- Don't be afraid to fail.



Presenter Michael Drues with Chapter Board Member Janet Tice

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- Don't go where a path may lead, go instead where there is no path and make a trail.

This session - with its focus on possibilities for the future - was definitely different than the typical ISPE event but provided an inspiring and thought-provoking learning experience. The evening flew by and left all of us thinking about the myriad of possibilities on the near horizon of medicine...and our next doctor's visit. Thanks to Michael Druess for taking us into the future!

### WPI Launches New Student Chapter with Plant Tour at Abbott in Worcester

*by Joshua Strauss, WPI Industry Advisor, and Hashim Ismail, WPI Student Chapter President*

Worcester Polytechnic Institute (WPI) has officially become the newest ISPE Boston Area Student Chapter. With over 15 members and officers, the Chapter has hit the ground running with a plant tour of Abbott (more on this to follow) and is already planning for guest speakers and other educational and professional events in the semester to come.

The Chapter was founded in 2010 by a small group of student professionals. The motive was a strong drive to learn more about the pharmaceutical and biotech industry, especially by connecting with industry professionals. The intent to serve fellow students in the Worcester area with similar interests was also of great importance and ultimately facilitated the startup of WPI's Student Chapter. With over eight colleges and universities in the Worcester area, the WPI is the only local ISPE Student Chapter.

The partnership between ISPE and WPI is a logical step that was a long time in the making. As the biotech sector continues to grow and engineering schools recognize that students will be choosing careers in R&D as well as manufacturing, professional societies like ISPE benefit both students and industry. WPI opened its first life science building in Gateway Park in 2007, combining academic research with "incubator" companies developing next generation therapies. With plans to further expand Gateway Park in the future, we expect ties between ISPE and WPI to strengthen further in the years to come.

On December 1st, just days after being officially recognized by ISPE, WPI students attended a plant tour at Abbott Bioresearch Center in Worcester. Attendees represented a range of majors including Biotechnology, Biochemistry, Chemical Engineering, Biomedical Engineering and Mechanical Engineering. As one of the participants put it, "a behind the scenes tour of Abbott was very insightful and educational. The Student Chapter is deeply grateful to ISPE Boston as well as Abbott for providing us with this opportunity."

The tour took the students through the process for culturing mammalian cell lines, beginning with raw materials and ultimately overseeing the purification steps. Clean steam, water for injection, and purified water were some of the basic GMP utilities introduced to the students. The tour guides described the differences in purity, quality and price between the municipal tap water and Abbott's purified plant steam, attesting to the effective water purification methods used by the plant. Moving on through the plant to the upstream equipment, the tour included a look at some of the seed reactors and larger 3000 liter reactors. CIP and SIP cycles were touched upon, as well as the differences between harvesting methods such as centrifugation and depth filtration. Some of the modern, price effective technologies used in various stages of the production process were also highlighted and discussed.

Tour guides Joshua Froimson, Mike Doucette and Lorraine Mathis of Abbott generously donated their time and made the tour a huge success. Being aware of commonly used acronyms such as CIP, SIP, WFI, etc. will give the students a leg-up when they begin interviewing for careers in the biotech industry in the months and years ahead. On behalf of WPI and ISPE we thank our tour guides and Abbott Bioresearch, Inc.

The WPI Student Chapter has many more tours, professional speakers and educational conferences to look

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forward to in the months and years ahead. All of these events and more will facilitate the professional development of its student members and the greater WPI community. With the rapid expansion of the biotech and pharmaceutical industries, the partnership between ISPE and WPI will help foster the education of young professionals and feed more talented, well-prepared individuals into the marketplace.

## E2500 Integrated C&Q Draws Standing-Room-Only Crowd to Genzyme

*article and photos by Joyce Chiu, CPIP, Honeywell Safety Products*

On the evening of December 15th in the Genzyme Cambridge auditorium, packed full with almost 100 attendees, Jack Greene gave an interesting and stimulating two-part presentation, titled "Integrated Commissioning & Qualification: Saving Time and Money without Compromising Quality." This topic came about because of the recent publication of ISPE's "Applied Risk Management for Commissioning and Qualification" Good Practice Guide. Although his presentation was reviewed by the ISPE Community of Practice on C&Q, Jack developed his presentations primarily based on his own 15 years plus experience in this area.



**Presenter Jack Greene (second from right) joins friends during the networking reception.**

1987. These resulted in two models of C&Q. Model 1 did complete C and Q, essentially replicating two identical sets of activities by two separate groups of people, Engineering and Quality. Model 2 skipped commissioning and went straight to qualification, with the rationale that since qualification was going to repeat commissioning, why not just do qualification? Each model had its benefits and pitfalls; neither was ideal.

Before Jack started part two, he got the audience engaged. Many shared their own experiences and the challenges they faced, and asked pointed questions. Jack then started introducing E2500, an updated approach toward C&Q significantly different from previous practice and a risk-based model that focuses efforts on areas with the greatest impact on product quality and patient safety. Only five pages long, E2500 is a high level guidance that provides a philosophy on C&Q, supported by ISPE guidance documents that show "how" to deploy such a philosophy.

E2500 philosophy says there is nothing special about validation, where the starting point follows ICH Q8 whereby a

As envisioned during the design of the program, the audience was very much part of the evening as they were encouraged to ask questions, share experiences and thereby help create a full interactive learning opportunity for all. The presentation consisted of a historical perspective and a current state, peppered with interesting anecdotes based on personal experience and pearls of wisdom.

The historical perspective started with an overview of nomenclature - what are Commissioning (IC/OC) and Qualification (IQ/OQ/PQ) - and how FDA justified cGMP in 1979 and issued guidelines on process validation in



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product is assigned a series of CQAs (Critical Quality Attributes) and the manufacturing process that makes it a series of CPPs (Critical Process Parameters) to control the CQAs. Those CPPs in manufacturing (components, instruments, process control elements, alarms, data, etc.) are then identified and designated in accordance to ICH Q9.

This then presents an entire continuum between two extremes. On the one hand is the traditional full commissioning followed by a full IQ/OQ/PQ, and on the other is the fully integrated verification ASTM E2500 advocates. Most companies, in reality, adopt an approach somewhere in between. Jack then presented scenarios that have been used, especially when "disaster" strikes. All integrated C&Q models require that a project follow Good Engineering Practices (GEP), thus the number of changes during C&Q should be relatively small. However, this requires that both the design and change management scheme be robust.

How does one implement a good E2500 based integrated verification model? Again, Jack offered two models that have been used. Model 1 is the Repeat Protocol model. In this model, commissioning is assessed, protocols are written and placed under change control, and the work summarized in reports. During qualification, only discrepant portions of commissioning are repeated after a review of the commissioning package. Jack gave an example of using a 5% AQL level, whereby 5% of the commissioning was repeated. The audience discussed the pros and cons of such an approach, which then led to Model 2.



Audience interaction adds another dimension to the information exchange.

everything was properly commissioned and all CPPs have been achieved.

For each of these models, Jack presented a case study. He also asked questions about how a full E2500 implementation would work. This seemed to pique the interest of many in the audience, especially those who are at the forefront of using this approach. Because of the newness of E2500, there have not been



Chapter President Brian Hagopian provides a Chapter update prior to the presentation.

Model 2 is the Risk Based Scheme, which still uses the commissioning package as a starting point, with analysis and assessment, but the qualification is based on the Critical Aspects traceability matrix to guide the testing. The testing can still be at the 5% level, however, it is now selected and prioritized based on criticality, namely, risk. Assuming good commissioning, qualification should be fast and result in a package that demonstrates



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sufficient data gathered in the industry to show "what is the payoff" and "how to do we justify our recommendation to our clients?" Because ISPE C&Q CoP members were also present in the audience, they got this feedback to take back to their community for further expansion and discussion.

Jack ended the lively evening by sharing the valuable lessons learned in his C&Q career - when to perform certain tests at critical junctures in a project based on GEP and common sense, tips on commissioning protocols and - possibly the most important lessons of all - successful C&Q starts with good, smart design. Do not skim on design reviews, which should engage all subject matter experts and encourage healthy rigorous debates, collaborative and clean handoff from design to construction to commissioning and qualification (no tossing over the wall) and do not outsource commissioning but rather use it as a training opportunity to retain the expertise in house.

### Industry News in Brief

*by Janet Tice, GMP Piping*

#### PCI Synthesis Continues Devens Expansion

Newburyport-based specialty chemical products manufacturer PCI Synthesis has filled 20 new positions at its Devens research and development plant in the past quarter and hopes to add five more in early 2012, according to company officials. PCI manufactures chemicals and pharmaceutical ingredients for drugs that are in clinical trials.

During the past three months, the company has ramped up its R&D facility in Devens, where about 25 people work. It has added 20 new workers, most of whom work in Devens, and about half of whom have doctorate degrees, according to Don Dickison, director of business development for the company. The company employs 91 people, and has openings for another five positions, he said.

PCI Synthesis has a collaboration with Biogen Idec - whose domestic headquarters is in Weston - to help the company produce new compounds. Source: Brandon Butler, Worcester Business Journal, 14 December, 2011)

#### Genzyme and Cystic Fibrosis Foundation Therapeutics Form Collaboration

Genzyme and Cystic Fibrosis Foundation Therapeutics Inc., the nonprofit affiliate of the Cystic Fibrosis Foundation, have announced a research agreement to support the discovery of new drugs to treat people with the most common mutation found in patients with CF, Delta F508. People with cystic fibrosis, a genetic disease, experience a cascade of symptoms that can lead to life-threatening lung infections and premature death.

The program's focus is to identify compounds known as "correctors," which may aid in the ability of the malfunctioning CFTR protein found in CF patients to operate correctly. In the Delta F508 mutation, the CFTR protein does not move to its proper place at the cell surface, impeding the flow of fluids into the airways. Nearly 90 percent of people with CF have at least one copy of the Delta F508 mutation.

In this collaboration, researchers will evaluate different compound libraries for correctors for Delta F508, and will take advantage of the vast compound libraries of both Genzyme and Sanofi. The research will take place throughout several Genzyme and Sanofi R&D facilities globally. Genzyme brings to the collaboration more than 20 years' experience exploring treatments for people living with CF. The company's efforts have ranged from improved molecular diagnostics to clinical trials with a gene therapy, and have included past

collaboration with the CF Foundation in the area of drug discovery.

"We are delighted to enter into a research collaboration with Genzyme, a company that has long dedicated itself to improving the lives of people with rare diseases," said Robert J. Beall, Ph.D., president and CEO of the CF Foundation. "Genzyme's capabilities and resources will help the CF Foundation accelerate its effort to find drugs to treat the most common mutation in CF and have the greatest impact on those with this disease."

"While there has been great momentum recently in cystic fibrosis research, there is still great unmet need," said Genzyme's president and CEO David Meeker, MD. "Together with the CF Foundation, we look forward to working to accelerate the pace of discovery on behalf of CF patients around the world." (Source: Genzyme Website, 16 November, 2011)

## Genzyme Appoints Leaders for Multiple Sclerosis and Rare Disease Businesses

Genzyme has announced the appointment of William "Bill" Sibold as Head of Multiple Sclerosis and Rogério Vivaldi as Head of Rare Diseases. Both will report to David Meeker, President and Chief Executive Officer of Genzyme, and will join the Genzyme Executive Team. The MS and Rare Disease businesses constitute Genzyme's core focus following its integration with Sanofi. "These appointments are a critical step in launching the new Genzyme," said David Meeker. "Bill and Rogério are dynamic leaders with the experience, energy, vision and commitment to patients needed to move us forward."

Bill Sibold has more than 20 years of experience in the biopharmaceutical industry, primarily in commercial operations, and has worked on multiple sclerosis products Avonex<sup>®</sup> and Tysabri<sup>®</sup>. He spent eight years in positions of increasing responsibility at Biogen Idec, where he was responsible for the company's \$2.5 billion neurology, oncology and rheumatology therapeutic areas consisting of approximately 800 employees. Bill joins Genzyme from Avanir Pharmaceuticals, where he was the Chief Commercial Officer, leading all of the company's commercial activities. Bill earned his MBA from Harvard Business School and his BA in Molecular Biophysics and Biochemistry from Yale University.

"Our goal is to build a world-leading multiple sclerosis franchise," said David Meeker. "Bill's substantial commercial experience and his deep knowledge of the MS field will be critical to the launch of Lemtrada<sup>™</sup> and Aubagio<sup>™</sup>, two investigational therapies with the potential to transform the lives of people living with MS."

Rogério Vivaldi joined Genzyme in 1997 and has held positions of increasing responsibility over his career with the company. Prior to this appointment, Rogério was President of Genzyme's Renal and Endocrinology Business. He previously served as Senior Vice President and President of Genzyme Latin America, responsible for the company's significant growth and diversification in the region, after founding Genzyme in Brazil.

Rogério was the first Brazilian doctor to treat a patient with Gaucher disease with enzyme replacement therapy in 1992 and has authored several publications on Gaucher disease. He was the founding partner of the Latin American Group on Gaucher. Rogério received his medical degree from Universidade do Rio de Janeiro Medical School, and received his MBA degree from Copead - Universidade Federal do Rio de Janeiro.

"Rogério's experience as a physician treating Gaucher patients in Brazil and his subsequent work in building our rare disease business in Latin America will provide both continuity and an energizing new beginning for our global rare disease business," said David Meeker. "Our highest priority is to resolve our product shortages and consistently meet the needs of patients." (Source: Genzyme Website, 10 November, 2011)

## Genzyme Plans to Grow in Massachusetts

Drawing on its new parent company's resources, Genzyme plans to grow over time in Massachusetts and increasingly apply its business model to drugs that serve larger patient populations, its new chief executive said yesterday. Genzyme, formerly the largest biotechnology company based in the state, was sold in April to the French pharmaceutical giant Sanofi SA in a \$20.1 billion deal.

Genzyme pioneered a system for developing drugs that treat rare genetic disorders, such as the enzyme deficiencies Gaucher and Fabry diseases, but is now pressing forward with treatments for more common afflictions, including multiple sclerosis, an autoimmune disease that attacks the central nervous system.

"This is a model that is absolutely scaleable and growable," chief executive David Meeker, who took on the top job at Genzyme in October, said in an interview after addressing a Greater Boston Chamber of Commerce breakfast at the Boston Harbor Hotel. Citing Genzyme's history of striking partnerships with patient advocacy organizations, physicians, and insurers, he said, "Our model is not defined by small-size disease or large-size diseases. Multiple sclerosis is a large-size disease."

Meeker said Genzyme plans to apply in the first quarter of next year for regulatory approval to sell its experimental MS drug Lemtrada in the United States and Europe. In October, the Food and Drug Administration agreed to review Genzyme's application for a separate oral MS treatment, Aubagio, and is expected to rule on it in the second half of 2012. Genzyme is currently readying an Aubagio application for European regulators.

But Genzyme, which has about 4,500 employees in Massachusetts and 10,000 worldwide, has not backed away from developing so-called personalized medicines to treat rare diseases. It has submitted an application in Europe for Kynamro, a drug to treat familial hypercholesterolemia, an inherited propensity for extremely high levels of cholesterol. It plans to seek FDA approval early next year.

Genzyme's drug shipments have been hobbled for the past two years as the company recovers from a 2009 viral contamination of equipment at its Allston Landing plant. But Genzyme is conducting trial production runs at a new plant in Framingham and expects the FDA will next year allow it to start shipping Fabrazyme, a treatment for Fabry disease, from the facility. Genzyme is on track to resume full Fabrazyme deliveries in the second half of 2012, Meeker said.

Speaking at the chamber's "innovation forum" breakfast, Meeker said Paris-based Sanofi is committed to expanding Genzyme's footprint in Massachusetts and using the company as a springboard into personalized medicine. "We're hiring aggressively now in our manufacturing and quality areas," he told the more than 100 business leaders. Meeker did not specify how many jobs Genzyme is likely to add. But he said the hiring in research and manufacturing is offsetting the loss of some "redundant" administrative jobs being eliminated at Genzyme headquarters.

Last month, Sanofi told employees it will close a research laboratory in Bridgewater, NJ, next year and move an unspecified number of jobs to the Boston area, where it has established its US research and development hub. The step is one in a series that will consolidate Sanofi's global research operations. (Source: Robert Weisman, The Boston Globe, 15 December, 2011)

## Vertex Announces CEO Succession Plan for 2012

Vertex Pharmaceuticals has announced that its Board of Directors has appointed Jeffrey Leiden, M.D., Ph.D., to the position of President and Chief Executive Officer (CEO), effective February 1, 2012. Dr. Leiden has been a Director on Vertex's Board since mid-2009 and brings to Vertex more than 20 years of scientific,

commercial and financial experience in the pharmaceutical and biotechnology industries and clinical experience in academia as a practicing cardiologist and molecular biologist.

Dr. Leiden began his employment with Vertex on December 14 as part of the transition period before he formally takes the role of CEO on February 1. Until February 1, Matthew Emmens will retain the role of Chairman, President and CEO, at which time he will retire from these duties to serve as the company's Executive Chairman through May 2012. In May, Mr. Emmens plans to retire from his full-time employment with Vertex but will continue to serve on the company's Board as a Director.

"Under Matt's leadership, Vertex established itself as a company capable not only of discovering important new medicines, but of successfully bringing those medicines to patients," said Dr. Leiden. "As a member of the Vertex Board, I have been extremely impressed with the company's ability to retain its clear focus on both groundbreaking science and improving the lives of people with serious diseases. It will be a privilege to lead Vertex at this exciting time and to further build the organization as we prepare for the global launch of our second new therapy, advance our diverse pipeline and build value for shareholders in the years ahead."

Dr. Leiden, 56, has been a member of Vertex's Board since July 2009. Dr. Leiden is a Managing Director at Clarus Ventures, a life sciences venture capital firm he joined in 2006. In 2000, he joined Abbott Laboratories as President and Chief Operating Officer where he had responsibility for running Abbott's global pharmaceuticals business. While at Abbott, Dr. Leiden helped launch multiple breakthrough medicines, including Humira for rheumatoid arthritis and other autoimmune diseases and Kaletra for HIV infection, among others. He also served as a member of the Board of Directors of Abbott Laboratories from 2001 to 2006.

Dr. Leiden began his career in academia as a practicing cardiologist and molecular biologist. From 1987 to 2000, Dr. Leiden held several academic appointments, including roles as Chief of Cardiology at the University of Chicago and Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital. During his academic career, Dr. Leiden was also involved in starting several biotechnology companies including Vical and Cardiogene.

Dr. Leiden held a number of board positions for pharmaceutical and biotechnology companies, including the role of non-executive Vice Chairman for Shire plc. He was also a member of the Board of Directors of Millennium Pharmaceuticals, Inc. Dr. Leiden received both his M.D. and Ph.D. degrees from the University of Chicago. (Source: Vertex Website, 15 December, 2011)

## FDA Grants Vertex Priority Review for Drug Treating Cystic Fibrosis

Vertex Pharmaceuticals has announced that the FDA has accepted the New Drug Application (NDA) for Kalydeco and granted the company's request for six-month Priority Review. The drug targets the defective protein that causes cystic fibrosis (CF) in a subset of people with the disease. If approved, it will be the first treatment to target the underlying cause of CF. Kalydeco (ivacaftor, VX-770) is Vertex's lead medicine in development for the treatment of people with cystic fibrosis. Known as a CFTR potentiator, this oral medicine in development aims to help CFTR protein function more normally once it reaches the cell surface, which is believed to help hydrate and clear mucus from the airways.

The FDA grants Priority Review to medicines that offer major advances in treatment or provide a treatment where no adequate therapy exists. A target review date of April 18, 2012 is set under the Prescription Drug User Fee Act (PDUFA) for the FDA's approval decision, which is four months earlier than the standard review time of 10 months.

In addition, Vertex announced today that its marketing authorization application (MAA) for Kalydeco has been validated by the European Medicines Agency (EMA). Validation indicates that the application is complete and starts the regulatory review process by the Committee for Medicinal Products for Human Use

(CHMP). Earlier this year, the EMA accepted Vertex's request for accelerated assessment, which is granted to new medicines of major public health interest and shortens the EMA's review time.

CF is caused by defective or missing cystic fibrosis transmembrane conductance regulator (CFTR) proteins resulting from mutations in the CFTR gene. The absence of functional CFTR proteins results in poor flow of salt and water across cell membranes in a number of organs, including the lungs. This leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage.

In people with CF who have a gating defect, CFTR proteins are present at the cell surface but do not function properly. The most common gating defect is caused by the G551D mutation. Approximately 4 percent of those with CF, or about 1,200 people in the United States and 1,000 people in Europe, are believed to have this mutation. Kalydeco is designed to keep the CFTR channels at the cell surface open longer to improve the transport of chloride ions across the cell membrane in people who have gating mutations. The US application seeks approval for the drug in people with the G551D mutation. The application submitted in Europe includes a request for all gating mutations. (Source: Vertex Website, 15 December, 2011)

## Covidien Plans Spin-Off of Pharmaceuticals Business

Covidien has announced that it plans to spin off its pharmaceuticals business into a standalone public company. Covidien's pharmaceuticals business is one of the world's largest producers of bulk acetaminophen, the largest United States supplier of opioid pain medications and is among the top 10 generic pharmaceuticals manufacturers in the US, based on prescriptions. Since 2008, this business has received FDA approval for eight new products, including two branded pain products launched in 2010.

In addition, Covidien's pharmaceuticals business is one of the world's leading suppliers of generators used to produce technetium-99m, a critical diagnostic medical isotope. It also is the only manufacturer that offers a fully integrated system of diagnostic contrast media in prefilled syringes and injectors.

"We've evaluated whether to separate these businesses for several years, due to the major differences between the medical products and pharmaceutical industries. We believe that now is the right time to do so because we have significantly improved the operations, performance and pipeline of our pharmaceuticals business," said José E. Almeida, President and Chief Executive Officer. "While both businesses hold industry-leading positions, they have distinctly different business models, sales channels, customers, capital requirements and talent bases. In addition, their respective innovation pipelines differ substantially in length, regulatory approval requirements, possible risks and potential returns.

"This transaction, if completed, would give both businesses greater flexibility to focus on and pursue their respective growth strategies, while potentially providing shareholders with greater value over the longer term," added Almeida.

If a spin-off is executed, the resulting Covidien medical products business would have annual sales of approximately \$9.6 billion (based on 2011 reported sales), about evenly split between the US and non-US markets. The Medical Devices business segment would represent about 80 percent of the company's sales, with Medical Supplies comprising the remainder. The company would hold the number one or number two market positions in categories representing approximately 90 percent of its sales, according to management estimates.

Covidien's pharmaceuticals business currently generates approximately \$2.0 billion in annual sales, with about two-thirds derived from the US market. This concentration in the US, where the business holds the significant leadership position noted above, would enable the new company to compete more effectively in the growing pain management category. The spin-off also would give the new company a better opportunity to bring to market innovative products currently in its pipeline and would give it the financial and strategic

flexibility to pursue its growth plans, including expansion outside the US. Covidien currently expects that completion of the transaction could take up to 18 months. (Source: Covidien Website, 15 December, 2011)

## Regulatory & Legislative Highlights

*by Janet Tice, GMP Piping*

### FDA Approves First Generic Olanzapine to Treat Schizophrenia and Bipolar Disorder

The FDA has approved the first generic versions of Zyprexa (olanzapine tablets) and Zyprexa Zydus (olanzapine orally disintegrating tablets) to treat schizophrenia and bipolar disorder.

Schizophrenia is a chronic, severe, and disabling brain disorder. About 1 percent of Americans have this illness. Symptoms people with schizophrenia have include hearing voices, believing other people are reading their minds or controlling thoughts, and being suspicious or withdrawn. Bipolar disorder, also known as manic-depressive illness, is a brain disorder that causes unusual shifts in mood, energy, activity levels, and the ability to carry out day-to-day tasks. The symptoms of bipolar disorder include alternating periods of depression and high or irritable mood, increased activity and restlessness, racing thoughts, talking fast, impulsive behavior, and a decreased need for sleep.

"The approval of generic olanzapine offers greater access to a widely used treatment for mental illnesses," said Keith Webber, Ph.D., deputy director of the Office of Pharmaceutical Science in the FDA's Center for Drug Evaluation and Research. "Having affordable treatment options is good for patients with long-term illnesses that must be carefully managed."

Olanzapine must be dispensed with a Medication Guide that describes the risks and adverse reactions people should be mindful of when using the product. Olanzapine has a boxed warning alerting that this type of drug can raise the risk of death in elderly people who have lost touch with reality (psychosis) due to confusion and memory loss (dementia). Olanzapine is not approved for treating psychosis in the elderly with dementia.

Other serious risks of olanzapine include, high blood sugar (hyperglycemia), high-lipid levels in the blood (increased cholesterol and triglycerides), and weight gain. Clinicians should take these effects into account when deciding to use this type of medication.

Generic olanzapine tablets will be manufactured by Dr. Reddy's Laboratories Ltd. and Teva Pharmaceuticals USA. Generic olanzapine orally disintegrating tablets will be manufactured by Apotex Inc., Dr. Reddy's Laboratories Ltd., and Par Pharmaceuticals Inc. (Source: FDA Website, 24 October, 2011)

### FDA Invests \$2 Million in Partnerships through Centers of Excellence in Regulatory Science and Innovation

The FDA has announced the award of \$2 million to support two regional Centers of Excellence in Regulatory Science and Innovation (CERSI). The centers, which will be located at the University of Maryland and Georgetown University, will focus on strengthening science and training needed to modernize and improve the ways drugs and medical devices are reviewed and evaluated, a major focus within the FDA. In August 2011, the agency released the strategic plan for: "Advancing Regulatory Science at FDA." More recently, the agency announced a related innovation initiative, "Driving Biomedical Innovation: Initiatives for Improving Products for Patients."

"These partnerships represent a critical, necessary and creative investment - one that will benefit not just FDA and academia, but also American consumers and industry," said FDA Chief Scientist Jesse L. Goodman, M.D., M.P.H. "The Centers of Excellence will create new scientific research, training and staff exchange opportunities for FDA and leading area institutions."

Working closely with FDA scientists, CERSI researchers will assist the FDA in driving innovation in medical product development as well as in advancing laboratory, population, behavioral, and manufacturing sciences. The agency chose to pilot the CERSIs in the Washington, D.C. area, to allow for the greatest possible face-to-face collaboration and training with FDA staff.

"These partnerships will promote faster and better scientific approaches to product development, helping people in need and supporting biotech innovation," Goodman said. (Source: FDA Website, 26 October, 2011)

## FDA Approves 35 Innovative New Drugs in Fiscal Year 2011

Over the past 12 months, the FDA has approved 35 new medicines. This is among the highest number of approvals in the past decade, surpassed only by 37 in 2009. Many of the drugs are important advances for patients, including two new treatments for hepatitis C; a drug for late-stage prostate cancer; the first new drug for Hodgkin's lymphoma in 30 years; and the first new drug for lupus in 50 years.

In a report recently released, FY 2011 Innovative Drug Approvals, the FDA provided details of how it used expedited approval authorities, flexibility in clinical trial requirements and resources collected under the Prescription Drug User Fee Act (PDUFA) to boost the number of innovative drug approvals to 35 for the fiscal year (FY) ending Sept. 30, 2011. The approvals come while drug safety standards have been maintained.

The report shows faster approval times in the United States when compared to the FDA's counterparts around the globe. Twenty-four of the 35 approvals occurred in the United States before any other country in the world and also before the European Union, continuing a trend of the United States leading the world in first approval of new medicines.

"Thirty-five major drug approvals in one year represents a very strong performance, both by industry and by the FDA, and we continue to use every resource possible to get new treatments to patients," said Margaret Hamburg, M.D., Commissioner of Food and Drugs. "We are committed to working with industry to promote the science and innovation it takes to produce breakthrough treatments and to ensure that our nation is fully equipped to address the public health challenges of the 21st century."

Among the new drugs approved in FY 2011, a number are notable for their advances in patient care and for the efficiency with which they were approved:

- Two of the drugs - one for melanoma and one for lung cancer - are breakthroughs in personalized medicine. Each was approved with a diagnostic test that helps identify patients for whom the drug is most likely to bring benefits;
- Seven of the new medicines provide major advances in cancer treatment;
- Almost half of the drugs were judged to be significant therapeutic advances over existing therapies for heart attack, stroke and kidney transplant rejection;
- Ten are for rare or "orphan" diseases, which frequently lack any therapy because of the small number of patients with the condition, such as a treatment for hereditary angioedema;
- Almost half (16) were approved under "priority review," in which the FDA has a six-month goal to

complete its review for safety and effectiveness;

- Two-thirds of the new approvals were completed in a single review cycle, meaning sufficient evidence was provided by the manufacturer so that the FDA could move the application through the review process without requesting major new information;
- Three were approved using "accelerated approval," a program under which the FDA approves safe and effective medically important new drugs quickly, and relies on subsequent post-market studies to confirm clinical benefit; and
- Thirty-four of 35 were approved on or before the review time targets agreed to with industry under PDUFA, including three cancer drugs that FDA approved in less than six months.

The Prescription Drug User Fee Act was established by Congress in 1992 to ensure that the FDA had the necessary resources for the safe and timely review of new drugs and for increased drug safety efforts. The current legislative authority for PDUFA expires on Sept. 30, 2012.

"Before the PDUFA program, American patients waited for new drugs long after they were available elsewhere," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research. "As a result of the user fee program, new drugs are rapidly available to patients in the United States while maintaining our high standards for safety and efficacy."

In October 2011, the FDA released a new plan, Driving Biomedical Innovation: Initiatives to Improve Products for Patients, to assist companies engaged in new product development, particularly smaller, entrepreneurial companies. (Source: FDA Website, 03 November, 2011)

## FDA Approves Xarelto to Prevent Stroke

The FDA has approved the anti-clotting drug Xarelto (rivaroxaban) to reduce the risk of stroke in people who have abnormal heart rhythm (non-valvular atrial fibrillation). Xarelto is marketed in the United States by NJ-based Janssen Pharmaceuticals.

Atrial fibrillation occurs in more than 2 million Americans and is one of the most common types of abnormal heart rhythm. In atrial fibrillation, the beating of the heart's two upper heart chambers (atria) is irregular and poorly coordinated. This leads to blood pooling in these chambers, resulting in blood clots. Non-valvular atrial fibrillation refers to atrial fibrillation in patients who do not have significant problems in their heart valves.

"Atrial fibrillation can lead to the formation of blood clots, which can travel to the brain, blocking blood flow and causing a disabling stroke," said Norman Stockbridge, M.D., Ph.D., director of the Division of Cardiovascular and Renal Products in the FDA's Center for Drug Evaluation and Research. "This approval gives doctors and patients another treatment option for a condition that must be managed carefully."

A stroke occurs if the flow of blood to a portion of the brain is blocked. If brain cells die or are damaged because of a stroke, symptoms occur in the parts of the body that these brain cells control. Stroke symptoms include sudden weakness; paralysis or numbness of the face, arms, or legs; trouble speaking or understanding speech; and trouble seeing.

The safety and efficacy of Xarelto were evaluated in a clinical trial with more than 14,000 patients comparing Xarelto with the anti-clotting drug warfarin. In the trial, Xarelto was similar to warfarin in its ability to prevent stroke.

As with other anti-clotting drugs, Xarelto can cause bleeding that, rarely, can lead to death. Bleeding was the most common adverse event reported by patients treated with Xarelto in the major clinical trial for the prevention of stroke in non-valvular atrial fibrillation. In that trial, Xarelto's risk of major bleeding was similar to that of warfarin; however, it caused less bleeding into the brain and more bleeding into the stomach and



intestines.

Xarelto has a boxed warning to make clear that people using the drug should not discontinue it before talking with their health care professional. Discontinuing the drug can increase the risk of stroke. An FDA-required Medication Guide, which will be given to patients and caregivers when Xarelto is dispensed, describes the risks and adverse reactions people should be mindful of when using the drug.

On July 1, 2011, the FDA approved Xarelto to reduce the risk of blood clots, deep vein thrombosis, and pulmonary embolism following knee or hip replacement surgery. (Source: FDA Website, 04 November, 2011)

## FDA Approves Erbitux to Treat Late-Stage Head and Neck Cancer

The FDA has approved Erbitux (cetuximab) for use with chemotherapy to treat patients with late-stage (metastatic) head and neck cancer. Erbitux is co-marketed by New York City-based Bristol-Myers Squibb and Eli Lilly and Company based in Indianapolis.

Combined with chemotherapy, Erbitux extended the lives of those receiving the treatment combination compared with those receiving chemotherapy alone. Erbitux already is FDA-approved for certain types of colon cancer, and has been approved since 2006 for treatment of non-metastatic head and neck cancer in combination with radiation therapy (first-line) or as a single agent (following standard treatment).

According to the National Cancer Institute, head and neck cancers account for 3 to 5 percent of all cancers in the United States. These cancers typically develop in the nose, throat or mouth and they are more common in men and in people older than 50.

"Erbitux's ability to extend the lives of patients with head and neck cancers is an important tool for oncologists who often rely on a multi-treatment approach for patients," said Richard Pazdur, M.D., director of the Office of Hematology and Oncology Drug Products in the FDA's Center for Drug Evaluation and Research." Given the aggressive nature of head and neck cancers that cannot be treated with surgery and radiation, it is important that patients have as many treatment options available as possible."

Erbitux was first approved by the FDA in 2004 to treat Epidermal Growth Factor Receptor (EGFR)-positive late-stage colon cancer after patients stopped responding to chemotherapy. The treatment can be used alone or in combination with chemotherapy. (Source: FDA Website, 07 November, 2011)

## FDA Approves First Drug to Treat a Rare Bone Marrow Disease

The FDA has approved Jakafi (ruxolitinib), manufactured by Incyte Corp. of Wilmington, Delaware, the first drug approved to specifically treat patients with the bone marrow disease myelofibrosis. In myelofibrosis, the bone marrow is replaced by scar tissue resulting in blood cells being made in organs such as the liver and the spleen. This disease is marked by an enlarged spleen, anemia, decreased white blood cells and platelets and myelofibrosis-related symptoms.

Jakafi, a pill taken two times a day, inhibits enzymes called JAK 1 and 2 (Janus Associated Kinase) that are involved in regulating blood and immunological functioning. Myelofibrosis is associated with the deregulation of JAK 1 and 2.

"Jakafi represents another example of an increasing trend in oncology where a detailed scientific understanding of the mechanisms of a disease allows a drug to be directed toward specific molecular pathways," said Richard Pazdur, M.D., director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research.

Jakafi was reviewed under the FDA's priority review program, an expedited six-month review of drugs that may offer significant advances in treatment over available therapy or that provide a treatment when no adequate therapy exists. The treatment was approved ahead of the drug's Dec. 3, 2011 review goal date under the Prescription Drug User Fee Act and has been designated as an orphan drug, which identifies the disease as affecting fewer than 200,000 people in the US. (Source: FDA Website, 16 November, 2011)

## FDA Revokes Approval of Genentech's Avastin for Breast Cancer

FDA Commissioner Margaret A. Hamburg, M.D. has announced that she is revoking the agency's approval of the breast cancer indication for Avastin (bevacizumab) after concluding that the drug has not been shown to be safe and effective for that use. Avastin will remain on the market as an approved treatment for certain types of colon, lung, kidney and brain cancer (glioblastoma multiforme).

"This was a difficult decision. FDA recognizes how hard it is for patients and their families to cope with metastatic breast cancer and how great a need there is for more effective treatments. But patients must have confidence that the drugs they take are both safe and effective for their intended use," Dr. Hamburg said. "After reviewing the available studies it is clear that women who take Avastin for metastatic breast cancer risk potentially life-threatening side effects without proof that the use of Avastin will provide a benefit, in terms of delay in tumor growth, that would justify those risks. Nor is there evidence that use of Avastin will either help them live longer or improve their quality of life."

Avastin's risks include severe high blood pressure; bleeding and hemorrhaging; heart attack or heart failure; and the development of perforations in different parts of the body such as the nose, stomach, and intestines.

The decision, outlined in Dr Hamburg's 69-page opinion, involves Avastin used in combination with the cancer drug paclitaxel for those patients who have not been treated with chemotherapy for their form of metastatic breast cancer known as HER2 negative. This indication must now be removed from Avastin's product labeling. Dr. Hamburg's decision is based on an extensive record, which includes thousands of pages submitted to a public docket, data from several clinical trials and the record from a two-day hearing held in June, 2011.

Avastin was approved for metastatic breast cancer in February 2008 under the FDA's accelerated approval program, which allows a drug to be approved based on data that are not sufficiently complete to permit full approval. The accelerated approval program provides earlier patient access to promising new drugs to treat serious or life-threatening conditions while confirmatory clinical trials are conducted. If the clinical trials do not justify the continued approval of the drug or a specific drug indication, the agency may revoke its approval. In this case, the accelerated approval was based on promising results from one study that suggested that the drug could provide a meaningful increase in the amount of time from when treatment is started until the tumor grows or the death of the patient.

After the accelerated approval of Avastin for breast cancer, the drug's sponsor, Genentech, completed two additional clinical trials and submitted the data from those studies to the FDA. These data showed only a small effect on tumor growth without evidence that patients lived any longer or had a better quality of life compared to taking standard chemotherapy alone - not enough to outweigh the risk of taking the drug.

FDA's Center for Drug Evaluation and Research, which is responsible for the approval of this drug, ultimately concluded that the results of these additional studies did not justify continued approval and notified Genentech it was proposing to withdraw approval of the indication.

Genentech did not agree with the Center's evaluation of the data and, following the procedures set out in FDA regulations, requested a hearing on the Center's withdrawal proposal, with a decision to be made by

the Commissioner. That two-day hearing, which took place June 28-29, 2011, included recommendations from the FDA's Oncologic Drugs Advisory Committee (ODAC), voting 6-0 in favor of withdrawing approval of Avastin's breast cancer indication.

"FDA is committed to working with sponsors to bring promising cancer drugs to market as quickly as possible using tools like accelerated approval," Dr. Hamburg said. "I encourage Genentech to consider additional studies to identify if there are select subgroups of women suffering from breast cancer who might benefit from this drug." (Source: FDA Website, 18 November, 2011)

## FDA Approves First Generic Version of Cholesterol-Lowering Drug Lipitor

The FDA has approved the first generic version of the cholesterol-lowering drug Lipitor (atorvastatin calcium tablets).

Ranbaxy Laboratories Ltd. has gained approval to make generic atorvastatin calcium tablets in 10 milligram, 20 mg, 40 mg, and 80 mg strengths. The drug will be manufactured by Ohm Laboratories in New Brunswick, NJ.

People who have high blood cholesterol levels have a greater chance of getting heart disease. By itself, the condition usually has no signs or symptoms. Thus, many people do not know that their cholesterol levels are too high.

"This medication is widely used by people who must manage their high cholesterol over time, so it is important to have affordable treatment options," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research. "We are working very hard to get generic drugs to people as soon as the law will allow."

Not all cholesterol in your blood is bad. There are three kinds of blood cholesterol that you should know about: high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides. HDL (good cholesterol) helps keep cholesterol from building up in the arteries. LDL (bad cholesterol) is the main source of cholesterol buildup and blockage in the arteries, which can prevent proper blood flow to your heart and lead to a heart attack. Triglycerides can lead to hardening of the arteries.

Atorvastatin is a statin, a type of drug that lowers cholesterol in the body by blocking an enzyme in the liver. Atorvastatin is used along with a low-fat diet to lower the LDL cholesterol and triglycerides in the blood. The drug can raise HDL cholesterol as well. Atorvastatin lowers the risk for heart attack, stroke, certain types of heart surgery, and chest pain in patients who have heart disease or risk factors for heart disease such as age, smoking, high blood pressure, low HDL, or family history of early heart disease. (Source: FDA Website, 30 November, 2011)

## FDA Proposes Draft Guidelines to Improve the Representation of Women in Medical Device Clinical Studies

Draft guidance aimed to address the historic underrepresentation of women in clinical studies has been issued by the FDA. Intended for medical device developers and manufacturers, the guidance outlines agency recommendations for designing and conducting device clinical studies that may enhance the enrollment of women in such studies, if appropriate.

"The FDA recommends that investigators and manufacturers strive to enroll representative proportions of both women and men in their device studies," said Jeffrey Shuren, M.D., director of the FDA's Center for

Devices and Radiological Health. "Our draft guidance outlines what we recommend for obtaining and improving the quality and consistency of sex-specific data on devices."

Certain medical products may elicit different responses in women than in men. This may be due in part to basic differences in men and women, including genetics, hormones, body size, diet, and sociocultural issues. In addition, certain variables associated with women, such as size or certain illnesses, may be responsible for certain differences between men and women in the safety and effectiveness of medical devices.

A 2001 report by the Government Accountability Office (GAO) on FDA-reviewed drug studies found that while women represented 52 percent of study enrollees, 30 percent of study documents did not report outcomes by sex and nearly 40 percent did not report enrollment demographics. A 2009 study of cardiovascular device pre-market applications showed that pivotal studies that reported sex enrolled an average of 33.9 percent women.

The draft guidance addresses study and evaluation of sex differences, data analysis and reporting in both pre- and post-market device clinical studies. In addition, it covers issues regarding statistical analyses of sex differences and how to report sex-specific information in summaries and labeling for approved devices. Devices intended for single-sex use, of course, would not be expected to address potential sex differences. (Source: FDA Website, 16 December, 2011)

## FDA Accepts Eliquis (apixaban) New Drug Application for Review

Bristol-Myers Squibb and Pfizer have announced that the FDA has accepted for review a New Drug Application (NDA) for Eliquis (apixaban), an investigational compound for the prevention of stroke and systemic embolism in patients with atrial fibrillation. The FDA accepted the filing and assigned a priority-review designation. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is March 28, 2012. As previously disclosed, an application for ELIQUIS for stroke prevention in atrial fibrillation has been validated for review by the European Medicines Agency.

The submissions were based on the results of the Aristotle and Averroes studies, two Phase 3 trials that evaluated the efficacy and safety of Eliquis for the prevention of stroke or systemic embolism in patients with atrial fibrillation. These two trials, which included approximately 24,000 patients, comprise the largest completed clinical development program for stroke prevention in atrial fibrillation among novel oral anticoagulants, and included patients eligible for anticoagulant therapy based on current treatment guidelines, as well as patients expected or demonstrated to be unsuitable for vitamin K antagonist (VKA) therapy. (Source: Bristol-Myers Squibb Website, 29 November, 2011)

### New Members

**Mr. Andrew Bartlett**, Millipore Corporation

**Mr. Steven P. Bevacqua**, *Student*, UMASS

**Mr. Paul C. Breen**, *Marketing Executive*, Enterprise Ireland

**Ms. Polly A. Brinkley**, *Automation Engineer*

**Mr. Mark Broadley**, *Vice President & General Manager*, Citra Labs, LLC.

**Mr. Charles T. Crooker, Jr.**, *Global Engineering*, Genzyme Corporation

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