Boston Area Chapter
ENGINEERING PHARMACEUTICAL INNOVATION

www.ispe.org/boston

NEWSLETTER

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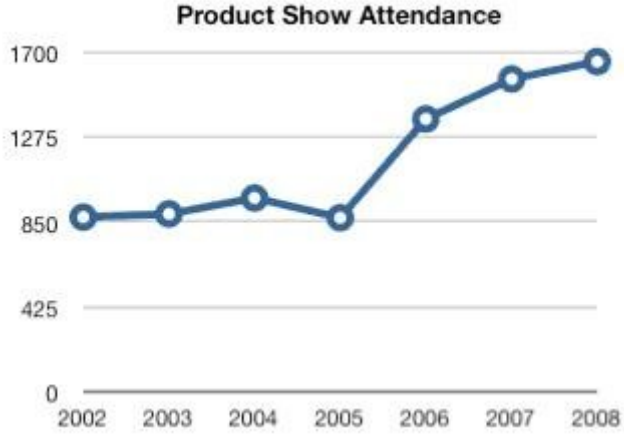
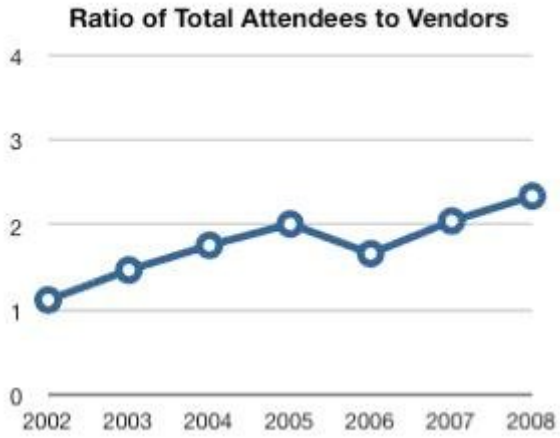
President's Message: Product Show, Annual Meeting, Fall Programs All a Success - Were You There?

The 2008 Product Show at Gillette Stadium was a rousing success with 1660 attendees, a new attendance record for the third year in a row. The graph below shows the growth in attendance for this event since 2002. Note that 2006 was the first year that the Product Show was held at Gillette Stadium.



Also noteworthy is the ratio of total attendees to vendors. This year set a new attendee:vendor ratio approaching 3 to 1. In other words, the Product Show is not just vendors talking to other vendors! Part of the reason for this growth is the increase in quality and quantity of the educational offerings at the Product Show. This year for the first time we had a

GAMP® 5 seminar which was very well attended, as well as an intensive Mixing in Biotech seminar and six other offerings.



Among the "other offerings" were the morning keynote address by Dr. Joey H. Norikane of the Fraunhofer Center for Molecular Biotechnology who described a plant-based biologics production system he is working on for the Department of Defense. You haven't lived until you have seen the movie of Nicotiana benthamiana sucking up agrobacterium solution! Just for fun, there was also an evening lecture by John Hannah, Pro Football Hall of Famer and former New England Patriot Offensive Lineman, who told some lively stories about his days as a football player.

The ISPE Annual Meeting at Boca Raton, Florida, was highlighted by two of the keynote addresses. One, by Janet Woodcock, MD, Director of CDER, FDA, spoke of the FDA future emphasis on preventing contamination of our foods and drugs from foreign suppliers. There will be challenges to companies to get their supply chains under control. The other keynote address I thought noteworthy was the single best lecture I have ever seen, by Hans Rosling, MD, PhD, cofounder of Doctors without Borders and Professor of International Health at the Karolinska Institute in Stockholm, Sweden. He used a deft sense of humor and the most amazing graphics to tell a poignant story about the delivery of health care in countries around the world through the past 100 years. I urge you to check it out here ("Debunking Myths About the Third World"): http://www.gapminder.org/video/talks/ted-2007---the-seemingly-impossible-is-possible.html

On the local level, the Chapter has been hard at work this fall organizing an impressive lineup of educational programs and plant tours throughout the greater Boston area for Chapter members and guests. (Please refer to the articles elsewhere in this issue for detailed summaries.) The September 16th program, **"Six Sigma Part II - Key to Efficient Innovation and Cost Effective Manufacturing Processes"** was held at the Genzyme Center in Cambridge and featured Dr. Philip Ramsey of North Haven Group and Philip Werth of Wyeth BioPharma whose presentations left many of the attendees thinking about how to apply what they had learned to situations in their own workplaces.

On September 24th, Chapter members traveled to Walpole for a **Siemens Healthcare Diagnostics Plant Tour** and a pair of presentations. Michael Canary, Siemens Director of Engineering, presented the challenges of the project from the perspective of what Siemens was looking to achieve. Fred Scribner, Project Executive for Columbia Construction, the project's general contractor, described how those challenges were met and overcome during implementation.

November 5th found members in Worcester at a very well-attended event entitled **"From Biotechnology to Bio-Fuels"** held at the WPI Life Sciences and Bioengineering Center at Gateway Park, a 12-acre, mixed-use development with a focus on the life sciences and biotech. Stephen Flavin from WPI spoke about the development itself and the joint venture between WPI and the Worcester Business Development Corporation that led to its creation. Christopher McPhee followed with an excellent presentation that covered "Biofuels: Ethanol for The Future." And, on November 18th, the Chapter traveled to Devens for a program on sanitary pumps featuring Allen LeBoeuf, Product Manager for Oliver M. Dean, and Mark Atkinson of Watson-Marlow Bredel Pumps. This event - with its catchy title, **"Sanitary Pumps 101: What They Didn't Teach You in College,"** and its novel location at Devens - drew many new faces.

The depth and breadth of our educational offerings over the past year has been due to a handful of volunteers and Dave MacDonald, Chairman of the Educational Program Committee and former Director at Avecia Biotechnology. Now, Dave has decided to take a job out in Colorado. Since we were already down one member, this means we seriously need two more volunteers for this critically important Committee.

In addition, one of the Chapter's key goals for 2009 is to attract more volunteers from operating companies. It may surprise some of you to know that Dave was one of the few volunteers from operating companies in the Boston Area Chapter. In fact, if we look at the nine operating companies with the greatest number of Chapter members (347 members, to be exact), only three of these members are active Chapter volunteers!

Since the Chapter's educational programs are primarily intended to benefit our operating company members and the Educational Program Committee has obviously flourished under Dave's leadership, I would love to see another member or two from an operating company step up and help. If you work at one of these companies, would you consider volunteering? The commitment is less than you might think. For instance, as a "meeting manager" your contribution could be to organize just one of the many programs held during the year. For more information, email us at mailto:ispe@camihq.org.

Thanks very much to you, Dave, for all the hard work and excellent results you have obtained for our benefit. Our loss is Colorado's gain! I hope you can make it back to Flat Top Johnny's in Cambridge to join us for the Chapter's "Holidays-are-Over" party on January 15th.

Sincerely,

Doyle Johnson

President, ISPE Boston Area Chapter

Upcoming Events - Mark Your Calendar!

Thursday, January 15, 2009
Annual Social
Flat Top Johnny's Billiards, Cambridge MA

Keep an eye out for registration information!

Check out the website at http://www.ispe.org/cs/boston_area_chapter/Boston_Area_Events for upcoming Events information.

Product Show Breaks New Ground - AGAIN!

by Brian Hagopian with photos by Peter Teague and Gail Fischer

The Boston Area Chapter recently held its flagship event, the 17th Annual Product Show, at Gillette Stadium. Attendance at the show reached record highs this year, thanks to the efforts of a large group of volunteers from the Chapter.

A few "firsts" at this year's show included:

* ISPE and GAMP synergized in a first ever, day long session

* ISPE International attended the show

* Patriot Hall of Famer John Hannah was a keynote speaker

* CNN (that's right, THE CNN we all watch on TV) visited the show and shot footage

Past President Rick Pierro, current President Doyle Johnson and audience show how much fun it can be to be a part of ISPE!

The day long event started earlier than ever before, with the Educational Committee adding two three-hour morning sessions, one covering fluid mixing and one covering GAMP. One informative session was presented by Chemineer which detailed fluid mixer design, application, and use. The GAMP® 5 session was presented by a team of instructors from Wyeth, Genzyme, and Novartis with high attendance. The Chapter also sponsored six afternoon sessions rich in content and covering pumps, automation, leadership, GAMP® 5, project management and chromatography. The subject matter was such that ISPE Members traveled from as far as California to attend these technical sessions.

The Boston Area Chapter broke new ground this year in working with the GAMP team to sponsor their presentations and breakout sessions throughout the day. Participants were able to attend these sessions for FREE. The success of this session was brought to the fore at the ISPE Annual Meeting in the hope that the winning formula in Boston can be replicated by other Chapters throughout the country.

New England Patriots Hall of Famer John Hannah entertains the crowd with great stories!

Students from UMass Amherst pore over employment opportunities at the Career Center.

Lynne Richards from ISPE's international headquarters in Tampa made the trip to Gillette as the Boston Area Product Show has received much national recognition in recent years. She staffed the ISPE membership booth and had the opportunity to take in all the Show had to offer. The Chapter added a record number of new members to ISPE during the Product Show thanks to Lynne's work and that of several local Board Members.

The Product Show held its second career fair this year with hiring companies Biogen, Shire, Bristol-Myers Squibb, Vertex, Astra Zeneca and others in attendance. CNN, which was researching a story for companies hiring in these trying economic times, learned of our career fair and visited the show to interview hiring companies, as well as candidates.

Last but not least, the Show featured two keynote speakers, one to open the show and a second in the late afternoon. Dr. Joey Norikane from Fraunhofer CMB spoke on the topic of producing vaccines using plant-based vehicles. New England Patriot and NFL Hall of Famer John Hannah, the most decorated Patriot of all time, regaled attendees with great stories from his life as a Patriot and had the audience in stitches. We learned that John is much more than just a retired football player. He continues his involvement with the Patriots and

regularly attends home games at Gillette, where he hosts "Hannah's Huddle."

Throughout the day, people I encountered described the reasons why they attended the show. From exhibitors:

* Our company exhibits at every local ISPE show and Boston's is by far the best local show in the country.

* Our company did a million dollars worth of business at the show.

From attendees:

* Everyone serving our industry is under one roof. I've never seen anything like this on a local level.

* I flew in from the west coast to attend the educational sessions.

* You'd be crazy to miss this show. It has everything.

* GAMP sessions for free, that's amazing!

About $2,000 in gift certificates and Patriots' memorabilia were raffled off throughout the day. Shawn Callahan from FW Webb was the lucky recipient of a Patriot jersey autographed by John Hannah.

It was great to see the entire Boston Area Chapter Board of Directors at the Show as well as many Members from the Chapter's Advisory Board. If you are looking to meet with the brain trust of the Boston Area Chapter, the Product Show is the best place to do so.

Amenities such as carving stations and hot and cold hors d'oeuvres were available throughout the day.

Product Show
roduct Show Committee Chair Brian Hagopian with CNN's Dan Lothian.

Keynote Speaker Dr. Joey Norikane with Past President Dave Novak.

to make each show new and exciting. Whether you attended or exhibited, you should have received a survey, which we encourage you to complete. This is our major vehicle for feedback and we want yours! If you have any suggestions, comments or input, either positive or negative, we would like to hear from you. If you prefer a different method of providing feedback, feel free to contact any member of the Product Show Committee or email us at ispe@camihq.com.

The Product Show Committee already has a few surprises planned for next year's show, so stay tuned for updates. The date has already been set - October 7, 2009 - so please mark your calendars and save the date. You can visit the Product Show website year round at http://www.ispeboston.org/ for updates and information.

Boston Area Students Sweep Nationals

article and photos by Rick Pierro

In an unprecedented event, two of the top winners of the 2008 ISPE International Student Poster Competition held in sunny Boca Raton last month were both from the Boston Area Chapter. They are Jason Lajoie from the University of Massachusetts, who was one of two winners in the undergraduate category (they actually tied) with his poster entitled "Directed Evolution of the RHil Protein." And, Padmaja Magdala from Northeastern University, also one of two winners in the graduate category (unbelievably, they tied also), with her poster entitled "Epidermal Growth Factor Receptor Targeted Engineered Gelatin Nanovectors for Gene Delivery and Transfection in Pancreatic Cancer Cells."

ISPE International Student Poster Competition winner
Padmaja Magdala from Northeastern (second from left).

These two students had won the local ISPE Boston Area Chapter Student Poster Competition held last May at Northeastern University and were sent to Boca Raton by the Chapter to compete at the international level. The competition was ferocious. Over 30 students from 12 Chapters nervously described their research in concise five-minute talks to six stern-looking and knowledgeable judges. They then handled numerous rapid-fire questions about their research with poise and skill. The competition was so tight that two winners for each contest were tied for first place by the judges. Each winner happily took home $500.

ISPE International Student Poster Competition winner
Jason Lajoie from UMass Amherst (second from left).

In all the years that this poster competition has been held, never have both contest winners originated from the same

Chapter. Boston was well served by these students. Congratulations to Jason Lajoie and Padmaja Magdala on a job fantastically well done!

ISPE Annual Meeting 2008: A Student's Perspective

by Jason Lajoie and Jeremy Sauer with photos by Doyle Johnson

Wow! I think this exclamation pretty much sums up my week as a student poster contest competitor at this year's ISPE Annual Meeting in Boca Raton Florida. But I won't leave it at that. As I flew into Ft. Lauderdale I wasn't sure what to expect, since this was my first trip to the ISPE Annual Meeting. When I arrived in Boca Raton on Saturday night the gorgeous and expansive Boca Raton Resort and Club was alight with activity. The resort, located on the beautiful Intercoastal Waterway, featured restaurants, bars, tropical plant life, and the one-of-a-kind architectural style of Addison Mizner. To say I was impressed with the location and facilities is an understatement.

The student activities kicked off on Sunday with the Student Luncheon. This luncheon offered the opportunity to meet other students from across the US and around the world. I met students who came from as far away as Singapore and Turkey. We also had the great pleasure of eating lunch with a number of industry leaders dedicated to mentoring the up and coming generation of ISPE. This is one of the greatest assets of ISPE membership from a student standpoint.

Meeting and interacting with pharmaceutical and biotech industry professionals allows us to learn the tricks of the trade and establish valuable relationships with people eager to help us succeed. These are things you can't learn from a textbook or in the lab but I consider them just as valuable as my education. It is simply amazing to be involved in an organization that shows such dedication to developing its student members.

Student Poster Competition winner Jason Lajoie (left) and UMass Amherst Student Chapter President Jeremy Sauer enjoying their "once-in-a-lifetime" visit to the ISPE Annual Meeting in Boca Raton.

I'm sure you are all wondering what it was like competing in the International Student Poster Competition. Up to this point in my ISPE career, I have never been disappointed with an event or activity and the poster competition was no exception. The caliber of students and their research was exceptional. I enjoyed speaking with many of my fellow competitors about their work and I certainly learned a lot about the research that is ongoing around the world. I'll admit I was a little nervous as I walked into the judging room. But once the butterflies settled I really enjoyed presenting my research and interacting with the judges.

I'm normally a pretty humble guy and I don't like to brag. But I am proud to say that I won first prize in the undergraduate category of the poster competition along with Maureen Cheung of the University of Akron. It was truly an honor to walk up to the stage and receive the award in front of hundreds of ISPE members. I was especially proud to be representing the University of Massachusetts Amherst and the Boston Area Chapter of ISPE.

On Monday night after the judging for the poster competition drew to a close, UMass ISPE president Jeremy Sauer and I had the great pleasure of going out to dinner with Rick Pierro, Mike Denault, and Andre Walker. We had a wonderful time and this was yet another example of how the senior members of ISPE are interested in mentoring and forming relationships with the student members.

This experience was truly once in a lifetime. The Boca Raton resort was magnificent and the program put on by ISPE

was first rate. All of the people that Jeremy and I met there were as enthusiastic and excited to talk to us students as we were to meet them. The Annual Meeting also gave us a great opportunity to meet with fellow students and talk about classes, the job search, and strategies for building a better Chapter. During the meeting, we even consulted with a student from Boston University on how to start up his own student chapter. For all of these experiences, we cannot thank ISPE enough. We only hope that as we embark on our careers that we can stay involved in this wonderful organization and continue to learn and grow within the industry.

Young Professionals Initiative First Meeting a Big Success

by Jim Grunwald with photos by Chris Ciampa

On Thursday, November 6th, the first official meeting of the ISPE Young Professionals Initiative was held at Flat Top Johnny's in Kendall Square. Attendees included Christopher Ciampa of Thermo Fisher, Anthony Giragosian, formerly of Epic Therapeutics, Carmen Ho of Shire HGT, Zeke Johnston of Genzyme, Joe Rajewski of Shire HGT, Chris Lewis of Beth Israel Hospital and Dan Ramsey of Commissioning Agents.

Attendees share their ideas with Chapter Board Member Jim Grunwald (right).

In addition to these young professionals, ISPE National Young Professionals Initiative Committee Chair, David Novak, ISPE Boston Area Chapter Vice President, Sylvia Beaulieu and Young Professionals Initiative Local Liaison and Boston Area Chapter Board Member, Jim Grunwald provided an introduction to the program and hosted this event. The premise underlying the Young Professionals Initiative is a desire to promote the development of our young professional membership and provide a dynamic environment where education, networking, career development and volunteer opportunities can be offered to these future Chapter and Society leaders.

Within a short period of time, it became obvious that our core group of attendees really had a lot of common concerns and aspirations and it didn't take long before an agenda was developed and a second meeting scheduled, this time at the Asgaard in Cambridge.

This is a great opportunity to get involved with like-minded professionals and help shape the future of ISPE and the industry. If you are interested in learning more about this dynamic group, please consider attending an upcoming meeting; or should you have questions regarding the program, please do not hesitate to contact jgrunwald@a-zcorp.com.

Six Sigma Part II - Efficient Innovation and Cost-Effective Manufacturing

by Jim Verhulst with photos by Doyle Johnson

On September 16, the Boston Area Chapter presented another educational seminar at the innovative, LEED-certified Genzyme Center corporate headquarters in Cambridge. The topic was Six Sigma Part II - Key to Efficient Innovation and Cost-Effective Manufacturing Processes. The speakers for the evening were Dr. Philip Ramsey, of North Haven Group, and Philip Werth, of Wyeth BioPharma.

Dr. Ramsey is an industrial statistician with more than 20 years of experience in applying statistical methods to products, processes and R&D programs across diverse industries. During that time, he has been designing and delivering industrial training courses in statistical process control, design of experiments and response surface methods for process optimization. In his presentation, *Design for Six Sigma*, Ramsey explained that today's highly competitive global markets and the rapid commoditization of new products require companies to innovate efficiently. Being early to market with the right product is now considered essential to long-term financial success.

Traditionally, management has focused on continuous improvement and cost reduction using Lean6Sigma, which integrates Lean and 6 Sigma tools and methods. Lean6Sigma programs have been very successful in helping companies improve quality and reduce costs for existing products and services. In contrast, Design for Six Sigma (DFSS) has evolved as an approach to shorten time to market, and to design and produce high quality products that are aligned with customer expectations.

Genzyme Center in Cambridge provided a spectacular backdrop for the September 16th program on Six Sigma.

Attendees were exposed to a full menu of jargon and acronyms. The talk covered the key elements and tools of DFSS, and linkages between DFSS and the traditional Lean6Sigma DMAIC (Define, Measure, Analyze, Improve, Control) process for continuous improvement. As Ramsey explained, the basic algorithm for all variants of DFSS is known as IDOV which is an acronym for Identify, Design, Optimize, and Validate. The first step in IDOV, identifying the Voice of the Customer (VOC) and translating and prioritizing the customer needs into functional responses (CTC's), is crucial.

So why are we interested in Design for Six Sigma? It turns out that nearly 80 percent of the overall costs of a product are established during the design phase. DFSS invests time and resources early in the product development cycle to lower overall product cost, speed time to market, utilize resources more efficiently, produce more robust designs and, in the end, better satisfy customer needs. DFSS helps move from "tested-in" to "designed-in" quality.

The presentation then turned to tools available to implement DFSS. Conjoint Analysis is a quantitative approach that can be used during the Voice of the Customer (VOC) phase. Conjoint Analysis is a cousin of design of experiments (DOE). It allows designers to uncover characteristics that are important to the customer as well as important interactions among those characteristics. A second tool, Quality Function Deployment (QFD), is used to facilitate requirements flow-down. The tool uses the concept of "houses" (named after the house-like appearance of the data graphs) to define relationships between functional responses (CTCs), design characteristics (DCs), process variables (PVs) and process controls. Other

QFD tools available include Transfer Functions, Scorecards, FMEA, Design Validation Test Plans, Communications Plans, Design of Experiments, Robust Design, Tolerance Design, and Control Plans. The presentation gave an overview of how these QFD tools can be used together.

A brief case study centered around how to build a better bicycle was presented to demonstrate some of the DFSS methodology. This was more complicated than it first appeared. The example showed how to use the basic tools, but it quickly became apparent that this was an involved effort that required trained resources.

Attendees from BIND Biosciences enjoy the reception prior to the presentations.

The second speaker for the evening was Philip Werth of Wyeth BioPharma, a chemical engineer with diverse industry experience. His presentation was entitled *Use of Statistical Quality Control to Improve the Productivity and Quality of a Biopharmaceutical Process*. Drawing on examples from his work at Wyeth, Werth explained how he has used statistical techniques to help define and implement numerous improvements to the manufacturing processes and demonstrated that monitoring a manufacturing process to detect costly and recurring problems can pay big dividends.

Furthermore, he explained that by carefully monitoring a process one occasionally finds opportunities for significant improvements. The presentation covered how this can be done from both univariate and multivariate points of view. It also examined how equipment and processes can be designed to facilitate the monitoring and gathering of relevant process data.

Univariate statistical process control (SPC) is the simplest type of analysis. The investigator looks at only one variable at a time to detect and learn from process changes over time. Because the changes may be small, one of the most important considerations in these kinds of investigations is the accuracy of the measurements. Multivariate SPC, as the name suggests, treats variables as a group. This has certain advantages in that one can see the covariance between the variables, and one can also see the effect when small changes in individual variables add up to a significant indication when viewed together.

A number of multivariate SPC techniques were presented using real life examples with two to seven variables. Batch histories may contain a lot of useful data. By plotting many batches, the many process variables measured can be summarized into a few new variables (scores) that create a fingerprint of a good batch. Scores provide overviews that are easier to use. Ultimately these can be used to facilitate a root cause analysis. Multivariate analyses are often restrained by having only partial data. Werth's advice: "build your skids and equipment to measure and record many variables." From an analyst's point of view, one cannot "over-instrument."

However useful that approach, it does leave the statistician with a huge volume of data. Werth described the utility of a Design of Experiments (DOE) approach. He pointed out that "one good DOE with 10 data points is better than thousands of points SPC."

The presentation offered suggestions on how best to do SQC and some common pitfalls to be avoided. Werth showed examples of problems with production data that may result in false correlations. In the end, the key to successful SQC is to develop a deep understanding of the manufacturing processes.

Many thanks to the Educational Program Committee for a stimulating program that left many of the attendees thinking about where and how to apply what they had learned to situations in their own workplaces.

Members Tour Siemens Diagnostic Healthcare State-of-the-Art Facility

by Lee J. Ward with photos by Peter Teague

September 24th found the ISPE Boston Area Chapter being hosted at another landmark facility within the life sciences realm, that of Siemens Diagnostic Healthcare located in East Walpole, MA. Following a sumptuous buffet dinner in the plant's cafeteria, 60 Chapter Members and guests were treated to a tour and presentation that illustrated the business needs and wants, project engineering and fiscal management that resulted in the world class, state-of-the-art facility we see today.

Michael Canary, Director of Engineering for Siemens Diagnostic Healthcare, presented the challenges of the project from the perspective of what Siemens (formerly Bayer) was looking to achieve. Fred Scribner, Project Executive for Columbia Construction, the project's general contractor, described how those challenges were met and overcome during the implementation phase. With a budget of $110 million and a schedule that could not change, they had a monumental mountain to climb and consequently conquer. Jacobs Engineering was enlisted as the process design company and, together as a cohesive team, worked with local government agencies, environmental groups and the Commonwealth of Massachusetts EPA such that all concerned reached their goals and objectives.

Gently nestled in a well-appointed, 81-acre site bordered on the east by I93 and on the west by residential properties, the Siemens facility fits in like a piece of a jigsaw puzzle. Great care was taken to ensure that the design of the building was environmentally responsible as well as aesthetically pleasing and the results were phenomenal. The landscaping artfully blends the 500,000 sq/ft structure into its surroundings, creating a vista that draws the visitor in. At the same time, the plant harbors engineering "secrets" that many owners would wish they had incorporated in their own facilities.

Michael Canary of Siemens Diagnostic Healthcare presents an overview of the project prior to the tour.

An example of the latter would be the genius that went into placing the HVAC equipment in the basement (instead of on the roof), a nontraditional approach and a testament to "smart design" that produced two major benefits. First, the equipment is protected from the elements and, second, with the nearby residential area in mind, both noise and aesthetics are successfully managed.

Another example was the approach to ground water management. A system was engineered that takes all the run-off from the site and directs it into the ground where it cannot impact the surrounding environment. "Who would have guessed we had the only creek where "cold stream" trout exist today in Massachusetts," said Mike when

The "viewing gallery" offers members a look into each manufacturing suite.

explaining how the design team worked with environmentalists during the planning phase to resolve the difficult challenges the scenic site presented.

The warehouse provides a lesson in efficient space utilization.

The tour that followed stressed that this is, first and foremost, a manufacturing facility and is pragmatically engineered as such. Care was taken to design in benefits to optimize operation of the plant. In addition, extensive use of predictive modeling was used in the design stage to ensure smooth progress during construction. As a seasoned professional who has spent a great deal of my working life in close proximity to construction engineering, I have to say this was achieved to great effect. Absolutely nothing was left to chance. For example, Fred described how the building had to be built to a point of near completion, then partially disassembled so that process equipment could be installed, all according to a carefully orchestrated plan that worked perfectly. In addition, forethought and planning ensured ease of future expansion, with extra space included in the manufacturing suites for additional reactor vessels.

And let me not forget the "piece de la resistance:" the viewing gallery overlooking each manufacturing suite where visitors are offered an awe inspiring view of the operation - in all of its gleaming, stainless steel complexity. A high tech console standing atop a pedestal in front of each operation displays a schematic providing visitors with an understanding of the inner workings of the equipment before them.

Members even got a tour of the vast basement area and the specialized equipment housed there.

It never ceases to amaze me that the tablet swallowed or the diagnostic test kit used - so often taken for granted - comes from the minds of researchers and the engineering marvels of facilities such as this one. The way in which the myriad elements of this project have culminated in healthcare products used every day by millions of people throughout the world will generally never be appreciated by the public. That is, except for those of us lucky enough to attend the evening's presentation and tour, where members and guests of the Boston Area Chapter were privileged in being able to see the results first hand. Finally, our visit above all else demonstrated that with constraints of cost and time, the right planning and a well-managed delivery organization, it truly is possible to complete a project of this magnitude, complexity and aesthetic appeal ahead of schedule and under budget.

"From Biotechnology to BioFuels" Draws a Crowd to Worcester's Gateway Park

by John Sheridan

On November 5, over 80 attendees spent an evening learning about cutting-edge technology for the production of cellulosic-based biofuels in a beautiful state-of-the-art academic research facility in Worcester, MA. On a site that once teemed with the machinery of the Industrial Revolution, the WPI Life Sciences and Bioengineering Center merges a new life sciences laboratory structure with a former industrial building constructed in the 19th century by Stephen Salisbury II, a Worcester merchant and a WPI founder.

The Center, built by Consigli Construction, is the first new structure built at Gateway Park, an 11-acre mixed-use life sciences-based campus that WPI is developing with the Worcester Business Development Corporation (WBDC). The project was completed in April 2007, on time and on budget, and consists of 124,600 square feet, four stories and a $50 million investment by WPI. Gateway Park will eventually host three additional laboratory buildings and will encompass about a half million square feet of space designed to help fuel the development of Central Massachusetts as a center for the emerging life sciences industry. But this is getting into the first speaker's presentation.

After announcements and introductions, Stephen Flavin, Associate Provost and Dean of WPI Corporate and Professional Education, spoke about all the exciting things happening not only on campus but all around Worcester. In his current role, Mr. Flavin works in close collaboration with faculty and staff to lead all aspects of corporate education programs. Talking about WPI, he noted that it was founded in 1865 by industrialists who recognized the need for a more highly skilled work force and currently offers over 50 graduate science, engineering and management programs plus over 60 professional development offerings.

To name only a few of its functions, the Center is home to four WPI Departments (Biology and Biotechnology, Biomedical Engineering, Chemistry and Biochemistry, and Chemical Engineering), WPI Interdisciplinary Research Groups ("Centers"), the Bioengineering Institute (an interdisciplinary organization dedicated to turning life-sciences technology into workable products) and houses the headquarters of WPI's Corporate and Professional Education Programs. Among its many amenities are an Internet café and a state-of-the-art amphitheater-style auditorium, where the ISPE event was held.

The presentation then shifted to the tremendous opportunities in Central Massachusetts and the biotech migration westward. Stephen spoke about the major investments the Commonwealth of Massachusetts is making in Central Massachusetts as a life sciences, bioengineering center. These include the BMC-Biomanufacturing Initiative in 2006 and the Massachusetts Growth District Initiative in 2008. In the past five years 20 biotech companies, including 14 from Cambridge, have moved into space along Route 128 and 49 of the 100 largest biotech firms in Massachusetts are located between 128 and Worcester. Although Genzyme's headquarters is in Cambridge, their largest research facility in the world is in Framingham.

Stephen described the vision for WPI as everything from acting as a launching pad to enhance its own leading-edge research programs in life sciences, biotechnology and bio/chemical engineering, as well as those of other academic and medical institutions; to adding new life to downtown Worcester by creating a mixed-use destination which includes companies, residential and retail establishments.

He also described partnering with industry to develop effective educational solutions and used Polaroid's efforts to transition its laid-off workers into biotech manufacturing as an example. When Polaroid was going under, a partnership was formed between WPI, industry and government to develop a custom re-training program utilizing WPI resources and bioprocessing knowledge, industry experts and government funding. The result was a five-week, hands-on training program conducted in a simulated cGMP environment. The program proved to be a great success, with a high percentage of the employees landing new jobs during or shortly after the training was completed.

Mr. Flavin's presentation was followed by a very detailed presentation on the research and development that sets WPI apart from other campuses. Although scheduled speaker Alexander Di Iorio, PhD, Director of the Bioprocessing Center at WPI and Affiliate Assistant Professor in the Department of Biology and Biotechnology, was unable to present, he was very ably represented by Christopher McPhee, MS, whose presentation covered "Biofuels: Ethanol for The Future."

Although some left WPI shaking their heads in wonderment at the complexity of the topic, it was apparent to all attending that Christopher had both complete mastery and real passion for the subject he spoke on.

He began by presenting the issues and roadblocks to biofuels but quickly got everyone's attention when he asked (and quickly answered) the question, "Why use ethanol?" He explained that ethanol is a relatively simple product to make, the technology for large scale production is already available, blending ethanol with gasoline increases oxygenation and boosts octane rating, ethanol can be used directly in fuel cells and enables independence from fossil fuel. After explaining the chemistry, he stressed that ethanol yield is critical to the overall cost of production and the economic viability of the process. Next question: where to get the biomass?

The initial development used food-starch crops however there is not enough cropland available to use corn-starch ethanol as the solution to our energy problems, in and of itself. This has forced research to examine other options like cellulosic ethanol with its low impact on food crops and agricultural land, higher yields and greater efficiency than corn, independence from foreign supplies of energy, and utilization of biomass that otherwise goes unused. Some candidate cellulosic crops are poplar, sugar cane, switchgrass, miscanthus and practically any crop residue. Christopher identified a number of development issues such as the typical two-stage system is time consuming and costly and it is apparent there is no silver bullet. At that point he was the professor discussing the idealized one-step process (where enzymatic digestion and ethanol fermentation occur simultaneously in the same bioreactor), biomining/strain improvement, process development, etc.

This is where a fascination for how nature works becomes a potential solution. He described biomining, nature's slow degradation process and how many organisms use wood for energy, including the homeowner's worst enemy: termites. Termites are cellulose-degrading machines that have proven to be one source of cellulolytic micro-organisms and after squashing many termites, BP Center is currently working with several termite microbes with proven potential for development. He went on discussing screening for enhanced cellulose and β-glucosidase, and other enhanced producers of enzymes and induction agents. He then pulled it all together with his summary and conclusions:

- Biofuels have made significant progress in the last decade.
- Corn-starch ethanol, the first large-scale biofuel, is insufficient to handle our energy needs.
- Cellulosic biomass appears to have advantages for the fuel ethanol market.
- The choice of crop will probably be specific to a given region.
- Technology advances in crop yields, enzymatic digestion and overall production are necessary for an economically feasible process.
- No alternate energy strategy will succeed without a healthy dose of conservation!

After acknowledgements, it became apparent that many in the audience not only understood what he was talking about but were hungry for more. There was over ten minutes of questions and a recognition that what is going on at WPI can and will make a difference in this world of bioengineering. The location outside of Boston and the reduced registration fee was intended to entice additional members to attend. Anyone who had the opportunity to see the facility, partake in the excellent cuisine and beverages (everything from cheese and crackers, fruit, vegetables and dip; to mini hamburgers, grilled sausages and open bar) and the excellent presentations on these interesting subjects will be back at the next ISPE Boston Area Chapter event. In the meantime, to view the actual PowerPoint presentations, please visit the ISPE Boston Area Chapter Website at www.ispe.org/boston.

Tech Talk:
An Introduction to the Stainless Steel Finishes of Mixers Used in Sanitary Processes

by David Wenzel

In order to meet the high standards of purity and cleanliness demanded by the pharmaceutical and biopharmaceutical

industries, it is necessary to use 316 stainless steel as the material of construction for mixing and blending equipment, not only for the wet end portion of the mixer, but also for portions of the drive end, which may include the motor, bearing frame or gear box.

It is also important that the surfaces of the mixers and blenders are smooth and clean, to minimize microbial contamination, reduce erosion corrosion and prevent the adherence of particulates to the surfaces of the equipment. The required surface characteristics may be obtained by electropolishing or by using a mechanical or chemical treatment.

A comprehensive inventory for sanitary standards and accepted manufacturing practices for the dairy, beverage and food processing industries has been established by 3-A Sanitary Standards Incorporated (3-A SSI) [1]. The 3-A symbol displayed on process equipment shows compliance with regard to the materials of construction, design and fabrication. New P-3A standards are being developed specifically for the pharmaceutical and biotechnology industries and expected to be issued within the next year [2].

In 2003, 3-A introduced the Third Party Verification (TPV) program to verify that process equipment meets established sanitary standards. The updated 3-A TPV number indicates that compliance has been independently verified by a certified conformance evaluator, resulting from a detailed inspection of all components on each machine at the manufacturer's facilities [3].

Within the 3-A manuals it is stated that the surfaces of process equipment - particularly those surfaces that contact the materials being processed - should be smooth, corrosion resistant, impervious, free of cracks and crevices, non-absorbent, non-toxic and cleanable. To meet these guidelines, stainless steel alloys have become the preferred materials of construction, being readily available and easily fabricated into complex structures. Furthermore the alloys provide superior corrosion resistance compared to mild steel or carbon steels, and the required surface properties can be obtained by a combination of mechanical or chemical polishing, electropolishing and passivation.

Many equipment manufacturers favor 316 stainless steel alloy for the construction of blenders and mixers, particularly for use in the pharmaceutical and biopharmaceutical industries. The 316 alloy contains molybdenum (2-3%), added to provide resistance to general corrosion that is superior to that of the 304 and 304L alloys more commonly used in the processing industries. The high purity requirements of the pharmaceutical and biopharmaceutical industries justify this position. The new standards that are being developed [2] will be directed to the equipment used in the production of Active Pharmaceutical Ingredients (APIs) and related materials and will overlap with ASME-BPE standards (directed to bioprocess equipment) and 3-A sanitary standards (directed to the food, beverage and dairy industries).

Why are smooth surfaces important?

Not only visually attractive, smooth surfaces can minimize the accumulation of products at the metal surfaces during mixing and other processing steps. Furthermore, the surfaces can be cleaned easily and effectively, since there are fewer sites available for the growth of microbial contaminants. It is also easier to visually confirm the cleanliness of a very smooth surface due to its optical properties. Perhaps more significantly, the rate of general corrosion of the metal depends upon the real surface area that is exposed to the corrosive environment. A smooth surface has a significantly lower, real area and therefore a lower rate of corrosion. In addition, the smooth surface reduces erosion corrosion, ie. the loss of metal from the surface due to the flow of the process fluids.

How are smooth surfaces obtained?

The surfaces of the stainless steel parts may be polished to a smooth finish by mechanical or chemical treatments or by electropolishing.

<u>Mechanical Surface Treatments</u>

Mechanical surface treatments of the stainless steel alloys include the use of abrasive compounds, grinding and buffing processes, sandblasting with silica, as well as shot, grit and wire blasting using stainless steel media. These methods are carried out carefully to avoid contamination of the polished surface with iron-containing materials. Furthermore, the parts that are polished mechanically are not as resistant to corrosion as those treated chemically or electropolished, due probably to the loss of chromium from the surface layer.

Several of the basic stainless steel mill plate finishes may be obtained by mechanical polishing. For example, the #4 polished finish (required to meet the basic 3-A standards for the processing industries) is obtained using a 120-150 mesh

abrasive and is a general purpose bright finish. The #7 and #8 finishes are highly reflective finishes that are obtained by polishing and buffing the surface with a series of fine abrasives.

Chemical Surface Treatment

Chemical surface treatment, also referred to as chemical polishing and steel pickling [4], is required to remove the scale formed at the surface of the steel during the hot rolling and annealing processes. Pickling is carried out by either the immersion of the part in a pickling bath or by coating the surface with a pickling paste. Presently, a solution of hydrochloric acid is the preferred pickling bath, providing faster reactions, greater flexibility, better quality control and lower costs. The pickling bath is typically heated to a temperature between 35 and 45¢ªC and the length of time of the treatment is dependent upon the thickness and composition of the scale.

Chemical treatment is also used to remove the debris (scale) from the surface of the steel, debris from grinding operations, abrasives and buffing compounds that can promote pitting and crevice corrosion. The presence of particles of iron on the alloy surface results in the formation of "rouge," a red-brown film of iron oxide. The presence of surface "rouge" is a concern when high purity is required and the part is usually chemically cleaned. The presence of impurities in or on the surface can also interfere with passivation of the steel substrate.

Electropolishing

Electropolishing [5] uses an electric current to uniformly dissolve the surface layers of the metal and has been termed "electroplating in reverse." Large and irregularly shaped parts are rapidly and efficiently polished electrolytically, though not necessarily at a lower cost than mechanical polishing.

In electropolishing, the substrate acts as the anode in the cell and is immersed in an electrically conductive solution, which is usually an aqueous solution containing mixtures of inorganic acids and organic additives. A counter electrode (the cathode in the cell) is also immersed in the electrolyte to complete the circuit and allow current to flow. The rate of dissolution of the metal is proportional to the applied current and the amount of metal electrochemically dissolved depends upon the composition of the electrolyte, time, temperature and the current density (the applied current divided by the surface area of the part).

Electropolishing is particularly suitable for components that have complex geometries, eg. the impellers in mixers, or components that are easily damaged. The configuration of the counter electrode can be critical, particularly when the part is an irregular shape, since it is necessary to provide the required current density across the whole surface being polished. Experience also teaches that the effects of gas evolution from the cathode can adversely affect the surface finish and it is necessary to use anions or solvent molecules that are difficult to discharge or to provide controlled agitation.

What is passivation?

Passivation refers to the formation of a film of chromium oxide, by the reaction of chromium atoms in the surface of the steel with atmospheric oxygen [6]. This film acts as a protective layer on the steel substrate and inhibits general corrosion reactions, enhancing the long-term performance of the equipment. The stainless steel alloys are often passivated to ensure that the process equipment meets the required standards for purity. The presence of impurities in or on the surface of the alloy can interfere with the formation of the passive, chromium oxide layer and therefore passivation is usually preceded by a chemical treatment or electropolishing.

How is surface smoothness measured?

Surface smoothness or, conversely, surface roughness has been described in various ways, eg. grit numbers, USA finish numbers, RMS, Ra (microinches) or Ra (microns). However, to allow specification of surface finishes for stainless steel equipment, a method has been adopted that conforms to the ANSI/ASME standard, B46.1. The surface roughness is measured with a profilometer, an instrument that uses a sensitive, diamond-tipped probe to trace the peaks and valleys as it moves across the surface. The roughness is then expressed as the arithmetic mean of the departure of the peak heights and valley depths from a centerline and the profile is recorded over several sampling lengths to obtain an average value. This average is termed the Ra value and is expressed in microinches [7]. The table below compares grit numbers, USA finish numbers and common names of surface finishes with the Ra number obtained using the profilometer.

Table 1. Terminology for Surface Finishes

Polish	Grit	Ra (Microinch)	Ra (Micron)
#3	#80	50	--
#4	#150	30-35	0.76-0.89
#4	#180	20-25	0.50-0.65
#6	#240	15-20	0.375-0.50
#7	#320	8-12	0.20-0.30
#8	#400	4-8*	0.10-0.20

* Ra (Microinch) values of 4-8 are typically obtained by electropolishing.

Which surface treatment is preferred by the process industries?

The high purity of pharmaceutical and biopharmaceutical processes and their sensitivity to traces of metal impurities requires the surfaces of the mixing and blending equipment to be very smooth ("mirror finish"). As stated earlier, electropolishing can be used effectively with large, irregularly shaped parts and the resulting surfaces are bright, very smooth, stress relieved and free of impurities. However, economics may dictate the use of abrasives and buffing compounds; if so, it is then essential to clean the surfaces of iron oxide and debris using a chemical treatment. Passivation may be selected as a final treatment to improve the long-term performance of the equipment.

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Industry News In Brief

by Patti Charek

Alkermes Plans Own Drug Lines

At nearly 20 years old, Alkermes Inc. is entering an era of "self discovery." It is moving away from a long-held strategy of making drug delivery tools and is now developing and commercializing its own products in-house.

Finally reaching profitability three years ago, it has been a long, hard road for Alkermes. The Cambridge-based company now wants to take a new path, one coupled with the uncertainty of rearing potential new therapies. Alkermes has put together a proprietary pipeline and has bold plans to put eight drugs into human trials by March 2009. Seven of its drugs are based on known compounds, but one, called ALK33, is an entirely new chemical entity.

What is making this transformation possible, is the company's healthy bottom line. In fiscal 2008, it netted $166 million on revenue of $240 million, up from a profit of $9.5 million on $239 million in revenue the year earlier. All that extra cash could have been invested back into its partnering and manufacturing efforts, but Alkermes decided to use the profits to back its new drug development model. It was just sound financial logic, according to James Frates, chief financial officer for Alkermes. "The drug delivery model only gets you so far. So once you've developed those delivery technologies, you can start to use those for your own. You can control your own fate much longer, and that just gives you greater growth opportunities," he said.

Alkermes CEO David Broecker explained that the company wanted a development element to its business, but the much-publicized collapse of its inhaled-insulin device deal with Eli Lilly forced Alkermes to lay off 150 employees and close its 4-year-old manufacturing plant in Chelsea. It cost the firm about $30 million in restructuring charges and ultimately caused company management to rethink its future. "Clearly the loss of the (Eli) Lilly program was disappointing to all of us ... and now we had this sense of urgency to really go after these proprietary products. That is when we put the stake in the ground," said Broecker.

Armed with its new strategic focus, the company went on a mission to "win the hearts and minds" of its 600-plus employees, according to Broecker. Scott Chizzo, CEO of the Waltham-based Maxiom Consulting Group Inc., said, "The concept is to take it from being a contract manufacturer of sorts, to a fully integrated pharmaceutical company. It is actually a very challenging strategy ... it involves a real change in mind-set," said Chizzo, whose company lists Alkermes as a client. Chizzo said the company's achievement in bringing the drug Vivitrol to market gave it the confidence to pursue becoming a full-fledged R&D biotech. (Source: Stephen DeSantis, Mass High Tech, 10 October, 2008)

J&J Study Finds Generic Less Effective in Treating Crohn's

Johnson & Johnson's Remicade fought the bowel disorder Crohn's disease better than the generic medicine prescribed by doctors, a result that may help J&J win thousands more patients for its second-best-selling drug. Remicade eased symptoms in 44 percent of patients when used on its own, and in 57 percent when combined with azathioprine, the generic that doctors typically turn to when initial treatments fail. Both of those regimens beat the 31 percent remission rate for azathioprine alone. The study also found Remicade to be about as safe as the generic.

About half of the 500,000 Crohn's patients in the US take azathioprine, said study author William Sandborn, a gastroenterologist at the Mayo Clinic in Rochester, Minn. J&J sponsored the study to see how many of those might do just as well starting off on Remicade, a switch that may earn the company as much as $22,000 per patient. Remicade, an anti-inflammatory also used against rheumatoid arthritis, generated $3.3 billion for the company last year. A boost among Crohn's patients could help J&J offset losses it is suffering as other top sellers, such as the schizophrenia pill, Risperdal, cede ground to cheaper generic copies.

Crohn's is a chronic disease that can cause abdominal pain, diarrhea, rectal bleeding, weight loss, and fever. There is no known cause, nor a cure. "Eighty percent of patients need surgery to repair bowel damage after 15 years, a sign of the inadequacy of treatment," Sandborn said.

The disease is typically treated first with steroids or aminosalicylates. If those don't work, doctors usually move to azathioprine and, if that fails, to Remicade. While the generic drug costs about $2,000 annually, as much as 11 times less than a year of Remicade, "what this data says is it's less expensive but it's also less effective," Sandborn said. (Source: Bloomberg News, The Boston Globe, 7 October 2008)

RXi Licenses UMass Technology

Worcester-based RXi Pharmaceuticals Corp. has licensed exclusive worldwide rights to University of Massachusetts Medical School technology for the oral delivery of RNAi-based drugs. The technology was developed by Dr. Michael Czech and Dr. Gary Ostroff, professors of molecular medicine at UMass. Czech is chairman of the school's molecular medicine department and an RXi co-founder. Ostroff is an RXi "collaborator." The company said oral delivery of RNAi-based drugs "could open up significant market opportunities for RXi." RNAi, which was pioneered by RXi founder, UMass professor and Nobel Prize winner Craig Mello, intends to treat diseases by interfering with the genes suspected of causing those diseases. (Source: Matthew L. Brown, Worcester Business Journal, 14 October, 2008)

Lilly to Acquire ImClone for $6 Billion

Eli Lilly & Co.'s winning bid of more than $6 billion for cancer drug maker ImClone Systems means a billion-dollar payday for former rival bidder Bristol-Myers and vindication for corporate raider and ImClone chairman Carl Icahn. Lilly said it would pay $70 per share for New York-based ImClone. The acquisition, Lilly's largest ever, helps the Indianapolis drug maker prepare for looming patent expirations and builds "a true oncology powerhouse," Lilly chief executive John Lechleiter said. Lilly will lose patent protection for its two top-selling drugs, the antipsychotic Zyprexa and the antidepressant Cymbalta, in 2011 and 2013, respectively. The deal also brings to an end one of the more dramatic buyout sagas in recent history.

Lilly's bid topped two previous offers from Bristol-Myers, which partnered with ImClone to develop and market the blockbuster drug Erbitux. In July, Bristol-Myers offered $60 per share for the 83 percent of ImClone it doesn't already own and later raised that bid to $62 per share. But Bristol-Myers said it would stop the bidding there. CEO James Cornelius, a former Lilly executive and board member, said his company was pleased to have started a process that led to a "substantial increase" in ImClone's value. Bristol-Myers stands to pocket about $1 billion for its 14 million ImClone shares, while still sharing in the revenue from Erbitux. The drug maker gets 61percent of the North American revenue from Erbitux and splits sales three ways with ImClone and Merck & Co. in Japan. (Source: The Boston Globe, 7 October, 2008)

Pfizer Alters Focus in Rush for New Drugs

Pfizer Inc. will abandon early stage research on heart drugs as part of a strategy to sharpen its focus on ailments such as cancer, Alzheimer's disease, and diabetes where the chances of a bigger profit are greatest. The company is in a rush to find new medicines for when the cholesterol pill Lipitor loses patent protection in 2011. Lipitor had $12.7 billion in sales last year, one-quarter of Pfizer's revenue.

As part of its shift, the company will sell or share rights to at least 11 medicines in early testing for diseases the company no longer believes profitable enough, said Martin Mackay, the head of research and development. That includes treatments for heart failure, high cholesterol, and obesity. Besides Alzheimer's, cancer, and diabetes, the company will pursue remedies for inflammatory diseases, pain, and schizophrenia. "These are the disease areas with a higher medical need where the science is really breaking," Mackay said. Pfizer's research budget of about $7.2 billion is unlikely to change next year, he said. The intensified focus won't affect drugs in the last of three stages of testing needed for US approval.

By ending heart disease research, Pfizer abandons an area of medicine that propelled its rise. Pfizer acquired Lipitor from Warner Lambert Co. in 2000, when the drug had less than $1 billion in annual sales, and transformed it into the best-selling pill in history. Lipitor sales have slumped since 2006, when generic copies of a similar drug, Merck & Co.'s Zocor, were introduced. The restructuring won't result in laboratories closing and will shift many research employees to other areas, the company said. (Source: Bloomberg News, 1 October, 2008)

Amgen's Osteoporosis Pill Shown to Reduce Spinal Fractures

Amgen's experimental bone drug reduced the risk of spinal fractures in women with osteoporosis by 68 percent in a pivotal clinical trial, a robust result that raises the probability the drug can help restore the luster of the embattled biotech company. The drug, called denosumab, also reduced the risk of hip fractures by 40 percent compared with a placebo and the risk of other fractures by 20 percent.

Amgen needs denosumab, the first potentially major drug from its research lab in years, to be a big success. Sales of its flagship anemia drugs have been battered by safety concerns. Amgen's stock, which was trading at $75 in early 2007, had fallen below $40 by March of this year. But the stock has since rebounded to more than $60 on the prospects for denosumab.

Amgen had announced in late July that denosumab had succeeded in the clinical trial, which involved 7,800 postmenopausal women with osteoporosis. But the company did not say at that time how much the drug had reduced the risk of fractures, which could help determine whether denosumab will be a blockbuster or just another competitor in a crowded global market for bone-density drugs that is valued at about $8 billion.

The 68 percent reduction in vertebral fractures compares favorably with the 40-50 percent reductions achieved in clinical trials involving other pills now mainly used to treat osteoporosis. However, one drug, Reclast from Novartis, has achieved a 70 percent reduction in spinal fractures compared with a placebo. The hip fracture reduction of 40 percent achieved by denosumab was generally in line with the reduction achieved by other drugs. Scientists cautioned that the best way to compare drugs is head-to-head in a clinical trial. Comparing across trials can be misleading because patients' characteristics can differ.

Amgen has said it planned to apply for federal approval of denosumab, which could reach the market next year. Analysts have been estimating sales of anywhere from $1 billion to several billion dollars just to treat osteoporosis. Amgen, which had revenue last year of $14.8 billion, is also testing denosumab as a treatment for bone complications arising from cancer or the treatment of cancer. The main drugs now used for osteoporosis are a class known as bisphosphonates, which include Fosamax from Merck and its generic equivalents; Boniva from Roche and GlaxoSmithKline; Actonel from Procter & Gamble and Sanofi-Aventis; and Reclast. The use of denosumab is likely to cost more than $1,000 a year.

About 10 million people in the US, mainly postmenopausal women, suffer from osteoporosis and more than 30 million others have low bone mass that puts them at risk of the disease. (Source: Andrew Pollack, New York Times News Service, 17 September, 2008)

In Largest Gift, Harvard Gets $125 Million for Biological Institute

Harvard University said it received the largest individual gift in its history, a $125 million donation from entrepreneur Hansjörg Wyss, an alum of Harvard Business School who is ranked on Forbes's list of billionaires. The money will underwrite a new biological engineering institute where scientists will research everything from new materials inspired by the natural world to restoration of diseased tissue.

"It's really wonderful," said Provost Steven E. Hyman of the gift, which creates the Hansjörg Wyss Institute for Biologically Inspired Engineering, to be located in the new science complex being built in Allston. "This is both an exciting cornerstone area for our new expanded efforts in biological engineering . . . [and] a way of tying together the Cambridge side of the river with the Boston side of the river - the medical school, but also our affiliated hospitals."

The institute's goal will be to bring together people from across disciplines, from computer science to surgery to physics. It reflects a continuing push away from Harvard's past philosophy of "each tub on its own bottom," the phrase used to

describe the fragmented relationship between Harvard's schools. The new thinking reflects the collaborative effort the Harvard Stem Cell Institute initiated in 2004, which brought together clinicians from affiliated hospitals, basic science researchers, and others to raise $70 million to date. Also, earlier this year, Harvard Medical School received $118 million in federal funding over five years to create a collaborative center to turn research into medicine more quickly.

The new institute also reflects a rise in status for engineering, which has gone from a division within Harvard to a school of engineering and applied sciences. "This gift underscores Harvard's ability to lead and to make very significant contributions in a field that is of increasing importance to scientists in a number of areas, and to science more generally," Drew Faust, president of Harvard, said in a statement.

The donation will fund seven faculty positions and provide operating funds for the institute. Donald Ingber, professor of bioengineering at the Harvard School of Engineering and Applied Sciences, will direct the institute, which will build on the "seed institute" that already existed, the Harvard Institute for Biologically Inspired Engineering. The institute will focus on several areas, including the emerging discipline of synthetic biology, which seeks to make working with cells and genes more like building circuits. It will also include a "living materials program" that will develop materials and devices that mimic the engineering principles of the natural world. It will also include the field of biological control, which looks at how living systems are organized and tries to develop ways to control them. (Source: Carolyn Y. Johnson, The Boston Globe, 8 October, 2008)

Broad Lands $86 Million in NIH Funds for Gene Research Tools

The Broad Institute of MIT and Harvard has been awarded a six-year, $86 million grant from the National Institutes of Health (NIH) to develop tools intended to dramatically aid researchers in taking genetic discoveries to treatments. The Institute, one of nine research centers in the program, is developing what are called chemical "probes," small molecules that can be used to discover targets, helping to bridge the gap between modern biological knowledge and human health.

The NIH selected Broad to be a major component of the Comprehensive Screening Centers in the Molecular Libraries Probe Production Centers Network (MLPCN). The centers will share in the work of building libraries of small-molecule probes that will be screened using high-throughput methods to identify compounds that could be potential drug targets. The institute will be using a portion of the grant to hire more researchers and purchase more equipment. Stuart Schreiber, director of the chemical biology program at Broad, stated that now is the right time for this kind of program because the sheer volume of data that researchers can now obtain from these types of high throughput experiments has increased exponentially while costs have dropped.

Broad will make its data from the program openly available to the scientific community, both academia and the biopharmaceutical industry alike. "I would be elated if industry were to utilize these tools. These kinds of probes can lead to drug targets, and will act to financially de-risk the specific projects for pharma companies," Schreiber said. The project at the Broad will place particular emphasis on the areas of diabetes, cancer stem cells, infectious disease and psychiatric conditions. (Source: Stephen DeSantis, Mass High Tech, 5 September, 2008)

Genzyme Marks MetroWest Growth

In September Genzyme officially opened its $125 million, 180,000-square-foot, 350-employee Framingham Science Center. Genzyme's 14-building, 1 million-square-foot Framingham campus now employs about 2,000 people, the biotech company's largest concentration of employees worldwide. The company has had a presence in Framingham for nearly 20 years.

Researchers at the new science center will focus on genetic diseases, cancer, immune diseases, kidney diseases, cardiovascular diseases, endocrinology and neurological disorders. "It's just a building, a tool," said Richard Gregory, Genzyme's senior vice president and its head of research, adding that it is the people inside the building, with a commitment to patients, which makes the company successful.

The center is part of an expansion of Genzyme's research, development and manufacturing operations around the world. In addition to the science center, a $250 million cell culture manufacturing facility is also under construction in Framingham. At some point in the future, a matching building to the new science center will be also added to the campus.

A $150 million expansion of the company's cell culture manufacturing facility in Allston began last year. The company is also building in France, Germany and China. The new science center is also Gold (LEED) certified for "green features" like high-efficiency lighting, heating and cooling systems. (Source: Eileen Kennedy, Worcester Business Journal, 29 September, 2008)

Gene-Targeted Drug Could Help Heart Patients

A drug touted as the first gene-targeted heart therapy reduced hospitalizations and deaths when given to heart failure patients with a specific genetic profile, researchers said. The drug, bucindolol, was dropped by its maker nearly a decade ago after it failed to top a placebo in a 2,700-patient study. But a new study of roughly 1,000 patients shows that it works more effectively than the standard drugs in its class in patients with "favorable" genetic features. Scientists have also developed a genetic test that predicts which patients will benefit most from the drug.

The patients are enrolled in a gene-targeting arm of a test of heart failure drugs called beta blockers, which reduce the heart's workload. The study, called the Beta-Blocker Evaluation of Survival Trial, or BEST, showed that researchers could predict how well the drug will work based on the presence of two mutations in genes that regulate the heart's activity. In patients with the most favorable genetic profile, bucindolol reduced: heart disease deaths by 48 percent; deaths from all causes by 38 percent; deaths and transplants by 43 percent; and hospitalizations for heart failure by 44 percent.

"These are the best results that have ever been achieved," says Michael Bristow, chairman of ARCA Biopharma, the company that resurrected the drug and is attempting to bring it to market. "These are very impressive results. They certainly could herald a new era in cardiovascular care," says Sidney Smith of the University of North Carolina at Chapel Hill and one of a handful of experts that set national heart-treatment guidelines. "This is what we've been hoping for - a way to predict which patients would respond to specific therapies," he says.

Based on the results of the new trial, Bristow says the FDA has agreed to review the company's application for government approval, along with a separate application for a genetic test. The agency's decision on the applications could come as early as May 1, 2009, he says. (Source: Steve Sternberg, USA Today, 22 September, 2008)

Sanofi-Aventis Acquires Zentiva for $2.6 Billion

French pharmaceuticals company, Sanofi-Aventis has won the approval of the board of Czech generic drug maker Zentiva for its takeover offer after raising its bid to about $2.6 billion. Jiri Michal will remain as CEO of Zentiva which makes and sells generic drugs in Central and Eastern Europe, including products for pain, cardiovascular diseases and disorders of the central nervous system. As part of its growth strategy, Sanofi-Aventis is expanding its presence into emerging markets that are characterized by high growth, low and medium disposable income, and affordable pharmaceutical products.

Sanofi-Aventis Europe and Zentiva have agreed that for the foreseeable future Zentiva will conduct its business under the brand names of Zentiva, whether alone or in association with Sanofi-Aventis brand names, and that its Prague headquarters will continue to be the center of expertise for Zentiva's development, manufacturing, supply chain and marketing activities in affordable medicines in the CEE regions.

The acquisition is the most recent case of consolidation in the generic drug industry. In other examples, Teva Pharmaceuticals is buying Barr Pharmaceuticals, and Daichi Sankyo has acquired Ranbaxy Laboratories. (Source: Sanofi-Aventis**,** 24 September 2008)

Biogen Idec MS Pill Found to Slow Damage

Biogen Idec Inc.'s experimental pill to treat multiple sclerosis prevented brain lesions associated with the disease from getting worse, a study found. The pill, called BG-12, reduced the conversion of new spots of inflammation into permanent damage in a trial of 56 patients.

In MS, neurons are stripped of an insulating coating known as myelin by the immune system, causing the cells to

malfunction. That leads to MS symptoms such as muscle weakness and loss of coordination, according to the Mayo Clinic. Biogen has received approval from US regulators to speed the review process for its pill. If cleared for sale in the US, BG-12 could be the first oral medication for MS patients to reach the market.

"There are two elements: You want to keep the lesions from forming in the first place and then, even if a lesion developed, you want to know the damage is reduced, and that's what you're seeing," said Mike Panzara, the chief medical officer for Biogen Idec. "Even if a lesion does develop on BG-12, injury is less because it's less often the lesions become permanent."

About 29 percent of the lesions in the brains of patients on BG-12 turned into signs of permanent damage, compared with 44 percent of those in the placebo group, the study showed. The company began final-stage testing on BG-12 in January. The trials, on more than 2,000 patients with a recurring form of the disease, will last two years. The drug is being compared with a placebo and with Teva Pharmaceutical Industries' Copaxone, an approved treatment for the disease.

Biogen Idec sells the MS drugs Avonex, which is given as a once-a-week injection, and Tysabri, an infusion given once a month in a doctor's office or hospital clinic. About 1 million people worldwide suffer from MS. (Source: Bloomberg News, The Boston Globe, 19 September, 2008)

Biogen Idec Ends Work on Rheumatoid Arthritis Drug

Biogen Idec has announced it will halt work on a drug for rheumatoid arthritis because it failed in studies. Baminercept missed its primary and secondary goals in a clinical trial with patients who did not respond to drugs known as disease modifiers, Biogen said. The company also based its decision on preliminary results from a study of patents who didn't respond to drugs called tumor necrosis factor inhibitors. (Source: Bloomberg News, The Boston Globe, 10 October, 2008)

Indevus Shares Double on Drug Agreement With Teva

Indevus Pharmaceuticals Inc. more than doubled in trading after it said Teva Pharmaceutical Industries Ltd. would pay as much as $142.5 million for rights to a drug for the treatment of stuttering. Pagoclone has already been shown in midlevel trials to work against stuttering. Indevus may receive as much as $92.5 million from Teva for testing and milestone payments and up to $50 million more in royalties. Teva will pay Indevus to complete the second round of trials needed before FDA approval, according to a statement. (Source: Bloomberg News, The Boston Globe, 27 September, 2008)

Novartis To Beef Up Vaccine Research in Cambridge

Novartis is doubling down on vaccine research. The Basel, Switzerland-based drug giant announced that it is opening a new facility and hiring an additional 150 people by the end of 2009 for a Research Center of Excellence in Virology in Cambridge. That will boost the company's employment in Cambridge to more than 1,800 workers.

Researchers in the new center will study vaccines for widespread viruses, including HIV, flu, cytomegalovirus, and respiratory syntical virus. The vaccine business, shunned as a backwater for cheap commodities as recently as five years ago, is suddenly booming - and Novartis clearly aims to capitalize on this growing field through its new center.

Vaccines generated an estimated $16 billion in sales in 2007. Premium-priced vaccines are back in. Merck's Gardasil, for a virus that causes cervical cancer, generated $1.5 billion in sales in 2007, its first full year on the market. That's enough to support quite a few research jobs. (Source: Luke Timmerman, Xconomy | Boston, 12 September, 2008)

Stem Cell Registry Set for Umass Medical School

Massachusetts has launched the International Stem Cell Registry, intended to be an online resource center for information on human embryonic stem cells for biomedical researchers and the public. The center is based at the University of Massachusetts Medical School in Shrewsbury, alongside the Massachusetts Stem Cell Bank. The stem cell

registry was partially funded by a $570,000 grant from the Massachusetts Life Sciences Center, a quasi-public organization established by the state. (Source: Todd Wallack, The Boston Globe, 12 September, 2008)

Boston Scientific Says Stents Cleared by FDA

Boston Scientific Corp., the leading seller of heart stents, says US regulators have agreed to lift the remaining restrictions preventing the company from issuing new versions of the artery-clearing devices. The FDA told the company it planned to remove the penalties imposed in January 2006 when the device maker was cited for manufacturing violations, said James Tobin, Boston Scientific's chief executive, in a conference call with analysts.

The move should lead to approvals for two new stents to open blockages in the carotid artery and kidney, and a balloon catheter for unclogging blood vessels. It also removes a potential hurdle for future products the Natick company aims to introduce in the $4 billion market for heart stents and other devices. (Source: Bloomberg News, The Boston Globe, 23 October, 2008)

Boston Scientific Stent Wins FDA Approval

Boston Scientific Corp. said the FDA approved the medical device maker's new Taxus drug-coated stent. The approval comes as Boston Scientific and its stent competitors try to recover from a yearlong downturn in sales for the devices, which are used to prop open clogged arteries. The drug-coatings are used to prevent the growth of scar tissue. The Taxus Express2 stent is the only stent on the market approved for use in vessels as small as 2.25 millimeters, the company said.

In 2006, studies began to show that patients with the drug-coated stents were more likely to develop potentially fatal blood clots months and even years after they were implanted. Doctors have since become more cautious about using them instead of bare-metal stents and companies have in turn released studies trying to shore up the safety profile of drug-coated stents.

Boston Scientific said Taxus is so far the world's most frequently implanted stent, with 4.6 million used and the drug already has an extensive record clinical trial and long-term follow-up record. The company plans to launch the new stent immediately. The stent is also approved to treat the recurrence of a narrowing artery in patients who have a bare-metal stent.

Taxus stents compete heavily with Johnson & Johnson's Cypher stent. Other competitors include Abbott Laboratories Inc.'s Xience V and Medtronic Inc.'s Endeavor drug-coated stents. (Source: Manufacturing.net, 25 September, 2008)

Waltham's ImmunoGen Grants License to Bayer Healthcare

Biotechnology company ImmunoGen Inc. said Bayer HealthCare has licensed a tumor-fighting technology developed by ImmunoGen for $4 million upfront. Bayer licensed the Tumor-Activated Prodrug technology, and will use it to develop cancer drugs. Along with the initial payment, Bayer will make development milestone payments to Waltham-based ImmunoGen if drug candidates made with TAP progress through clinical testing. Those payments could reach $170.5 million per drug, and if the products reach the market, ImmunoGen would also receive royalties on sales. (Source: The Boston Globe, 22 October, 2008)

Major Drug Makers' Sales Suffer in the Third Quarter

Drug makers Merck & Co., Wyeth, and GlaxoSmithKline PLC all posted lower profits for the third quarter, partly due to the intensifying generic competition weighing on the entire pharmaceutical industry. And in what it characterized as an advance strike to counteract that and other problems, Merck said it will slash about 7,200 jobs, or nearly 13 percent of its workforce, in its second major restructuring in less than three years.

Merck, which currently has 250 employees at its research center in Boston's Longwood Medical Area, plans to expand its

Massachusetts operations as part of the restructuring. Spokesman Ian McConnell said the company is shifting its molecular profiling group from Seattle to Boston by 2009. Merck is also shifting its basic research for the oncology and Bone Respiratory Immunology and Endocrine groups to Boston by year's end. McConnell said the company, which already has partnerships with many Bay State institutions, such as Harvard University and Vertex Pharmaceuticals Inc., also hopes to forge more partnerships with outside groups.

The restructuring is "not a reaction to our performance in 2008 or the economy," chief executive Richard Clark said. "I think it's a competitive advantage" to make the company leaner and more flexible. Clark said 60 percent of the job cuts will come overseas, and they'll affect workers in sales and marketing, manufacturing, administration, and even basic research. Three research centers will be closed - Seattle, Japan, and Italy - and the company is evaluating which factories will be closed in a few years.

Sales were hurt by the continuing decline of Merck's cholesterol drugs Vytorin and Zetia, lower sales for nearly all its vaccines, partly related to manufacturing problems, and generic competition for former blockbuster osteoporosis drug Fosamax, which saw sales cut in half this quarter to $354 million.

Wyeth reported a slight drop in its third-quarter profit as it continues with a restructuring program meant to brace for generic competition. Earlier this year, blockbuster heartburn drug Protonix lost patent protection and top-selling antidepressant Effexor will soon face generic competitors as well. So like other drug makers, Wyeth has been focusing on international expansion and diversifying to increase revenue and has already begun a cost-cutting program that could slash up to 10 percent of its 50,000 employees by 2011. (Source: Associated Press, The Boston Globe, 23 October, 2008).

Regulatory & Legislative Highlights

by Deepen Joshi

FDA Approves DNA Test to Measure Hepatitis B Virus Levels

The FDA approved the first nucleic acid test for hepatitis B virus (HBV) that measures the amount of viral DNA (viral load) in a patient's blood. Assessing a patient's viral load provides health care professionals with a highly sensitive method for gauging the progress of antiviral therapy in patients with chronic HBV infections.

The COBAS TaqMan HBV Test, manufactured by Roche Diagnostic Division, Basel, Switzerland, extracts and then amplifies sections of viral DNA from human plasma or serum. The viral DNA sections are measured to establish a baseline level before beginning treatment, and then used again during treatment to assess an individual's response to therapy.

HBV is spread through sexual exposure, use of infected needles, and transmitted from infected mother to child during birth. Symptoms occur in about 70 percent of patients, and include abdominal pain, jaundice, fatigue, loss of appetite, nausea, and vomiting. (Source: FDA Website, 4 September, 2008)

FDA Creates Single Web Page with Drug Safety Information

Consumers and health care professionals can now go to a single page on the FDA's Web site to find a wide variety of safety information about prescription drugs. The Web page, http://www.fda.gov/cder/drugSafety.htm, provides links to information in these categories:

- Drug labeling, including patient labeling, professional labeling, and patient package inserts;
- Drugs that have a Risk Evaluation and Mitigation Strategy (REMS) to ensure that their benefits outweigh their risks;
- Clinicaltrials.gov, a searchable database of clinical trials, including information about each trial's purpose, who may participate, locations, and useful phone numbers;

- Drug-specific safety information, including safety sheets with the latest information about the drug as well as related FDA press announcements, fact sheets, and drug safety podcasts;
- Warning Letters, Import Alerts, Recalls, Market Withdrawals, and Safety Alerts;
- Regulations and guidance documents;
- Consumer information about using medications safely and disposing of unused medicines;
- Instructions how to report problems to the FDA through its MedWatch program;
- Consumer articles on drug safety; and
- The FDA's response to the Institute of Medicine's 2006 report on the future of drug safety.

Establishing such a Web page is one of the requirements of the Food and Drug Administration Amendments Act of 2007, and is among FDA's many efforts to address the safe use of drugs throughout their lifecycle. (Source: FDA Website, 15 October, 2008)

FDA Web Site to Post Quarterly Report of Potential Safety Issues

The FDA announced that it has posted on its Web site its first quarterly report listing certain drugs that are being evaluated for potential safety issues. The drugs have been identified based on a review of reports in FDA's Adverse Event Reporting System (AERS). This information is being provided under provisions of the Food and Drug Administration Amendments Act, signed into law Sept. 27, 2007.

The appearance of a drug on this list does not mean that FDA has concluded that the drug has the listed risk, or that FDA has identified a causal relationship between the drug and the listed risk. It is on the list only because FDA has identified a potential safety issue. Drugs that appear on the new AERS-based table, titled "Potential Signals of Serious Risks/New Safety Information," are identified by FDA reviewers based on reports from the FDA's AERS database, which contains millions of reports of adverse events submitted to FDA by drug manufacturers, health care professionals and patients.

A new quarterly report listing additional drugs for which new safety information or potential signals of serious risks have been identified through AERS will be posted to the FDA's Web site every three months. (Source: FDA Website, 5 September, 2008)

FDA Issues Warning Letters to India's Ranbaxy Laboratories

The FDA issued two Warning Letters to Ranbaxy Laboratories Ltd., of the Republic of India, and an Import Alert for generic drugs produced by Ranbaxy's Dewas and Paonta Sahib plants in India. The Warning Letters identify the agency's concerns about deviations from US current Good Manufacturing Practice (cGMP) requirements at Ranbaxy's manufacturing facilities in Dewas and Paonta Sahib (including the Batamandi unit) in India. One Warning Letter addressed problems at Ranbaxy's Dewas facility found during an inspection conducted by FDA in early 2008. The second Warning Letter addressed the Paonta Sahib facility following an inspection at its Batamandi unit, also in early 2008.

Because of the extent and nature of the violations, FDA issued an Import Alert, under which US officials may detain at the US border any active pharmaceutical ingredients (API) and both sterile and non-sterile finished drug products manufactured at these Ranbaxy facilities and offered for import into the United States.

The FDA will continue to work with Ranbaxy's Dewas and Paonta Sahib plants to resolve these issues. (Source: FDA Website, 16 September, 2008)

FDA Analysis Shows Statins Do Not Increase Risk of Lou Gehrig's Disease

FDA's analysis provides new evidence that the use of statins does not increase incidence of amyotrophic lateral sclerosis

(ALS), a neurodegenerative disease often referred to as "Lou Gehrig's Disease."

Statins -- HMG-CoA-reductase inhibitors -- are the most commonly-prescribed medications to treat elevated cholesterol levels in the United States. ALS is a fatal neurodegenerative condition with an overall annual incidence of 1 to 2 per 100,000 people in the general population. The incidence of ALS increases with age.

Statins have also been shown to reduce the risk of heart disease in a wide variety of patients. Based on currently available information, health care professionals should not change their prescribing practices for statins and patients should not change their use of statins. FDA is examining the feasibility of conducting additional epidemiologic studies to examine the incidence and clinical course of ALS in patients taking statins. (Source: FDA Website, 29 September, 2008)

FDA Awards $2.5 Billion to Modernize Information Technology over Ten Years

The FDA announced the selection of ten contractors to receive up to a total of $2.5 billion for information technology (IT) and data center management services over the next ten years. The contract is the cornerstone of the FDA's Information Technology for the 21st Century (ICT21) bioinformatics initiative, an extensive IT modernization program encompassing data management, data warehousing, IT infrastructure and IT security.

The ten contractors will compete for data information technology task orders through this contract. The FDA has awarded three task orders under the ICT 21 contract for the design and migration of all systems applications to two new data centers, which will be the cornerstone of the FDA IT infrastructure and bioinformatics modernization for the next decade. All FDA software applications and hosting operations will transition to the new data centers over a two-year period. The resulting enhanced computing power and greater responsiveness will provide the FDA with the tools it needs to ensure that all products reaching the American public are safer and more effective. (Source: FDA Website, 30 September, 2008)

FDA and PATH Malaria Vaccine Initiative Announce Research Collaboration

The FDA has announced a collaboration with the PATH Malaria Vaccine Initiative (PATH-MVI) to develop laboratory tests to better predict the level of safety and effectiveness of experimental malaria vaccines before they are used in human clinical trials.

"This collaboration with the PATH-MVI supports the overall mission of the FDA and specifically the Agency's work under our Critical Path Initiative," said Jesse L. Goodman, M.D., M.P.H., director of the FDA's Center for Biologics Evaluation and Research. "We are actively seeking ways to help organizations such as PATH develop safe and effective products that can benefit the public health both in the United States and globally."

PATH is an international, nonprofit organization that creates sustainable, culturally relevant solutions to improve global health and well-being. PATH-MVI supports the development of malaria vaccines and is expected to spearhead the efforts to ensure their availability and accessibility in the developing world once a safe and effective vaccine becomes available.

The PATH-MVI collaborative project is expected to span about three years and is being conducted under the Cooperative Research and Development Agreement (CRADA) program, which allows federal laboratories and businesses to form partnerships that help expedite research activities. Recent scientific advances suggest that vaccines based on live, weakened (attenuated) malaria parasites may be possible in the future but assessing safety and effectiveness in the early stages of product development is challenging. Under this CRADA, PATH-MVI provides the FDA with about $1.5 million to develop tests for evaluating malaria vaccines early in their development.

To date, there are no approved vaccines to prevent malaria but several vaccines are in development. This CRADA will help develop laboratory tests to assess whether a vaccine candidate is safe enough to begin Phase I clinical trials.

Each year 350-500 million cases of malaria occur worldwide, killing an estimated one million people, most of them young children in sub-Saharan Africa. Travel between the United States and the affected areas, as well as men and women in

the US military who are stationed in regions at high risk for malaria, can bring the disease into the United States.

The Center's Global Vaccine Initiative fosters the development, evaluation and availability of vaccines needed to protect against major global infectious diseases and is part of the Center's commitment to work with others, including the World Health Organization, in advancing global public health. The Critical Path Initiative is the FDA's effort to stimulate and facilitate a national effort to modernize the sciences through which FDA-regulated products are developed, evaluated and manufactured. (FDA Website, 7 October, 2008)

FDA Approves Use of Temporary Pump to Assist Heart's Right Side

The FDA approved a Humanitarian Device Exemption (HDE) for the first heart pump that provides certain critically ill patients with temporary support for the right side of their heart. Heart assist devices are mechanical pumps that aid in the pumping action of a weakened heart. Most heart assist devices support the heart's left ventricle, which pumps oxygen-rich blood to the rest of the body. The CentriMag Right Ventricular Assist System, manufactured by Levitronix LLC of Waltham, MA, is intended for patients requiring support for the heart's right ventricle, which passes oxygen-depleted blood to the lungs to be refreshed with oxygen.

HDEs facilitate the development of medical devices intended to treat or diagnose a disease or condition affecting fewer than 4,000 people in the United States every year. To receive approval of an HDE application, a company must demonstrate the product's safety and probable benefit. The CentriMag system is for critically ill patients with a failing right ventricle when other therapies have failed. It is intended to be used for up to 14 days to keep the patients alive until their heart recovers or until a heart transplant or long-term heart assist device can be implanted. (Source: FDA Website, 7 October, 2008)

FDA Approves Updated Labeling for Genentech's Psoriasis Drug Raptiva

The FDA announced labeling changes, including a Boxed Warning, to highlight the risks of life-threatening infections, including progressive multifocal leukoencephalopathy (PML), with the use of Raptiva (efalizumab). Raptiva, approved in 2003, is manufactured by Genentech. The labeling changes are based on the FDA's post-market surveillance.

The FDA is also requiring the submission of a Risk Evaluation and Mitigation Strategy (REMS), which will include a Medication Guide for patients and a timetable for assessment of the REMS.

Raptiva is a once-weekly injection approved for adults with moderate to severe plaque psoriasis who are candidates for systemic (whole body) therapy or phototherapy to control their psoriasis. The now-required Boxed Warning will highlight the risk of bacterial sepsis, viral meningitis, invasive fungal disease, progressive multifocal leukoencephalopathy and other opportunistic infections. (Source: FDA Website, 16 October, 2008)

HHS Preparing to Open FDA Offices in China, India, Europe and Latin America

The Department of Health and Human Services will send the first FDA staff to China, India, Europe, and Latin America before the end of 2008. The first overseas office will be in China. The U.S. government recently secured formal approval for the office from the People's Republic of China. The first staff will be in place in Beijing this year, with additional staff to be posted in 2009. Staff is also scheduled to be posted in Shanghai and Guangzhou next year.

HHS/FDA plans on establishing its second overseas office in the Republic of India, with staff first posting to New Delhi in 2008 and at least one additional office to follow in 2009. Plans at present are for 10 US nationals to be posted in India. HHS/FDA will also be opening overseas offices in Europe and Latin America before the end of 2008, with a fifth office in the Middle East to follow soon in early to mid-2009.

Last year, the United States imported more than $2 trillion worth of products, from roughly 825,000 importers, through

over 300 ports of entry. All projections indicate this volume will continue to rise sharply over the coming years as the scale and complexity of international trade multiplies. (Source: FDA Website, 16 October, 2008)

FDA Issues Warning Letters to Bayer HealthCare

The FDA sent Warning Letters to Bayer HealthCare concerning two unlawful, over-the-counter (OTC) aspirin products: Bayer Women's Low Dose Aspirin + Calcium (Bayer Women's) and Bayer Aspirin with Heart Advantage (Bayer Heart Advantage).

The products, which contain aspirin with either phytosterols or calcium, are unapproved new drugs that require an approved new drug application in order to be legally marketed. In addition to being labeled for use as a pain reliever, both products are labeled for use in reducing the risks of heart disease. Bayer Women's is also labeled for use in "fighting" osteoporosis. Neither product has been approved by the FDA for such uses. These drug uses require a health care professional's diagnosis and supervision, and therefore these products cannot be labeled for use by consumers and sold over-the-counter (OTC).

Under its OTC drug monograph system, FDA allows some drugs to be marketed without first obtaining agency approval. Bayer Heart Advantage and Bayer Women's do not meet the conditions in any applicable OTC monograph, and do not have FDA approval. Therefore, Bayer Heart Advantage and Bayer Women's are unapproved new drugs.

Companies that do not resolve violations in FDA Warning Letters risk enforcement action, such as injunctions and/or seizure of illegal products. (Source: FDA Website, 28 October, 2008)

Sanofi-Aventis Temporarily Suspends Marketing of Acomplia

Sanofi-Aventis has announced that the European Medicines Agency (EMEA) recommended to the European Commission (EC) the temporary suspension of the marketing authorization of Acomplia (rimonabant) for the approved indication of overweight and obese patients.

Since the start of the commercialization of Acomplia, Sanofi-Aventis has been closely collaborating with both the regulatory authorities and healthcare providers to monitor on an ongoing basis the real life use of the product and to ensure its use in the right patient population.

Sanofi-Aventis believes that Acomplia will remain an important therapeutic answer to a highly prevalent and increasing unmet medical need. As discussed with the EMEA, the company will continue the ongoing clinical trial program except phase IV and is committed to providing additional evidence for the positive re-evaluation of the benefit/risk profile of the drug. (Source: Sanofi-Aventis Website, 23 October, 2008).

New Members

Mr. Edgar G. Aguilar, Webb Bio-Pharm

Mr. Rick F. Baggio, Millipore Corporation

Mr. Octavian Boca, Genzyme Corp

Zachary J. Brentzel, University of Massachusetts Amherst

John Bric, Vertex Pharmaceuticals

Ami Canzano, Massachussetts Biologic Labs

Mr. Frank Cava, Mettler-Toledo, Inc.

Varun Chalupadi, University of Massachusetts Amherst

Curtis Chase, Parsons Corporation

Mr. Robert A. Coggon, Superior Controls Inc

Mr. Paul A. DePriest, Parsons

Brian DiLuiso, Winter Street Architects

Mr. Dennis L. Doody, Bristol-Myers Squibb

Mr. Thomas J. Egan, Thermo Scientific

John C. Feeley, University of Massachusetts Amherst

Ms. Tamara B. Fridman, Vanasyl LLC.

Kathryn G. Geldart, University of Massachusetts Amherst

Sean R. Grandfield, University of Massachusetts Amherst

Mr. Stephen D. Hammitt, Parsons

Josephine L. Harrington, University of Massachusetts Amherst

Mr. Jeffrey J. Hays, Pall Biopharmaceuticals Corp

Orain A. Hibbert, University of Massachusetts Amherst

John C. Hickey, University of Massachusetts Amherst

Mr. John F. King, Parsons

Ms. Keely K. Kwok, University of Massachusetts Amherst

Mr. Bryan Laskowski, Cascade Solutions

Jason S. Lee, University of Massachusetts Amherst

Mr. Mark A. Libby, Parsons

Ms. Abigail Lynn, University of Massachusetts Amherst

Mr. John A. MacBlane, Atlantic Climate Control Inc

Mr. Anthony C. Malette, Tri-Stae Packing Supply, Inc.

Lorraine E. Mathis, University of Massachusetts Amherst

Marissa J. McGarry, University of Massachusetts Amherst

Frank E. Morse, Walsh Brothers Incorporated

Mr. Scott M. Nelson, Lonza

Mr. David A. Newman, Bristol-Myers Squibb

Mr. Donald R. Norris, New England Water Purification

Mr. Pat T. O'Donnell, Parsons

Mark Poulicakos, iPura Consulting Group LLC

Dan A. Ridenhour, Bio-Rad Laboratories

Dr. Karl Rix, DASGIP BioTools, LLC

Mr. Henrique Rodrigues, Bristol-Myers Squibb

Mr. Marco Rotondo, iPura Consulting Group, LLC

Joanna Rucker, Lonza Biologics

Mr. Blaine Sanborn, Watson-Marlow Flexicon

Jeremy P. Saver, University of Massachusetts Amherst

Jordan F. Schleeweis, University of Massachusetts Amherst

Dan R. Schreck, Lj Star

Sarah A. Scott, Northeastern University

Narendra Sharma, Boston University

Laura E. Smith, University of Massachusetts Amherst

Ms. Suzanne L. Stuhler, Shire Human Genetic Therapies (HGT)

Dr. Jesse P. Sullivan, Amgen Inc

Mr. Stephen P. Sylvester, Parsons

Mr. Juan Valdes, AstraZeneca

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