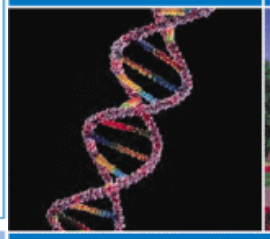
ISPE Boston Area Chapter
ENGINEERING PHARMACEUTICAL INNOVATION

www.ispeboston.org




NEWSLETTER

September 2009, Volume XIX, No. 5

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President's Message: Back to School!

Dear ISPE Boston Area Chapter Members,

Back to school. Those dreaded words every student hates to hear and a relief to all parents of school-aged kids. Well, it is back to work for the Boston Area Chapter Board of Directors. I am very honored to be the 17th President of this great Chapter and I look forward to an exciting year ahead. I would like to begin by introducing the new Board of Directors:

Vice President	Jim Grunwald	A/Z
Treasurer	Doyle Johnson	CDI Life Sciences
Secretary	Janet Tice	GMP Piping
Directors	Brian Hagopian	Mar Cor Purification
	Deepen Joshi	Sepracor
	Marita King	Maritek
	Kevin Lynch	Shire HGT
	Chrisopher Opolski	Alexion Pharmaceuticals
	Pietro Perrone	Millipore
	Monique Sprueill	Bristol Myers Squibb
	Lee Ward	Rockwell Automation
	Jay Zaino	GxP Automation

I also want to recognize past Board Members Jim Berry, Rick Pierro, Mike Denault, Dan Paquette and Jim Verhulst, all of whom have moved on to new adventures, and thank them for their tireless dedication to the Boston Area Chapter and their never-ending enthusiasm for the Chapter and its mission. They will be missed.

Equally important, I would like to thank all the members who have volunteered their time to serve on a committee this past year. I have been on committees for years and can't say enough about how beneficial committee membership has been for me personally and professionally. If you are not on a committee, I strongly urge you to consider joining one. We have many to choose from that should pique your interest: Membership, Educational Programs, Communications, Student Affairs, Young Professionals, Product Show and Social (which is near and dear to my heart).

The Board will be meeting in September for a full-day strategic planning session. We will be planning all of the events for 2009-10 and will advertise our final plans as soon as possible. If you have any suggestions for educational topics, social events or recreational activities, please email them to me at sbeaulieu@columbiacc.com. We always want to hear from our members.

This past month we held another successful Annual Golf Outing, this time at Ferncroft Country Club in Middleton. I want to thank Chris Opolski who did a wonderful job coordinating the event this year. I hope he decides to do it again next year! It was a very hot and steamy day but, as always, everyone had great time (the scotch and cigars were a nice touch...) See the write-up and photos in this newsletter and find out who the winners were.

Our kickoff educational program for 2009-10 held on September 14th, "Process Analytical Technology (PAT) / Quality by Design (QbD): Integrated Systems in the Future Pharma Business Landscape," was very successful and will be followed by upcoming facility tours scheduled at Bristol-Myers Squibb in Devens and Lonza in Portsmouth, NH. More details will follow, so be sure to check our Chapter Web site at http://www.ispeboston.org for program updates and be sure to read those ISPE emails. Online registration makes it easy to sign up to attend.

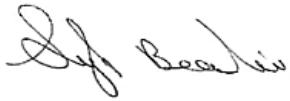
On October 7th we will again be hosting our Annual Product Show at Gillette Stadium and once again we have sold out the exhibitor tables. Board member Brian Hagopian

and the Product Show Committee have again done an outstanding job pulling this together, while Lee Ward and the Educational Program Committee deserve kudos for developing the educational sessions which I promise you will be outstanding. We have a fantastic keynote speaker, Juan Enriquez, who is famous for his ability to shed light on the links between science, business and society. His thought-provoking presentation, "As the Future Catches You: How Genomics & Other Forces are Changing Your Life, Work, Health and Wealth," is not to be missed.

For those of you attending the ISPE Annual Meeting in San Diego, November 8-11 at the Manchester Grand Hyatt, please join the Boston delegation at 9pm on Sunday, November 9th for cocktails and light appetizers at the Top of the Hyatt, the bar on the top floor with outstanding views of San Diego. This will be a Boston Area Chapter-only event. I look forward to seeing you there!

To end my first President's Message I need to mention Doyle Johnson, Chapter President this past year. Doyle did a wonderful job leading the Board and the Chapter through difficult economic times, with members being laid off and companies closing, but he was also a terrific mentor. He helped me learn more about leadership, patience and how to have fun, relax and enjoy our time as Officers. Doyle, you are a dear friend and I hope to make you proud of your decision to nominate me as your Vice President. You have given me the chance to shine as President of this exciting Chapter and I hope to live up to your expectations.

Sincerely,



Sylvia Beaulieu
President, ISPE Boston Area Chapter

Upcoming Chapter Events - Mark Your Calendar

Wednesday, October 7, 2009
Annual Product Show

- Source new products - View new technology and innovations from over 250 exhibitors
- Improve your knowledge - Attend any of the 9 Broad Based Educational sessions
- Develop new resources - Connect with 2000 biopharmaceutical professionals
- Emerging trends - Learn about the future of Genomics in Society from World Renowned Keynote Speaker - Juan Enriquez - 1:00 pm, Arrive Early for Premium Seating
- Enjoy yourself - Free parking, sustenance and non-alcoholic beverages

Gillette Stadium Clubhouse, Foxborough, Massachusetts

Click Here to Register to Attend. Its Free!

Wednesday, October 7, 2009
GAMP Forum

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

Gillette Stadium Clubhouse, Foxborough, Massachusetts

Click Here to Register

Thursday, November 19, 2009
Tour and Educational Program

Save the Date!
Registion Will Open Soon at www.ispeboston.org/events

Tuesday, December 8, 2009
Tour and Educational Program

Save the Date!
Registion Will Open Soon at www.ispeboston.org/events

Join the Excitement: Visit Product Show XVIII at Gillette Stadium on October 7th

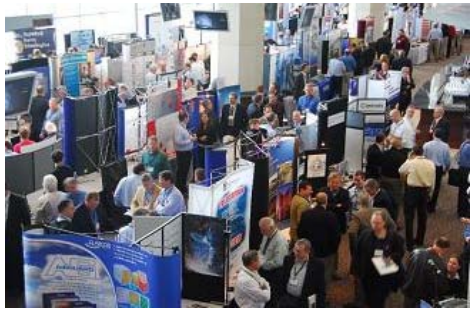
by Brian Hagopian, Mar Cor Purification / Fluid Solutions with photos by Peter Teague and Gail Fischer

This year, the 18h Annual ISPE Boston Area Chapter Product Show will be held on Wednesday, October 7th. at Gillette Stadium in Foxboro. It will be the biggest and best Product Show ever, loaded with more products and educational content than ever before. If you've attended prior shows at Gillette, you already know what a great venue it is. If you haven't been to Gillette before - you really have to make a point of visiting the show.

A spectacular view of Gillette Stadium provides a backdrop for the Annual Product Show.

Why?

- Free admission and free parking - only 35 minutes from Boston
- Over 250 exhibitors - including over 40 exhibitors you've never seen here before
- Exciting keynote speaker Juan Enriquez on the future of biotech
- Expanded educational program with 9 afternoon/evening sessions and a morning GAMP seminar
- Free hot/cold buffet plus free bottled water and non-alcoholic beverages all day
- Student Chapter meeting - meet the industry's future leaders
- Raffle with valuable prizes given away throughout the day
- Stadium tours



Over 1600 attendees and 250 exhibitors packed the Show floor last year.

There is no other single venue where members of the local life sciences community can mingle with one another and meet the ISPE Boston Area Chapter Board of Directors, Past Presidents and Advisory Committee Members (many of whom are local industry leaders) - all while viewing new and exciting products and services offered by the exhibitor community. The Product Show Committee has always sought to bring new products and educational topics of interest together with the companies that need them in a fun, exciting and hospitable location. And again they've succeeded admirably!

Since its humble beginnings, the Product Show has evolved into much more than a vendor and product-based event and has truly become a one-of-a-kind extravaganza. We've heard from so many exhibitors that this Product Show surpasses other local events and *is the one* activity that everyone should attend. In fact, the Product Show has received such acclaim that it recently won a national award for the best ISPE "special event."

The bar is a convenient "break" area where attendees and exhibitors can mingle throughout the day.

Gillette Stadium provides a unique venue that holds a special place in the hearts of New Englanders. We've taken advantage of some of Gillette's specific offerings including stadium tours (40-minute guided tours of the press box, visitor's locker room and the stadium field) along with raffles of autographed memorabilia and gift certificates to the pro shop and area restaurants. Attendees will be able to enjoy Gillette's outdoor "red seats" during the show (an area normally reserved for season ticket holders) and possibly even one of Gillette's luxury club boxes. This year, with the expansion at Patriot Place, Gillette is a better venue than last year, featuring a newly-opened Renaissance Hotel.

Gillette Stadium is about a 30-35 minute ride from Kendall Square (we timed it ourselves!), Boston, and a bit longer from Worcester, so it's really closer than you think. We suggest that you plan to beat the traffic (the show opens at noon, with the morning GAMP session beginning at 8:30am) and take full advantage of the day-long event.

Multiple carving stations serve

This year we have another excellent lineup of speakers for our keynote address and educational program. We've expanded our educational offerings with 9 afternoon and evening sessions. In addition, GAMP will present a morning-long session and two afternoon breakout sessions. There is a fee for attending the GAMP session, mainly to defray the cost of lunch being furnished to session attendees. Visit our Web site at www.ispeboston.org for a complete roster of programs and speakers and to register to attend these sessions. Last year, participation at seminars and the keynote address reached record levels, with over 600 attendees taking advantage of scheduled events. Save your spot by pre-registering for the Show and the seminars of your choice on our Web site.

The Product Show runs from 12noon until 8pm, so you can get your work done early and still have plenty of time to attend and participate. (The morning GAMP sessions begin at 8:30am.) Plan to arrive early to beat the rush and take advantage of the many opportunities offered. We promise you a rewarding day well worth the short trip from your workplace. And remember, the Show, including keynote presentation and educational program (with the exception of the GAMP sessions), is completely free (free parking, too), with complimentary food and non-alcoholic beverages served throughout the day,

hand-carved beef, ham & turkey.

complimentary lunch for exhibitors and cash bar for that cold beer. The food at Gillette is top-shelf all the way - just ask anyone who attended last year!

The ISPE Boston Area Chapter Product Show generates the funds needed to operate the Chapter, so your attendance not only provides you with valuable and pertinent information but helps to attract the exhibitors whose participation ensures that the Boston Area Chapter continues to be financially successful. Because of the funds raised by this event, the Chapter is able to sponsor top flight educational programs, social events, facility tours, workshops, Student Chapters and much more throughout the year.

Please register at our Web site (http://www.ispeboston.org) and help support the Boston Area Chapter by attending this event. It will be a smart decision that you will not regret, we promise! We look forward to seeing you on October 7th.

Rick Pierro & Doyle Johnson enjoy a light moment during last year's keynote address.

Keynote Speaker & Global Thinker Juan Enriquez Takes a Look into the Future

by Doyle Johnson, CDI Life Sciences

In the past, Product Show keynote speakers have typically been leaders in our industry or political figures who have focused on local topics - the new plant they are building in Massachusetts or how the Commonwealth is attempting to attract more biotech investment. At this year's Show, we are proud to bring you one of the best keynote speakers we've ever had, global thinker Juan Enriquez.

Dubbed "Mr. Gene" in a recent *Fortune* magazine profile, Juan Enriquez is not your typical scientist. He's a best-selling author with a special interest in the intersection of science, business and society and a background in high-level government service. In addition to the profile in *Fortune* magazine, *Time* magazine chose him to co-organize the life sciences summit commemorating the 50th anniversary of the discovery of DNA.

His keynote address, "As the Future Catches You," will describe how genetics is becoming the dominant language of the 21st century and how countries that keep up with the rapid advances in this area will be the future drivers of the global economy. His broad background and many accomplishments provide the background for his presentation and include:

- Founding Director of the Harvard Business School's Life Sciences Project.
- Managing Director at Excel Venture Management, a life sciences venture management company which launched a new $125 Million fund in July 2009.
- Chairman & CEO of life sciences research & investment firm Biotechonomy LLC.
- Author of the bestselling book, "As the Future Catches You: How Genomics & Other Forces are Changing Your Life, Work, Health & Wealth," chosen as one of the best business books of the year by Amazon's editors.
- CEO of Mexico City's Urban Development Corporation, where he played a role in reforming Mexico's domestic policy; and Chief of Staff for Mexico's Secretary of State.

So plan to join us at 1:00pm in the northeast lounge the Show floor and be sure to arrive early to get a good seat. We expect an overflow crowd will want to hear this great thinker and world-class speaker give what is sure to be a stimulating and entertaining lecture about our future.

Triple-track Educational Program Offers Something for Everyone

by Lee Ward, Rockwell Automation

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

Can't get enough education? No? Well then the 2009 Boston Area Chapter Product Show could be just what you need to satisfy your craving. Join us at Gillette Stadium, home to the New England Patriots and the New England Revolution, on Wednesday, October 7th. This year sees a diverse array of subject matter presented by industry leader experts in their given fields. The Educational Programs Committee, dedicated to delivering world class educational programs on a regular monthly basis, has again put together an amazing collection of seminars. The program is designed to serve a wide range of interests and needs, from individuals new to the biopharm industry through to leading-edge professionals seeking to further expand their knowledge and experience.

Seminars are grouped into three "tracks" running concurrently, not necessarily subject matter specific but providing a convenient way to navigate which sessions you would like to attend. In addition, there is a GAMP Forum taking place in conjunction with the Show, with both morning and afternoon sessions (see companion article below for more information on this special event).

TIME	TRACK 1	TRACK 2	TRACK 3
2:30 - 3:30	***Biotech 101*** James Vogel, Process Facilities Services, Inc	***Future Trends in Manufacturing*** Robert Conway, PhD, Xcellerex	***Wish I Would Have Known: From Site Selection to Grand Opening*** Moderator and Panelists: H. Steven Kennedy, Parsons Don Reitano, CFM, Alkermes Peter Cramer, AIA, Parsons Fred Scribner, Columbia Construction Ted Lyon, DTZ FHO Partners
4:00 - 5:00	***ASME BPE Guidelines Update*** Jay Ankers, LifeTek Solutions	***Leadership in Biotech*** Moderator and Panelists: Joyce Chiu, Perceptive Informatics, PAREXEL Walt Bassett, Millipore Joe Maressa, CMF, Fitzgerald, Stevens and Ford/OI Partners Beth Wescott, Wyeth BioPharma Joyce Whitehead, PhD, Shire Human Genetic Therapies Lesley Wood, Lonza Biologics	***What to do with Your Shrinking Facilities Budget*** Moderator and Panelists: Dick Priester, Strategic Facility Planning LLC David Wilson, Abbott Bioresearch Center Anthony J. Meenaghan, EMD Serono Henry Fitzgerald, Genzyme Steven Kassack, Novartis Vaccines & Diagnostics, Inc. Pat Sacco, Shire HGT

Previous Issues

		Patricia Seymour, BioProcess Technology Consutlants	Gil Stevens, Wyeth
6:00 - 7:00	***Principles of CIP*** Mark Pelletier, CRB Consulting Engineers Chris Pacheco, Amgen	***Energy Saving Projects: Creating an Energy Usage and Management Program - Reducing Operating Costs and Embracing Corporate Sustainability Goals*** Tom Pagliuco, Schering-Plough	***Transferable Skills in Biotech*** Panelists: Aaron Conant, Biogen Idec Jodi Allen, Shire HGT Rachel Yamartino, WPI Corporate and Professional Education

We have looked at the industry, taken into account the economic climate, considered the future, and then chosen topics that are the "right fit" for the times in which we find ourselves. Track 1 leans toward the discerning young professional or newcomer to the industry with a focus on core competencies: Biotech 101, ASME BPE guidelines and CIP basics.

Track 2 initially takes a look at the growing trend of "modular manufacturing" and how one company approaches the needs of flexibility. Biotech leadership is the focus during the second session which brings industry leaders together for a free-wheeling panel discussion. And session three looks at what you can do within your facility to achieve energy savings.

Track 3 begins with a panel discussion focused on the facility lifecycle, with panelists sharing their experiences and discussing lessons learned. Session two, addressing what facility owners can do in light of the diminished

Educactional sessions & panel discussions
cater to a wide range of interests and experience.

funding for projects in today's economy, is another panel discussion with industry headliners more than willing to share their thoughts and answer your questions. We round up this track by sharing what externally-derived skills are readily transferable when looking at adding to or building a technical team.

We hope you agree that this is one of our strongest Product Show programs ever and that you will make every effort to join us and participate in our premier educational event of the Chapter year. Be sure to visit www.ISPEBoston.org/Events to pre-register online for the programs of your choice...See you there!

Attend GAMP Forum for a Comprehensive Look at Good Automated Manufacturing Practices

GAMP (Good Automated Manufacturing Practice) is a community of practice (CoP) within ISPE that works internationally with the life sciences industry and regulatory agencies. Its goal is to develop guidelines and best practices that help companies achieve compliant computer automated manufacturing and manufacturing support systems. GAMP hosts forums and other events to gather and communicate information from around the world to facilitate continual improvement in compliance activities for systems developers/suppliers and end users.

There is a nominal fee for this special event which includes lunch. Since we expect a high level of interest and space is limited, pre-registration is mandatory for this event. Please visit www.ISPEBoston.org/Events to pre-register online.

Morning Sessions		
Time	Speaker	Topic
8:00-8:30	-- Registration --	
8:30-9:00	Greg Ruklic, Wyeth Randy Perez, Novartis	Welcome and Introduction GAMP 2009 Update
9:00-10:00	John English	Cloud Computing and Compliance
10:00-11:00	Frederick Simard & Heather Schwalje, BMS	A Paperless Plant: BMS Devens
11:00-11:30	-- Lunch --	
11:30-12:00	Armen Nahabedian, Wyeth	ASTM Common Approach to Specification & Verification
12:00-12:30	Randy Perez, Novartis & Winnie Cappucci, Bayer	Intro to Outsourcing & Offshoring in a Regulated Environment
Afternoon Breakout Sessions (concurrent)*		
Time	Speaker	Topic
2:00-3:30	Armen Nahabedian, Wyeth	Workshop: ASTM Common Approach to Specification & Verification
2:00-3:30	Randy Perez, Novartis & Winnie Capucci, Bayer	Workshop: Intro to Outsourcing & Offshoring in a Regulated Environment

* Please note: Afternoon breakout sessions are available only to registrants attending the morning session.

Product Show Schedule of Events

8:30 - 12:00	***GAMP Forum*** Separate pre-registration and a fee is required for this program.		
1:00 - 2:00	Opening Keynote Address As the Future Catches You: How Genomics & Other Forces are Changing Your Life, Work, Health and Wealth Juan Enriquez, Managing Director, Excel Venture Management, Chair and CEO, Biotechonomy		
2:00 pm	Door Prize Drawing #1		
2:30 - 3:30	***Biotech 101*** James Vogel, Process Facilities Services, Inc	***Future Trends in Manufacturing*** Robert Conway, PhD, Xcellerex	***Wish I Would Have Known: From Site Selection to Grand Opening*** Moderator and Panelists: H. Steven Kennedy, Parsons Don Reitano, CFM, Alkermes Peter Cramer, AIA, Parsons Fred Scribner, Columbia Construction Ted Lyon, DTZ FHO Partners
3:45 pm	Door Prize Drawing #2		
4:00 - 5:00	***ASME BPE Guidelines Update*** Jay Ankers, LifeTek Solutions	***Leadership in Biotech*** Moderator and Panelists: Joyce Chiu, Perceptive Informatics, PAREXEL Walt Bassett, Millipore Joe Maressa, CMF, Fitzgerald, Stevens and Ford/OI Partners Beth Wescott, Wyeth BioPharma Joyce Whitehead, PhD, Shire Human Genetic Therapies Lesley Wood, Lonza Biologics Patricia Seymour, BioProcess Technology Consutlants	***What to do with Your Shrinking Facilities Budget*** Moderator and Panelists: Dick Priester, Strategic Facility Planning LLC David Wilson, Abbott Bioresearch Center Anthony J. Meenaghan, EMD Serono Henry Fitzgerald, Genzyme Steven Kassack, Novartis Vaccines & Diagnostics, Inc. Pat Sacco, Shire HGT Gil Stevens, Wyeth
5:45 pm	Door Prize Drawing #3		
6:00 - 7:00	***Principles of CIP*** Mark Pelletier, CRB Consulting Engineers Chris Pacheco, Amgen	***Energy Saving Projects: Creating an Energy Usage and Management Program - Reducing Operating Costs and Embracing Corporate Sustainability Goals*** Tom Pagliuco, Schering-Plough	***Transferable Skills in Biotech*** Panelists: Aaron Conant, Biogen Idec Jodi Allen, Shire HGT Rachel Yamartino, WPI Corporate and Professional Education

8:00 - 10:00	Open Reception

Fun in the Sun at the Boston Area Chapter's 7th Annual Golf Outing

by Chris Opolski, Alexion Pharmaceuticals, with photos by Sylvia Beaulieu, Columbia Construction

On August 17th, the Boston Area Chapter hosted our annual golf tournament at the gorgeous Ferncroft Country Club in Middleton for the second year in a row. And just like last year, during a summer plagued by nonstop rainy days, we lucked out with beautiful, sweltering hot weather. Congratulations to all of the day's winners.

The winning teams:

First Place (57)	Second Place (60)	Third Place (62)
Skanska	Erland Construction	A/Z Corporation
Joe Devlin	Mike Phillips	Dan Paquette
Mike Benedetto	Chuck Vaciliou	Jim Grunwald
Darrin Ball	Bob Lewis	Herb Aiken
Steve Jackson	Bob Liptrot	Steve Webber

And the individual winners:

	Men	Women
Longest Drive	Mike Phillips	Leena Asplund
Closest to Pin	Mike Walsh	Debbie Crooke
Straightest Drive	Glenn Bohling	Colleen Clifford

And many, many thanks to our Golf Outing corporate sponsors: DECCO, GxP Automation, Cotter Brothers, Superior Controls, Erland Construction, North Shore Mechanical Contractors, Middlesex Gas & Technologies, AES Clean Technology, American Plant Maintenance and NNE Pharmaplan who helped to make this event another big success for the Chapter.

Golf Tournament Photo Gallery

Overlooking the course at Ferncroft Country Club..

First Place winners, sponsored by Skanska
(l to r): Joe Devlin, Darrin Ball, Mike Benedetto, Steve Jackson

Second Place winners, sponsored by Erland Construction (l to r):
Bob Lewis, Mike Phillips, Chuck Vaciliou

Third Place winners, sponsored by A/Z (l to r):
Herbie Aiken, Steve Webber, Jim Grunwald, Dan Paquette

"Longest Drive" winners Leena Asplund and Mike Phillips

"Closest to the Pin" winners Debbie Crooke and Mike Walsh

"Straightest Drive" winner Glenn Bohling

Tech Talk: An Introduction to Single-Use Technology: Flexible Technology That Gives the User Choices

by Pietro Perrone, Millipore Corporation

The need for operating plants to be flexible, minimize costs and risk, while keeping ahead of the ever-ticking clock has created opportunities for single-use products that can

address these immediate needs. Numerous papers have been written that assess the benefits; some of these are referenced at the end of this article. Here we highlight fundamental components that are available and are applied in single-use equipment or systems. Familiarity with these components is the first step to capitalize on the benefits of single-use technology.

Make It Simple to Make It Easy and Fast

The main categories of single-use products are:

- base components - such as bags and tubing; and
- assembled kits or systems - from sample kits to bioreactors.

Many of the individual components have been around for a while in commercial operations. The components (bags, tubing, filters, etc.) would often be obtained from various sources and assembled in the most expedient and acceptable way in the process plant. While the components are readily available, their assembly into a concerted process line often causes issues. Components obtained from multiple suppliers require special attention. Connections must match to make these interfaces smooth transitions. Sorting this out causes work and potential delays. Getting all the components set up in a relatively smooth assembly is a time-consuming and unpredictable activity.

One critical time-saving advantage that single-use products provide is that the products are based on assembled components or at least components with matching connections from the same supplier. This saves time and keeps the personnel focused on getting the plant operational.

The flexibility of single-use products combined with their low initial investment makes it easier to customize to the specific needs of the drug product. This flexibility is particularly important in situations where the user is unsure of what drug product needs to be processed next or has little time to set up a new process. If planned properly, the technology allows the user to select or develop a process line specifically suited to the drug product with minimal impact on the critical path of a project. To take advantage of this flexibility, the user needs to understand the capabilities of the single-use products available.

A Flexible and Complex World of Choices

Having flexibility is great. Having flexibility, while minimizing cost and risk, and still being able to respond to market fluctuations, gives the drug product manufacturer the ability to respond quickly. This is where single-use products can provide the drug manufacturer competitive advantages. While the combinations that can be developed from the basic components provides the user great flexibility to design to the specific need, this flexibility requires the user to have a basic understanding of what is available and then apply it effectively. As an introduction to what is available, the following expands on the main categories of tools. These include:

- base components
  - Bags
  - Tubing
  - Instruments
    - Pressure
    - Temperature
    - pH
    - Conductivity
  - Mixers
  - Filters
- assembled kits or systems
  - Storage containers
  - Mixing totes
  - Sample kits
  - Filter systems
  - Bioreactors

Suppliers for each of the items above are developing product lines to give the drug manufacturer lots of choices. Given time, the drug manufacturer can optimize the available products to the needs of the process by extracting maximum performance from the single-use products during their one time use. However, time is usually at a premium and the optimization is often made from educated decisions based on self-acquired data, published information and assistance from the various suppliers.

Implementation of single-use technology in a complete process line is a significant undertaking that requires planning and upfront work. There is literature and case studies[5] that address design, compliance, and validation and can be used as examples of what needs to be investigated. There are also ISPE Communities of Practice (COPs) [6] dedicated to this endeavor. These resources should be used by those considering evaluating and implementing single-use technology.

In addition to the published literature and case studies there are simulation tools [4] that also help in getting your process optimized quickly. The simulation tools can provide ways to predict the impact of single-use technology after scale-up. Optimization of a process can provide a cost advantage but most importantly it can reduce the time to come to an acceptable solution with minimum analysis. This in turn minimizes risk. The simulation tools can provide critical evaluations such as comparisons of production cost between stainless steel and single-use components at various scales of operation (see Figure 5 in Reference 4).

Flexibility and Speed with Minimum Risk and Up-Front Cost

One of the main benefits of single-use technology is the speed of setting up a process. Single-use technology provides the user flexibility that can prove valuable in light of today's evolving needs. However the components are assembled, the main questions that are critical to implementing single-use technology are:

- ***Can it save me money?*** The low initial investment for the single-use components provides an advantage. The long-term cost comparisons between single-use vs. stainless steel needs to be done on a product-specific basis as it is contingent on utilization of the equipment.[2]
- ***Will it minimize risk?*** While there are numerous advantages that minimize risk with the single-use products, there are some issues that could cause adverse results and therefore need special review. These include: extractables, contamination, dimensional integrity, impact on product characteristics, and chemical or physical interactions.

These issues typically need input from various disciplines in the organization on a case-by-case basis. It requires a concerted effort up front to yield the best chance of success. The homework to minimize risk done in this area will pay big dividends in time and acceptability of the single-use technology.

In summary, finding the right solution for using either stainless steel or single-use options requires an objective assessment as early in the process as possible. The solution is a balance that needs to be found for each unique situation. Single-use technology has the inherent flexibility to meet many of the unique industry needs.

- 1. Lifecycle Cost Analysis for Single-Use Systems; B. I. Bamoon and B. Bader; BioPharm International, 2 Nov 2008.
- 2. Disposables Cost Contributions: A Sensitivity Analysis; A. Sinclair and M. Monge; BioPharm International, April 2009, pages 28-32.
- 3. The Environmental Impact of Disposable Technologies, A. Sinclair, L. Leveen, M. Monge, J. Lim, and S. Cox; BioPharm International, 2 Nov 2008.
- 4. Systematic Evaluation of Single-Use Systems Using Process Simulation Tools; V. Papavasileiou, C. Siletti, and D. Petrides; BioPharm International, 2 Nov 2008.
- 5. Methods and Considerations for Disposable Implementation; A. Goldstein, D. Schieche, J. Harter, R. Samavedam, L. Wilkinson, A. Manocchi; BioProcess International, October 2005, pages 20-27.
- 6. Disposables COP and Implementation of Disposables COP.

Pietro Perrone, P.E. is a Proposals/Projects Manager at Millipore Corporation. He is a Professional Engineer registered in Massachusetts. Pietro has a degree in chemical engineering from Tufts University with 20+ years of purification/separation technology experience in process development/optimization, equipment scale-up, and project management.

Industry News In Brief

by Patti Charek, Linbeck

GE Healthcare and Geron Enter Stem Cell Alliance

GE Healthcare and biotechnology firm Geron Corp. said that the two companies have formed an alliance to develop testing and analysis products based on human embryonic stem cell lines that Geron licenses from the Wisconsin Alumni Research Foundation. The products developed under the alliance are expected to allow researchers to determine toxicity problems with drug candidates earlier in the drug development process. Earlier detection of toxicity problems could reduce both overall drug development costs and potentially harmful patient exposure in clinical trials, where most toxicity problems currently are detected.

Under the global exclusive license and multi-year alliance agreement, GE Healthcare and Geron intend to develop and commercialize cellular assay products derived from stem cells for use in drug discovery, development and toxicity screening. GE Healthcare will fund the research and development program and will be responsible for manufacturing, sales and distribution of products developed under the agreement.

The program will use stem cells derived from human embryonic stem cell (hESC) lines listed on the NIH Human Pluripotent Stem Cell Registry, which are eligible for federal funding. "This agreement marks a further step in GE Healthcare's cell technology strategy aimed at addressing the potential of stem cell applications in the drug discovery and therapy markets," said Konstantin Fiedler, general manager, cell technologies, GE Healthcare. "Combining GE Healthcare's reach into the drug discovery and research markets, as well our expertise in cell manufacturing, with Geron's expertise and intellectual property in hESCs, means that together we will be able to accelerate the development of hESC-derived products for drug discovery and development."

The first products developed in the GE Healthcare and Geron alliance are expected to be available by early 2010, with a pipeline of products to follow. Intellectual property rights arising from the alliance program research will be shared, with GE Healthcare receiving rights for the development of drug discovery technologies, and Geron receiving rights for cell therapy applications.

GE Healthcare, a unit of Fairfield, Connecticut-based General Electric Co., is based in the UK but maintains extensive operations in the Milwaukee area. Geron is based in Menlo Park, California. (Source: The Business Journal of Milwaukee, 30 June 2009)

Glaxo Hopes to Supply Flu Vaccine by Early 2010

GlaxoSmithKline PLC hopes to supply swine-flu vaccine to all of the governments it is in discussions with by the first part of 2010, but that will depend on some quirks in the production process. So far, 16 governments have ordered 195 million doses from Glaxo, but the company is talking to 50 governments at the moment and expects total orders to be "substantially" higher, Chief Executive Andrew Witty said. Mr. Witty's remarks came as the company reported a 12 percent rise in second-quarter profit.

How quickly Glaxo can deliver will depend on how much active ingredient, or antigen, it can produce, Mr. Witty said. But the H1N1 virus being used for swine-flu vaccine is so far yielding a low level of antigen, he said. If production levels remain roughly where they are now, "we believe we could meet the kind of demands we're being told [governments] want" by "the first part of 2010," he said.

In addition to the vaccine, Glaxo is increasing production of antiviral medication Relenza that is being prescribed by some doctors to relieve the symptoms of swine flu. Mr. Witty said he expects the pandemic to make a "significant contribution" to Glaxo's profit, which he said is justified given the company's investment over the years in developing Relenza and flu vaccines.

Glaxo is charging wealthy nations about $10 a shot for the H1N1 vaccine and developing countries less, he said. It is also donating 50 million doses to the WHO. Governments buying H1N1 vaccine from Glaxo are agreeing to indemnify the company against some legal liabilities that may arise from a mass vaccination program, Mr. Witty said. He added that he expects regulators, including the FDA and the European Medicines Agency, to sign off on the vaccine before it is used in any consumers. (Source: Jeanne Whalen and Jason Douglas, The Wall Street Journal, 23 July 2009)

Sanofi Plans to Overhaul Research and Development

Sanofi-Aventis SA will announce a reorganization of its research and development operations in coming weeks, CEO Chris Viehbacher said. "We have a number of things to address in terms of how we get our people to work together, how we can provide more latitude for creativity, how we can develop them scientifically and how we can encourage external collaboration, because there is a world of science out there," Viehbacher told Reuters in an interview.

Viehbacher, who joined Sanofi from GlaxoSmithKline in December, is overhauling the research effort after the obesity pill Acomplia, once Sanofi's most promising new medicine, was rejected by regulators. The company also faces generic competition to drugs that make up about 20 percent of revenue.

In a letter to employees the week he joined, Viehbacher said that rethinking the organization and the management of Sanofi's R&D teams was one of his priorities. On Feb. 11, he said the division, run by Marc Cluzel, would now show "lower spending internally" and "higher spending externally." "The company's R&D track record is seen as weak," Tero Weckroth, an analyst at Kepler Capital Markets in Zurich, wrote in a June 16 note to clients. "Discipline in R&D could increase value creation."

The 49-year-old executive began his overhaul in April, when he announced Sanofi was dropping 14 of its 65 research projects and that more may be terminated in the coming months. He also started making acquisitions, including the purchase of BiPar Sciences Inc. of Brisbane, California, seeking to fill up the company's pipeline.

Sanofi will announce cost cuts when it releases second-quarter results, CFO Jerome Contamine said during the Bank of America and Merrill Lynch health-care conference in New York. "We are working on various ways to reduce the costs," Contamine said. In research, "we have reduced the portfolio, we have decided to open up the R&D to external R&D and it's clear that we also will have to adapt the internal structure to this new shape of R&D," Contamine said. (Source: Albertina Torsoli, Bloomberg, 24 June 2009)

Sanofi Agrees to Take Control of India's Shantha

Sanofi-Aventis SA, France's biggest drugmaker, agreed to take control of Shantha Biotechnics in an acquisition valuing the Indian vaccine maker at 550 million euros ($784 million). Under terms of the agreement, Sanofi's vaccine unit will buy ShanH, which owns 80 percent of Shantha Biotechnics, from the Merieux Alliance. The French drugmaker is paying about 440 million euros for the purchase. The transaction is set to close before the end of the third quarter, Sanofi said.

The purchase gives Sanofi a platform in India as well as access to Shantha's pipeline of new products, including an experimental typhoid vaccine. Prior to this acquisition, Sanofi's Indian operations had a total of 2,870 employees, mostly based in Mumbai "Shantha brings in the low-cost production facilities that ease access to emerging markets," Peter Duellmann, an analyst at Oppenheim Research GmbH in Cologne, Germany, wrote in a note to clients.

Sanofi CEO Chris Viehbacher has been looking for outside growth opportunities since taking over eight months ago. In a June 17 interview, the 49-year-old executive said he was committed to expanding Sanofi's vaccine business. He cited growth in developing countries, including India, as another priority. Of the four acquisitions Viehbacher has made since his appointment, three were in emerging markets. (Source: Albertina Torsoli, Bloomberg News, 27 July 2009)

Bristol-Myers Squibb to Acquire Medarex

Bristol-Myers Squibb Company and Medarex, Inc. announced that the companies have signed a definitive merger agreement providing for the acquisition of Medarex by Bristol-Myers Squibb, for $16 per share in cash. The transaction, with an aggregate purchase price of approximately $2.4 billion, has been unanimously approved by the boards of directors of both companies. Medarex's projected $300 million in net cash and marketable securities at closing would be an asset acquired by Bristol-Myers Squibb resulting in an implied purchase price of approximately $2.1 billion.

"Medarex's technology platform, people and pipeline provide a strong complement to our company's biologics strategy, specifically in immuno-oncology," said James M. Cornelius, chairman and CEO, Bristol-Myers Squibb. "With its productive and proven antibody discovery capabilities, ability to generate interesting therapeutic programs and unique set of pre-clinical and clinical assets in development, Medarex represents what we're looking for in terms of our String of Pearls strategy. This acquisition is another important step in our BioPharma transformation."

"We believe that this combination with Bristol-Myers Squibb, a global leader in oncology, provides an excellent opportunity to realize the full potential of Medarex's development portfolio and our UltiMAb technology platform through a transaction which also provides an attractive valuation for our shareholders," said Howard H. Pien, chairman and CEO, Medarex. "Medarex has evolved significantly over the past two decades from a research platform to a development company. We believe that this transaction represents a great opportunity to place our clinical programs and technology assets in the hands of one of the world's premier biopharmaceutical companies with the expertise, resources, motivation and dedication to bring innovative cancer treatment options to patients in need."

"We welcome the opportunity to further collaborate with the Medarex scientific leadership," said Elliott Sigal, M.D., Ph.D., executive vice president and president, research and development at Bristol-Myers Squibb. "In addition to our Adnexus team, which has been expanded since it was acquired in 2007, Medarex scientists will help us create an industry-leading biologics capability. We believe Medarex's antibody generation expertise, located in California and New Jersey, will complement our existing biologics efforts with a dedicated discovery and development capability in immuno-oncology." (Source: Business Wire, 22 July 2009, through Drugs.com)

GTC Agreement Takes Aim At MS

Framingham-based GTC Biotherapeutics Inc. now has the rights to develop and commercialize a protein that could be used to treat multiple sclerosis and other autoimmune diseases. The protein is recombinant human alpha-fetoprotein (rhAFP) and it has been in development by Cambridge-based Merrimack Pharmaceuticals in the milk of genetically modified goats at GTC's facilities. Under the new agreement, GTC will receive enough rhAFP from Merrimack for use in clinical studies and will assume control of the goats. Financial terms of the deal were not disclosed.

Human AFP is a blood protein produced in very high levels in women during pregnancy. It plays a role in strengthening women's immune systems in order to protect gestating fetuses. Apart from pregnancy, AFP is produced in very low levels. GTC plans to study whether human AFP produced by genetically modified goats can treat autoimmune diseases multiple sclerosis and myasthenia gravis. (Source: Matthew L. Brown, Worcester Business Journal. 8 July, 2009)

Genzyme Sues Sandoz over Dialysis Drug Patent

Genzyme Corp. sued the Sandoz Inc. unit of Novartis AG, alleging infringement of a patent for Hectorol, used to treat patients on kidney dialysis. Genzyme and patent partner Bone Care International LLC contend that Sandoz is planning to market a generic copy of injectable Hectorol before the patent expires in 2014. Sandoz is seeking FDA approval to sell a copy of the medicine. Genzyme wants a court to block approval until the patent expires. The drug is used to treat overactive parathyroids in patients with chronic kidney disease who are on dialysis. (Source: Bloomberg News, 18 July 2009)

Biopure Files Chapter 11, Plans Sale

Biopure Corp., the ambitious Cambridge biotech firm that was working on developing a human blood substitute, has run out of time and money. The company said it filed for Chapter 11 bankruptcy protection and will sell most of its remaining assets to OPK Biotech LLC, a Delaware company.

If the sale is approved in court, it will mark the end of a firm that once was one of the state's most promising biotechs. Hemopure, made from cow hemoglobin, long seemed on the verge of emerging as a potential life-saving breakthrough. But Biopure could never clear regulatory hurdles that would have turned Hemopure into a mainstream medical product.

At one time, the company, which was founded in 1984, had 250 employees, but only four remained at the time of the bankruptcy filing. The once-hot stock, which reached a record $49.37 price in March 2000, closed at under 7 cents. The bankruptcy also triggered a delisting notice from the Nasdaq stock market. In the bankruptcy petition, Biopure said it had $5.08 million in assets and $2.73 million in liabilities.

A major part of the Biopure story was driven by the exciting promise of its technology. By isolating cow blood hemoglobin - a chemical that binds with oxygen - the company said it was on the way to creating a blood substitute that could fill a crucial need in the medical community. Hemopure showed many benefits compared with real blood: a three-year shelf life, the ability to be used by patients of any blood type, and freedom from diseases and pathogens that could be transmitted by human blood.

The path to FDA approval, however, was rocky. Although the Navy was interested in using the experimental product to treat military personnel wounded in battle, where traditional blood transfusions aren't readily available, the FDA consistently rejected Biopure and the Navy's efforts to test the product in clinical trials, citing safety worries and other concerns. (Source: D.C. Denison, Boston Globe, 22 July 2009)

Early Rollout of Shire's Drug for Gaucher Disease Okayed by FDA

British drug maker Shire PLC stepped up the pressure on Cambridge biotechnology company Genzyme Corp., reporting positive test results for a competitor to Genzyme's drug for Gaucher disease and disclosing that US regulators will let doctors prescribe the rival drug before it is approved for commercial use.

Supplies of Genzyme's enzyme replacement therapy Cerezyme, currently the only drug on the market to treat the rare genetic disorder, were interrupted in June when a virus was detected in the company's Allston Landing plant. While the plant resumed production after the decontamination of its bioreactors, Genzyme, the state's largest biotechnology company, will continue rationing drugs to the least vulnerable patients until late this year, when new batches of the drugs can be shipped and inventories return to their full strength.

Shire's competing drug, velaglucerase alfa, could be administered to some Gaucher disease patients in a matter of weeks, following FDA approval of a company plan for introducing the drug, called a treatment protocol. The agency solicited the protocol, a relatively uncommon arrangement that allows doctors to prescribe drugs for up to 12 months before they have received FDA approval. A treatment protocol is typically reserved for situations such as supply disruptions, where there are acute medical needs.

The early rollout of Shire's drug could give the company a leg up in its efforts to grab a share of the market for Gaucher disease treatments. But the company had planned to submit a new drug application to the FDA even before Genzyme's supply interruption. "We're just responding to the patient need at this point, which is what matters most," said Sylvie Gregoire, the president of Shire's human genetic therapies division, which produces velaglucerase alfa, and other enzyme replacement drugs. "That's what the FDA wants. If this turns into an opportunity for us, that's fine."

Gaucher disease is an enzyme deficiency in which fatty substances accumulate in the spleen, liver, lungs, bone marrow, and sometimes, the brain, causing bruising, enlarged organs, and lung and kidney ailments. It affects only about 5,700 people worldwide. But the treatment for it, which is often subsidized by governments or insurance companies, costs approximately $200,000 per year per patient, bringing the potential market for drug makers to about $1.2 billion.

In addition to Shire, two other drug companies, Actelion Pharmaceuticals Ltd. of Switzerland, and Protalix BioTherapeutics Inc. of Israel, are developing drugs to treat Gaucher disease.

Genzyme is likely to keep the lion's share of the market in the near future, but finds itself under increasing regulatory and competitive pressure, said Christopher J. Raymond, senior biotechnology analyst for financial services firm Robert W. Baird & Co. in Chicago. "They've had a string of setbacks," Raymond said of Genzyme, citing the FDA inspection and the intensifying competition

On the competitive front, Shire, which has nearly 1,000 employees in Lexington and Cambridge, reported positive results from the first of three phase 3 studies of veraglucerase alfa. The data were consistent with previous studies that helped convince the FDA to accept the company's treatment protocol that will allow doctors to prescribe the drug before it wins final approval by the agency. Shire said it began a "rolling submission" of its new drug application three weeks after it received fast-track designation from the FDA. The designation enables companies to file sections of the application as they become available, and allows the agency to review those sections before the entire application is filed. (Source: Robert Weisman, Boston Globe, 4 August 2009)

New England Biotechnology Firms get Venture Capital Boost

Biotechnology firms received most of the venture capital that went to New England companies in the second quarter of this year, accounting for $168.7 million, or 36 percent, of the total invested in the region. Medical devices and equipment, the second most active category in New England, brought in $111 million.

The New England industry breakdown reflected the national trend. The life sciences sector (biotechnology and medical device industries combined) represented 41 percent of all investment dollars and 26 percent of all deals in the three months that ended June 30.

Eight of the 10 largest deals in New England were in life sciences. The largest New England deal to close in the second quarter was a $40 million early stage investment in Aileron Therapeutics Inc. in Cambridge, which is developing new technologies to help treat cancer. It was followed by investment in ConforMIS Inc. of Burlington, which raised more than $35 million for its minimally invasive medical implants for orthopedics.

New England was the second most active US region for venture capital investment, with 76 deals worth $467 million, 13 percent of total US venture capital invested. However, venture investment in the region was down sharply, with 43 percent less invested than the $826 million in the same period last year. More than half of the total for the quarter went to life sciences companies in the region. The number of deals for the quarter also fell, from 128 to 76 over the same period a year earlier.

The data appeared in the MoneyTree Report, which is produced by the accounting firm PricewaterhouseCoopers and the National Venture Capital Association, using data

from research firm Thomson Reuters.

New England was still a distant second behind California's Silicon Valley, which landed 174 deals totaling nearly $1.2 billion. Venture investment in Silicon Valley companies accounted for 32 percent of venture investment nationwide. However, both regions and the rest of the country are struggling with fewer opportunities for venture capitalists to cash out their investments, according to Mark Heesen, president of the National Venture Capital Association. "We're still facing an extremely poor exit market," Heesen said. "There were only six venture-backed initial public offerings in 2008, and so far there have only been six this year. In a good year, we've seen a hundred or more. That is having a dampening effect on venture investing."

The decline mirrored a national downturn in venture funding, as the total number of dollars invested in the United States fell to just under $3.7 billion from more than $7.5 billion during the same period last year. "The comparison, year over year, is stark, because if you think about the economy a year ago - that was before the downturn really started," said Kevin Shaw, a partner in the Emerging Company Services practice at PricewaterhouseCoopers LLP in Boston. "The companies that were funded a year ago got their investments before the downturn."

Although the data show that venture investment declined dramatically year over year, the second quarter was actually a slight improvement over the previous quarter. In New England, venture investment was up $61.5 million over the first quarter of this year; US venture investment was up $500 million. (Source: D.C Denison, Boston Globe, 25 July 2009)

Epix Pharmaceuticals to Shut Down

Epix Pharmaceuticals, Inc. has announced it will quietly wind down operations after a hard fought battle to keep the company afloat. The Lexington-based company's officials said Epix was unable to raise enough money or enter into a partnership in time to remain a going concern. It has since filed paperwork to provide for an orderly liquidation of its assets.

As of Dec. 31, the company had 91 full time employees. However, in March it oversaw an unspecified number of job cuts to reduce its overhead. A more recent employee figure was not immediately available. Elkan Gamzu, president and CEO of Epix, stated, "It is with great disappointment that the company must proceed with this decision. Over the past several months we had taken several actions in an effort to improve the financial health of Epix ... Despite this and the efforts of our financial advisors who approached numerous third-parties over the past several months, we were unable to obtain additional funding to continue our operations or consummate a strategic transaction."

In April, Epix announced the sale of the US, Australian and Canadian rights of its vascular imaging agent Vasovist to Lantheus Medical Imaging for $28 million. The biotechnology company targeted $10.5 million of the proceeds to pay off debts to a former partner, Germany-based Bayer Schering Pharma. That same day, Epix also announced a deal to wipe out $100 million of debt by offering bondholders shares of the company and cash payments.

But these moves were not enough to prevent the company from being delisted by Nasdaq on May 14th. The delisting followed repeated warning letters that the company failed to meet the minimum requirements of the stock exchange, including failure to maintain a $35 million market capitalization for 10 consecutive trading days. Signs of the company's troubles were evident at the end of 2008, when Epix had $24.6 million in cash on hand. Epix burned through $36.45 million last year. The company received a going-concern letter - a red flag that a company may not survive another full year - from its auditor as part of its year-end earnings statement.

Epix has laid off all of its employees. CEO Elkan Gamzu, will stay on for a short period of time to assist in the liquidation. (Source: Julie M. Donnelly, Boston Globe, 22 July 2009)

WPI, CellThera Researchers Turn On Stem Cells

A team of researchers at Worcester Polytechnic Institute's Life Sciences and Bioengineering Center at Gateway Park in Worcester has found a way to turn on stem cell genes in human skin cells without inserting extra genes or using viruses. The team responsible for the discovery is made up of WPI faculty and investigators at CellThera, a private company located at the life sciences center.

According to the team, the discovery may be beneficial to the development of patient-specific cell therapy. Also, using skin cells means that tissue can be regenerated without some of the problems associated with using embryonic stem cells to do so, including ethical concerns and the potential for embryonic stem cells to be rejected by a patient's immune system or to grow out of control and cause tumors.

The team turned on stem cell genes already present in skin cells by lowering the amount of oxygen the cells were exposed to and adding a naturally occurring protein necessary for maintaining stem cells. The team said its research also suggests that there is a natural mechanism at work, yet unknown, in skin cells that regulates stem cell gene expression.

The work was funded by WPI, a grant from the National Institutes of Health and funding to CellThera from the U.S. Defense Advanced Research Projects Agency and the Army Research Office. (Source: Matthew L. Brown, Worcester Business Journal. 29 July, 2009)

RXi Pharmaceuticals Acquires Exclusive License to RNAi Delivery Technology

Worcester-based RXi Pharmaceuticals, a biopharmaceutical company pursuing the development and commercialization of proprietary therapeutics based on RNA interference (RNAi), has exercised its option to an exclusive worldwide license to novel technologies from Advirna LLC to enable *in vivo* delivery of RNAi therapeutics.

The RNAi delivery technologies licensed from Boulder, Colorado-based Advirna encompass four distinct approaches, with the primary focus on "self-delivery" of RNAi therapeutics; that is, RNAi delivery without the use of a separate delivery vehicle. In evaluating the Advirna technology, RXi observed that this technology delivers RNAi molecules to cells spontaneously upon direct administration, both *in vitro* and *in vivo*, without requiring a delivery vehicle or transfection formulation. RXi has reproduced this result in many cells, and has seen activity even with cells that are difficult to transfect.

RXi President and CEO Tod Woolf, PhD stated, "The ability to create self-delivering RNAi therapeutics promises to provide significant competitive advantages in efficacy, toxicity, ease of administration and manufacturing costs. This unique capability is creating a great deal of interest in the scientific and business community and we believe this exciting technology could simplify clinical development of RNAi therapeutics and could position RXi to take the lead in the area of RNAi therapeutics."

RXi is integrating its comprehensive delivery platform, including the new technologies licensed from Advirna, with its proprietary rxRNA compounds to develop a sustainable pipeline of products for unmet medical needs. RXi has a strong IP position in both RNAi compounds and delivery approaches and is using its scientific expertise in these areas to identify lead therapeutic candidates for inflammatory diseases, such as rheumatoid arthritis, diabetes, and Crohn's disease, as well as other indications. (Source: Business Wire, 27 July, 2009)

Regulatory & Legislative Highlights

by Deepen Joshi, Sepracor

FDA to Require Boxed Warning for Chantix (Pfizer) and Zyban (GlaxoSmithKline)

The FDA has announced that it is requiring manufacturers to put a Boxed Warning on the prescribing information for the smoking cessation drugs Chantix (varenicline) and Zyban (bupropion). The warning will highlight the risk of serious mental health events including changes in behavior, depressed mood, hostility, and suicidal thoughts when taking these drugs. The FDA's request for the additional warnings is based on a review of reports submitted to the agency's Adverse Event Reporting System since the time the products were marketed and on an analysis of information from clinical trials and scientific literature. The analyses revealed that some who have taken Chantix and Zyban have reported experiencing unusual changes in behavior, become depressed, or had their depression worsen, and had thoughts of suicide or dying.

In addition to the Boxed Warning, the FDA also is requesting more information in the Warnings section of the prescribing information and updated information in the Medication Guide for patients that further discuss the risk of mental health events when using these products. Manufacturers also will be required to conduct a clinical trial to determine how often serious neuropsychiatric symptoms occur in patients using various smoking cessation therapies, including patients who currently have psychiatric disorders. The FDA's review of adverse events for patients using nicotine patches did not identify a clear link between those medications and suicidal events. (Source: FDA Website, 1 July, 2009)

FDA Approves Sanofi-Aventis Drug Multaq to Treat Heart Rhythm Disorder

The FDA has approved Multaq tablets (dronedarone) to help maintain normal heart rhythms in patients with a history of atrial fibrillation or atrial flutter (heart rhythm disorders). The drug is approved to be used in patients whose hearts have returned to normal rhythm or who will undergo drug or electric-shock treatment to restore a normal heart beat. The drug's label will contain a boxed warning, the FDA's strongest warning, cautioning that the drug should not be used in severe heart failure patients. (Source: FDA Website, 2 July, 2009)

FDA Approves First Maintenance Drug Therapy for Advanced Lung Cancer

The FDA has approved Eli Lilly's Alimta (pemetrexed), the first drug available for maintenance therapy of advanced or metastatic lung cancer. Patients with cancer often receive maintenance therapy to prevent the disease from progressing after their tumor has shrunk or the disease has stabilized in response to chemotherapy. Alimta disrupts metabolic processes that are dependent on the B-vitamin folate, a necessary ingredient for cell replication.

Alimta initially was approved in 2004 for the treatment of patients with mesothelioma, a cancer frequently related to asbestos exposure. The drug was later approved for the treatment of patients with non-small cell lung cancer whose disease worsened on prior chemotherapy drugs and also as an initial therapy for advanced non-small cell lung cancer. (Source: FDA Website, 6 July, 2009)

FDA Approves Eli Lilly's Effient to Reduce the Risk of Heart Attack in Angioplasty Patients

The FDA has approved the blood-thinning drug Effient tablets (prasugrel) to reduce the risk of blood clots from forming in patients who undergo angioplasty, a common procedure to unblock a clogged coronary artery.

During an angioplasty, a balloon is used to open the artery that has been narrowed by atherosclerotic plaque. Often, a stent is inserted into the blood vessel to help keep the artery open after the procedure. Platelets in the blood can clump around the procedure site, causing clots that can lead to heart attack, stroke, and death.

The drug's labeling will include a boxed warning alerting physicians that the drug can cause significant, sometimes fatal, bleeding. The drug should not be used in patients with active pathological bleeding, a history of mini-strokes or stroke, or urgent need for surgery, including coronary artery bypass graft surgery.

Effient is manufactured by Eli Lilly and Company of Indianapolis, in partnership with Tokyo-based Daiichi Sankyo Ltd. (Source: FDA Website, 10 July, 2009)

FDA Reviewing Preliminary Safety Information on Genentech's Xolair

The FDA has announced that it is conducting a safety review of Xolair (omalizumab), a drug used to treat certain adults and adolescents with moderate-to-severe persistent asthma. Reviewers are looking for a possible association between patients who use Xolair and an increased risk of heart attack, abnormal heart rhythm, heart failure, and stroke. The possible association has been identified based on interim results from an ongoing study of Xolair known as Evaluating the Clinical Effectiveness and Long-Term Safety in Patients with Moderate to Severe Asthma (EXCELS). The study is being conducted by the manufacturer, San Francisco-based Genentech Inc.

An FDA Early Communication is available online. The Early Communication is in keeping with the FDA's commitment to inform the public about its ongoing safety reviews of drugs. Once its review is completed, the FDA will communicate its findings and any resulting recommendations to the public. Until the evaluation is completed, health care professionals and patients should be aware that the agency is reviewing data that may suggest a risk of adverse events. The FDA is not advising a change in prescribing or use of the drug. (Source: FDA Website 16 July, 2009)

FDA Approves Vaccine for 2009-10 Seasonal Influenza

The FDA has announced that it has approved a vaccine for 2009-2010 seasonal influenza in the US. The seasonal influenza vaccine will not protect against the 2009 H1N1 influenza virus that resulted in the declaration of a pandemic by the World Health Organization (WHO) on June 11, 2009. The FDA continues to work with manufacturers, international partners and other government agencies to facilitate the availability of a safe and effective vaccine against the 2009 H1N1 influenza virus.

Each year, experts from the FDA, WHO, CDC and other institutions study virus samples and patterns collected from around the world in an effort to identify strains that may cause the most illness in the upcoming season. The six vaccine brand names and manufacturers are: Afluria (CSL Limited), Fluarix (GlaxoSmithKline Biologicals), FluLaval (ID Biomedical Corporation), Fluvirin (Novartis Vaccines and Diagnostics Limited), Fluzone (Sanofi Pasteur Inc) and FluMist (MedImmune Vaccines Inc). (Source: FDA Website, 20 July, 2009)

FDA Authorizes Emergency Use of Another Test for H1N1 Influenza Virus

The FDA has announced it has issued an Emergency Use Authorization (EUA) for another diagnostic test for the 2009 H1N1 influenza virus. Emergency Use Authorization is part of Project BioShield, which became law in July 2004.

The EUA for the Focus Diagnostics Influenza H1N1 (2009) Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) diagnostic test is the third diagnostic test authorized under an EUA by the FDA since the public health emergency involving the 2009 H1N1 influenza virus was declared on April 26, 2009.

The EUA allows Focus Diagnostics to distribute the test to laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) to perform high complexity tests. This test is not typically utilized in a doctor's office; it is a complex laboratory test performed in an environment that has the necessary equipment. These tests are intended for use in the detection of the 2009 H1N1 influenza virus in patients with symptoms of respiratory infection.

The EUA authority allows the FDA to authorize the use of unapproved medical products or unapproved uses of approved medical products following a determination and declaration of emergency. The Focus Diagnostics test is an unapproved device whose use is authorized by the EUA. The authorization ends when the declaration of emergency is terminated or when the FDA revokes the authorization. (Source: FDA Website, 24 July, 2009)

FDA Approves Colchicine for Acute Gout and Mediterranean Fever

The FDA has approved Colcrys (Mutual Pharmaceutical Company, Inc.) to treat acute flairs in patients with gout, a recurrent and painful form of arthritis, and patients with familial Mediterranean fever (FMF), an inherited inflammatory disorder. The medication's active ingredient is colchicine, a complex compound derived from the dried seeds of a plant known as the autumn crocus or meadow saffron (Colchicum autumnale).

Colchicine has been used by healthcare practitioners for many years to treat gout but had not been approved by the FDA. The FDA has an initiative underway to bring unapproved, marketed products like colchicine under its regulatory framework. This initiative promotes the goal of assuring that all marketed drugs meet modern standards for safety, effectiveness, quality and labeling. The FDA is alerting healthcare professionals to this new dosing regimen and also warning about the potential for severe drug interactions when patients take colchicine.

The medicinal value of using colchicum was first identified in the first century AD and its use for treating acute gout dates back to 1810. Physicians have prescribed the medication since then. Although single-ingredient colchicine has not been approved by the FDA until now, a combination product containing colchicine and an agent that increased the excretion of uric acid in the urine was approved by the FDA in 1939. (Source: FDA Website, 30 July, 2009)

FDA Approves New Drug Treatment for Type 2 Diabetes

The FDA has approved Onglyza (saxagliptin), a once-daily tablet to treat Type 2 diabetes in adults. The medication is intended to be used with diet and exercise to control high blood sugar levels. Onglyza is manufactured by Bristol-Myers Squibb and marketed by Bristol-Myers and AstraZeneca Pharmaceuticals.

The hormone insulin keeps blood sugar (glucose) levels within a narrow range in people who don't have diabetes. People with Type 2 diabetes are either resistant to insulin or do not produce enough insulin to maintain normal blood sugar levels. Onglyza is in a class of drugs known as dipeptidyl peptidase-4 (DPP-4) inhibitors which stimulate the pancreas to make more insulin after eating a meal.

Approval of Onglyza was primarily based on the results of eight clinical trials. The application seeking FDA approval was submitted before December 2008 when the agency recommended that manufacturers of new diabetes drugs carefully design and evaluate their clinical trials for cardiovascular safety. Although Onglyza was not associated with an increased risk for cardiovascular events in patients who were mainly at low risk for these events, the FDA is requiring a postmarket study that will specifically evaluate cardiovascular safety in a higher risk population. (Source: FDA Website, 31 July, 2009)

FDA and EMEA Launch Good Clinical Practices Initiative

The FDA and the European Medicines Agency (EMEA) have announced an agreement to launch a bilateral Good Clinical Practices (GCP) Initiative, designed to ensure that clinical trials submitted in drug marketing applications in the US and Europe are conducted uniformly, appropriately and ethically. The initiative will begin with an 18-month pilot phase on September 1, 2009 and will focus on collaborative efforts to inspect clinical trial sites and studies. Products regulated by the FDA's Center for Drug Evaluation and Research in the United States, and by the EMEA for the European Union will be the focus of the initiative.

Key objectives of the FDA-EMEA GCP initiative will be:

1. To conduct periodic information exchanges on GCP-related information.

2. To conduct collaborative GCP inspections by sharing information, experience and inspection procedures, cooperating in the conduct of inspections, and sharing best-practice knowledge.

3. To share information on interpretation of GCP, by keeping each regulatory agency informed of GCP-related legislation, regulatory guidance and related documents, and to identify and act together to benefit the clinical research process.

At the conclusion of the pilot phase, a joint assessment will be made by the FDA and the EMEA, with the scope and process modified and amended as needed.

Companies planning on submitting their marketing applications simultaneously to the FDA and the EMEA, and interested in participating in the joint inspections component of the initiative should contact Leslie Ball, MD, director, Division of Scientific Investigations, Center for Drug Evaluation and Research, at Leslie.Ball@fda.hhs.gov. (Source: FDA Website, 3 August, 2009)

FDA Requires Cancer Warnings Required for TNF Blockers

The FDA is requiring stronger warnings in the prescribing information for a class of drugs known as TNF blockers. The warnings, which include an updated boxed warning, highlight the increased risk of cancer in children and adolescents who receive these drugs to treat juvenile rheumatoid arthritis, the inflammatory bowel disorder, Crohn's disease, and other inflammatory diseases. In addition, the FDA is working with manufacturers to explore new ways to further define the risk of cancer in children and adolescents who use these drugs. Additional required updates to the prescribing information include incorporation of reports of psoriasis associated with the use of TNF blockers. (Source: FDA Website, 4 August, 2009)

FDA Commissioner Outlines Vision on Enforcement to Support Public Health

Commissioner of Food and Drugs Margaret A. Hamburg outlined her commitment "to prevent harm to the American people" through swift, aggressive, and effective enforcement of FDA laws and regulations. Commissioner Hamburg highlighted six initial steps designed to hone the effectiveness and timeliness of the FDA's regulatory and enforcement system:

- Set post-inspection deadlines.
- Take responsible steps to speed the warning letter process.
- Work more closely with FDA's regulatory partners.
- Prioritize follow-up on warning letters and other enforcement actions.
- Be prepared to take immediate action in response to public health risks.
- Develop and implement a formal warning letter "close-out" process.

By taking these steps, Commissioner Hamburg said, the FDA will ensure that "violative inspection results are taken seriously, that warning letters and enforcement actions occur in a timely manner and that steps are taken to protect consumers in cases where immediate enforcement action is not possible." (Source: FDA Website, 6 August, 2009)

FDA Issues Final Rules to Help Patients Gain Access to Investigational Drugs

The FDA has published two rules that seek to clarify the methods available to seriously ill patients interested in gaining access to investigational drugs and biologics when they are not eligible to participate in a clinical trial and don't have other satisfactory treatment options.

To support the effort to help these patients, the agency also is launching a new Web site where patients and their health care professionals can learn about options for investigational drugs. In general, these options include being treated with a drug that has been approved by FDA, being given an investigational drug as part of a clinical trial, or obtaining access to an investigational drug outside of a clinical trial.

The new rule, "Expanded Access to Investigational Drugs for Treatment Use," makes investigational drugs more widely available to patients by clarifying procedures and standards. The other rule, "Charging for Investigational Drugs Under an Investigational New Drug Application," clarifies the specific circumstances and the types of costs for which a manufacturer can charge patients for an investigational drug when used as part of a clinical trial or when used outside the scope of a clinical trial.

The FDA has allowed expanded access to experimental drugs and biologics since the 1970s. That access has allowed tens of thousands of patients with HIV/AIDS, cancer, and other conditions to receive promising therapies when no approved alternative is available. (Source: FDA Website, 12 August, 2009)

FDA Approves Schering-Plough's Saphris for Schizophrenia and Bipolar Disorder

The FDA has approved Saphris tablets (asenapine) to treat adults with schizophrenia, a chronic, severe and disabling brain disorder, and to treat bipolar I disorder in adults, a serious psychiatric disorder that causes shifts in a person's mood, energy, and ability to function.

The most common symptoms of schizophrenia include hearing voices, or seeing things that are not there, having false beliefs (for example, believing that others are controlling thoughts, reading minds, or plotting harm), and being inappropriately suspicious or paranoid. These thoughts may be terrifying and can cause fearfulness, withdrawal, agitation or violence. Bipolar I disorder is a chronic, severe, and recurrent psychiatric disorder that causes alternating periods of depression and high, increased activity and restlessness, racing thoughts, talking fast, impulsive behavior, and a decreased need for sleep.

Saphris is in a class of drugs called atypical antipsychotics. All atypical antipsychotics contain a boxed warning that alerts prescribers to an increased risk of death associated with off-label use of these drugs to treat behavioral problems in older people with dementia-related psychosis (a brain disorder that lessens the ability to remember, think, and reason). Saphris is not approved for these patients. (Source: FDA Website, 14 August, 2009)

European Commission Approves Genzyme's Mozobil

Genzyme has announced today that the European Commission has granted marketing authorization for Mozobil (plerixafor injection), providing a significant new option for patients with the blood cancers lymphoma and multiple myeloma who require an autologous stem cell transplant.

In Europe, Mozobil is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to enhance mobilization of stem cells to the bloodstream for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma whose cells mobilize poorly. This indication allows physicians to use Mozobil in the broad group of patients who are at risk of poor mobilization, as well as those who have previously failed conventional treatment. The product has been granted orphan drug status in the EU and US.

Mozobil, in combination with G-CSF, is designed to release hematopoietic stem cells from the bone marrow into the bloodstream where they can be collected, making it more likely for patients with certain types of cancers to proceed to autologous transplant. Currently, before a transplant can take place, patients may receive a prescribed dose of chemotherapy and/or other drugs called growth factors to help mobilize their hematopoietic stem cells into the bloodstream. Once the cells are released into the bloodstream, they are collected in preparation for a transplant.

Approximately 55,000 hematopoietic stem cell transplants are performed each year globally for multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma, and other

conditions. Genzyme expects that over time and with further clinical development, Mozobil will be used in the majority of these procedures. Peak sales of the product in the transplant setting are projected to reach $400 million annually. (Source: Genzyme Website, 5 August, 2009)

Anika Therapeutics Receives Health Canada Approval for Monovisc

Anika Therapeutics, a leader in products for tissue protection, healing and repair based on hyaluronic acid (HA) technology, has announced that it received Health Canada approval for Monovisc, its single-injection viscosupplement approved for the treatment of osteoarthritis of the knee. Monovisc has been broadly available in the European Union since the second quarter of 2008.

"Health Canada approval marks an important next step as we continue to expand the geographic reach of our novel osteoarthritis treatment therapy and establish Monovisc as the premier single-injection product on the market worldwide," said Charles H. Sherwood, Ph.D., Anika's President and CEO. "We are successfully moving forward on our goal of achieving FDA approval for Monovisc in the US. The initial PMA modules have been submitted to the FDA and are currently under review. We expect to submit the final module containing the clinical study data prior to year-end 2009..." (Source: Anika Therapeutics Website, 20 August, 2009)

FDA Moves to Speed Access to Gaucher Drugs in Wake of Genzyme's Plant Shutdown

The FDA has moved to speed up access to experimental drugs for Gaucher disease to help offset likely shortages of Cerezyme, the world's leading treatment for Gaucher disease, made by Genzyme. Cambridge-based Genzyme recently shut down its plant in Allston after a virus halted production of Cerezyme and Fabrazyme, its treatment for Fabry disease, another rare condition.

Protalix BioTherapeutics Inc. and Shire PLC both said that they have been approached by the FDA about expanding access to their experimental drugs for the rare but serious disorder. Patients with Gaucher are deficient in an enzyme that breaks down a certain type of fat molecule. Fatty cells accumulate in the body, including in the spleen, liver, and bone marrow.

Protalix said the FDA has asked the company to consider submitting a treatment protocol that would allow use of its treatment, prGCD, under an expanded access program. Under this program, a treatment protocol may be submitted for a drug that has not yet been approved, but is in development for a serious disease for which no other therapy is available. Shire said it has already filed a treatment protocol for its drug, velaglucerase alfa (see related article below). Both Shire and Protalix said they would provide their drugs free of charge.

David Aviezer, chief executive of Protalix, expects approval of the treatment protocol within 60 days. He said the company is on track to file an application for full approval of the drug by the end of this year. Some analysts said the FDA's action gives a good indication of how the agency views the Protalix drug. "We view the FDA's request as clearly positive for Protalix, as it indicates FDA's comfort with prGCD's safety and efficacy data, and increases the likelihood of ultimate prGCD approval," said Brian Abrahams, an analyst at Oppenheimer & Co.

Cerezyme, an enzyme replacement therapy, is Genzyme's biggest-selling product and, at $200,000 a year, is one of the world's most expensive drugs. Cerezyme and Fabrazyme represented about 37 percent of the company's 2008 revenue of $4.6 billion. "The fact that the FDA has reached out to Protalix is not unexpected," said Geoff McDonough, senior vice president of the genetic diseases business at Genzyme. "They would be looking at all possible avenues." (Source: Toni Clarke, Reuters, 7 July, 2009)

FDA Accepts Shire's Treatment Protocol for Gaucher Disease Drug

Shire has reported positive results from the first of three Phase III studies of velaglucerase alfa, its enzyme replacement therapy in development for the treatment of Type 1 Gaucher disease. The company also announced that the FDA has accepted Shire's treatment protocol for velaglucerase alfa. The acceptance of the treatment protocol by the FDA will enable physicians to treat Gaucher patients with velaglucerase alfa prior to commercialization. Shire will initially provide velaglucerase alfa free of charge to patients who are enrolled in the protocol.

In addition, Shire has begun a rolling submission of a New Drug Application (NDA) to the FDA for velaglucerase alfa to treat patients with Type 1 Gaucher disease. The submission was initiated on July 30, 2009, three weeks after Shire received Fast Track designation. Fast Track designation allows a company to file the sections of the NDA as they become available and enables the agency to commence its review on a rolling basis. The company expects to complete the NDA submission by the end of this quarter.

"We are very pleased with the progress of the velaglucerase alfa program from both a clinical and regulatory perspective," said Sylvie Grégoire, President of Shire Human Genetic Therapies. "We will continue to work diligently with the FDA and other regulatory agencies to make velaglucerase alfa available as soon as possible to help meet the needs of the Gaucher community." (Source: Shire Website, 3 August, 2009)

New Members

Mohammed S. Akhtar, *Student,* Worcester Polytechnic Institute

Dr. Robert R. Boulanger, Jr., *Manager,* Protein Sciences

Michael Brundage, *Student,* Tufts University

Mr. Steven N. Brunner, *Director of QD,* InterSystems Corporation

Mr. Michael Cahill, *Facilities Manager,* Biomed Realty Trust Inc.

Mr. Russell M. Carson, *Associate Director, Facilities,* Mannkind Corporation

Mr. Robert L. Coulter, Jr., *Associate Director of Facilities,* University of Massachusettes Biologic Labs

Ms. Melissa Cutler, *Knowledge Mgmt Specialist,* Wyeth Pharmaceuticals

Mr. Paul J. Doherty, *Sr. Project Manager,* CRB Builders

Mr. David M. Dube, *Sr Comp. Val Eng.,* Shire HGT

Mr. Peter Ferguson, Bristol-Myers Squibb

Mr. Robert Fitts, *Life Scienes Application Engineer,* Spraying Systems Company

John Greco, *Process Engineer,* Genzyme Corporation

Mr. Vinh Huynh, *Validation Engineer/Compliance,* Genzyme Corp

Mr. Andrew R. Jankovich, *Senior Automation Engineer,* Independant Contractor

Dennis T. Kassick, *MEP Manager,* Whiting-Turner Contracting

Mr. Jeffrey Maciak

Mr. Foster Malcom, *Associate Process Engineer,* Parsons Corporation

Mr. Jeff N. Pearsons, *Automation Engineer,* Millipore

Ms. Susan M. Richter, *Principal Engineer,* Wyeth

Mr. John F. Ryan, *Process Engineer,* Pall Biopharmaceuticals Corp

Mr. Erik D. Sandler, *Facilities Manager,* Biomed Realty Trust Inc

Tim Schmidt, *Engineer*

Dr. Stacy L. Springs, *Biomanufacturing Program Director,* MIT Center for Biomedical Innovation

Mr. Erik W. Swanson, *Manager,* AstraZeneca

Mr. Ronald E. Whelan, *Sales Manager,* Atlas Copco Compressors LLC

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