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Newsletter

A publication of the Controlled Release Society

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CRS Newsletter
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Table of Contents

Advertisers' Index

Cover photo from the Young Scientist Committee Event at the BridgePort Brewery.

The CRS Newsletter is the official newsletter of the Controlled Release Society. The newsletter is published five times annually providing scientific and technical information pertinent to the controlled release community and news about society and chapter activities. Members can receive the newsletter via mail. The newsletter may also be viewed online at www.controlledreleasesociety.org.

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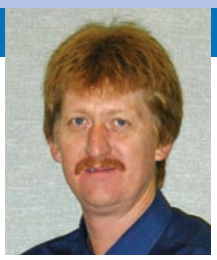
From the Editor



Prof. Roderick B. Walker
Rhodes University
Republic of South Africa

Portland, Beer, World Cup Soccer, and Vuvezelas

The 2010 CRS Annual Meeting & Exposition in Portland, OR, has come and gone and with it the memories of an excellent scientific programme and a meeting with a number of firsts, as Mark Tracy mentions in his first "From the President" column. Indeed, the last time I wrote the "From the Editor" column I mentioned that CRS is an organization on the move and that change is afoot. This has been seen with the introduction of Innovation Sunday, the announcement of a College of Fellows, the Women in Science luncheon, and various new awards amongst a whole lot of other events. However, I would like for the organizers of future conferences to consider inviting people to give a plenary lecture who are not leading scientists in various fields of research, but who have made sacrifices to go and work in the developing world, in regions that have no access to first world healthcare, and who have made a significant impact on the quality of life in those regions. Perhaps they could also consider Bill and Melinda Gates and other funders of research who are trying to alleviate the disease burden in a global sense.

This edition of the *CRS Newsletter* includes photographs and snippets of news from the annual meeting so those members of our Society who could not make the conference can at least share a little of the meeting.

There was beer at the meeting too, and plenty of it, from a multitude of breweries in what has been called the beer capital of the world. In fact, it seems that there may be a need to establish a new section of CRS that deals specifically with the "Science that Is Beer." An article detailing the events of the night at the BridgePort Brewery can be found in this issue. Congratulations must go to the Young Scientist Committee for organizing what appeared to be a highly informative and successful event. Another successful initiative of the Young Scientist Committee is the Mentorship Programme, and this issue contains a summary of what mentoring is for those embarking on this journey.

There are also some regular features in the *Newsletter*, and as always, I found these to be enlightening and interesting. The Scientifically Speaking articles are fascinating, covering topics related to magnetic droplets as drug carriers and SMEDDS. The veterinary article on pharmacogenetics makes one realise that the results of animal studies must be interpreted with care and that knowledge of genetic variation in animals is as important as it is in humans. There is also Chapter news from Italy, news from around the globe in the "In the News" section, and a summary of the R&D resources at the Southwest Research Institute. The "Back to Basics" article covers important aspects of dissolution testing using apparatus 2.

In closing, it would be remiss of me not to mention the showcase event that was World Cup Football (if you are from the United Kingdom) or Soccer (if you are from the United States), which was hosted in South Africa during June and July. The event was amazing for South Africa, and we were able to showcase our country in a positive way. There were also a number of firsts in the World Cup, including the first time it was held in Africa, the first time the host nation and a defending champion was eliminated in the opening round, the first time Spain won the event, and of course the vuvuzela was heard throughout the world. In fact there were one or two in Portland. The word "*kinako*," a Xhosa word that means "feel it, it is here," was used to mobilize a nation for the World Cup. Perhaps the time is right to take the "Science of Controlled Release" to other parts of the world, so that we scientists too can shout "*kinako*!" ■

Mark A. Tracy
Alnylam Inc.
Cambridge, MA, U.S.A.

I am grateful, excited, and above all honored to have the opportunity to serve the Controlled Release Society and you, our members, as president over the upcoming year. I would like to thank immediate Past President Diane Burgess for her service as president over the last year and for her dedication and commitment to the CRS. I have big shoes to fill!

As I write this column, I am on a plane returning home from our 37th Annual Meeting & Exposition in Portland, OR, admiring from my window the beautiful and majestic Mt. Hood proudly rising above the clouds and, just below her, the mighty Columbia River. Portland is indeed a special place, and the CRS Annual Meeting, held July 10–14, was a special meeting. The scientific and technical program was world-class. I would especially like to thank our meeting program chairs Ick Chan Kwon, David Putnam, Leila Zarif, Christophe Barbe, James Oxley, Mike Rathbone, and Jim Riviere, supported by Scientific Secretary Ijeoma Uchegbu, for their exemplary efforts in assembling such a strong scientific and technical program with contributors from around the world.

In addition, the Portland meeting marked several firsts for CRS. The Innovation Sunday program brought together, on a single day, activities focused on delivery science and technology in the commercial sector, including the Soapbox Sessions, Releasing Technology Workshops, new panel discussions on starting-up delivery companies and building partnerships, the State of the Industry Keynote, our new CRS Partnering program, and the grand opening of the exposition and welcome reception. A special thanks to Marketing Committee Co-chairs Claire Madden-Smith and Vinay Chhatre and Soapbox Chair Eyal Ron, supported by Treasurer Debra Bingham and CRS staff, for producing such a successful event.

Bringing our members together both professionally and socially is a key goal of our meetings, so we held several new networking events, including a networking night at the BridgePort Brewery organized by the Young Scientist Committee; a Women in Science Luncheon championed by Diane Burgess; and an After Party following our Closing Banquet at the beautiful Portland Art Museum organized by the Membership Committee. All of these events were wonderful ways to catch up with long-time friends and make new acquaintances.

We also announced our 2010 award winners, including a new award for our chapters, the new Jorge Heller Postdoctoral Fellowship, and our new College of Fellows. Congratulations to all 2010 award winners and to our inaugural class of Fellows! In addition, we announced a new CRS journal, *Drug Delivery and Translational Research*, which will focus on translational aspects of delivery as a complement to our premier journal, the *Journal of Controlled Release*, and a new CRS book series, both in collaboration with Springer. Both new publications are scheduled to debut in 2011.

What a meeting! We had cutting-edge delivery science and technology plus a vibrant exposition, the announcement of a new journal and book series, innovative industry and young scientist programs, greater recognition of excellence in our field, and increased networking opportunities. We are fortunate to have such dedicated volunteers, sponsors, and staff to make all of this happen. Thank you! Be sure to mark your calendars for our 38th Annual Meeting, which will be held July 30–August 3, 2011, near Washington, DC. You do not want to miss what promises to be another special event. Also, please check our website for information on our upcoming workshops and the new Product Development Forum in January, another first as we strive to enhance our benefits to our members year-round. In addition, CRS also approved a bylaw change that will give you a full 12 months of membership regardless of when you join or renew your membership.

As reflected in the Portland meeting, it is a great time to be a member of CRS and to work in our field of delivery science and technology. Advances in research are enabling solutions to challenging problems in delivery. Scientific advances are also resulting in the development and commercialization of an increasing number of novel delivery-based products that are expanding the field. As CRS president, I will continue to work with the Board, staff, our committees, sponsors, and you, our members, to initiate and promote activities that prepare the Controlled Release Society for the new decade and enhance your ability to contribute to and benefit from the rapid developments in delivery science and technology. My vision is to provide enhanced member benefits year-round and greater awareness of the CRS as the premier society worldwide for delivery science and technology. I look forward to sharing our progress toward these goals with you through this column, our website, and in person over the next year. I also welcome hearing your thoughts and ideas. I encourage you to help as a volunteer and give back to your Society in support of these exciting goals and activities. I very much look forward to the coming year!

Mark A. Tracy ■

Interview with Barbara J. Mock

Brian Kilfoyle and Bozena Michniak-Kohn, Ph.D.
Ernest Mario School of Pharmacy, Rutgers-The State University of New Jersey, Piscataway, NJ, U.S.A.

Barbara J. Mock is a CPA, CMA, MBA, and MLS currently working for six international non-profit member associations, including The American Phytopathological Society, AACC International, the International Society for Molecular Plant-Microbe Interactions, the American Society of Brewing Chemists, the Master Brewers Association of the Americas, and the Controlled Release Society. From 2005 to present, she has been the vice president of finance and administration for the Controlled Release Society. In this position, she has numerous duties, including overseeing finance, human resources, information technology, and administration. Her responsibilities are typical of those of senior financial management and include being a liaison to the CRS Board and Treasurer with regard to strategic financial planning and reporting, budgeting, and business modeling, forecasting, auditing, and tax return preparation. She recently led the request for a proposed process for banking and cash management services, investment manager selection, health insurance, general liability insurance, and audit services resulting in overall organizational savings.

CRS Treasurer Debra Bingham, who interacts with Barbara on a nearly daily basis, calls Barbara the "key financial contact on staff. She is the staff accountant. She keeps the Society books, coordinates our annual audit, and supports the Finance Committee and Board of Directors with all of the financial duties and responsibilities that we have." When asked what personal qualities make Barbara successful, Debra continued, "Barbara is very organized, detailed oriented, and educationally qualified. She has a kind and service oriented way of conducting the duties of tracking expenses."

Before working for the six non-profit member societies mentioned above, Barbara worked as a controller at American Public Media Group (1998–2005), a controller at the American Academy of Neurology (1993–1998), at Health Systems Minnesota as the manager of treasury and operations analysis (1991–1993) and as a senior accountant (1987–1991), and at Deloitte & Touche as a senior accountant (1983–1987). Barbara has also served as a part-time instructor with Employers Association, Inc. (2003–present), Minnesota Bankers Association (2000–present), and at Rasmussen College (1995–1997).

Barbara obtained her B.S. degree in accounting and finance from Mankato State University (1983); her MBA, with a concentration in finance and management, from the University of St. Thomas (1994); a mini-master's degree in software design and development from the University of St. Thomas (2001); and a master's of liberal studies degree with an Innovation Studies Certificate from the University of Minnesota (2007). She is a Certified Public Accountant (1983) and a Certified Management Accountant (1995).

Barbara was kind enough to work with us on a brief interview to provide some insights for our readers into the behind-the-scenes work that goes on at the Controlled Release Society headquarters.

Interview

Q ***In the role of vice president of finance and administration for the Controlled Release Society, what are your key responsibilities? Could you elaborate on the importance of these responsibilities to the Society?***

A I work very closely with Debra Bingham, the CRS Treasurer, in relation to CRS financial statement reporting, budgeting, tax reporting, investment management, and risk management. I work with the CRS Finance Committee to provide detailed analysis of specific programs and build business plans for the future. CRS is audited annually by an outside Certified Public Accounting firm.

Q ***How has your career prepared you for these responsibilities?***

A I have been an auditor with Deloitte Touche, one of the big 4 public accounting firms. I am a nonprofit specialist with previous controller responsibilities for American Public Media Group and the American Academy of Neurology.

Q ***What do you enjoy most about your position?***

A Our staff enjoys working with the members to create new strategies that will build services and value for the future.

Q ***What do you enjoy least about your position?***

A I am fortunate to enjoy my work, so this is a difficult question to answer.

Q ***What is the financial state of the Controlled Release Society? Has the CRS been affected by the global economic downturn?***

A CRS is in good financial shape. Yes, CRS was affected by the global economic downturn. CRS equity investments declined in accordance with the overall market decline in 2008, but they have recovered.

Q ***Are all of our revenues from member dues? If not, where else do we derive revenue from? What types of investments does the CRS make to secure its future?***

A About 10% of the CRS revenues are derived from member dues. The annual meeting and exposition is the largest contributor of revenue at about 70% of the overall total revenue. Other sources of revenue include satellite meetings, journal revenue, and investment income.

Q ***Do you have a role in planning the annual CRS meeting? If so, could you please elaborate?***

A I have a limited role in planning the annual meeting. I work closely with the Treasurer in the meeting budget process.

Q ***Would you like to recognize anyone who works closely with you at CRS headquarters?***

A While five or six staff work closely with CRS, there are over sixty staff who work in St. Paul at Headquarters for the multiple societies. Many of these staff also contribute to CRS. Staff who I work closely with include Amy Hope and Jody Grider, who handle the CRS Annual Meeting, membership, and committees, and Kim Flanegan, our accounting manager.

Q ***Outside of working at the CRS, what are your other interests?***

A I volunteer for Midwest Avian Adoption Rescue Services. We take care of unwanted pet birds such as cockatoos, macaws, cockatiels, etc. My partner and I have farm land in southern Minnesota and a lake home in northern Wisconsin that keep us busy. We recently worked with the Department of Natural Resources to restore the lake shore to a natural shoreline for the benefit of the wildlife. ■

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Congratulations 2009 and 2010 CRS Awardees!

The Controlled Release Society's awards ceremonies held during the 37th CRS Annual Meeting & Exposition in Portland, OR, honored and recognized deserving scientists from around the globe. Thank you to the many sponsors who provided their time and financial support to promote the talented scientists and innovative science. ■

Mark Tracy presents Vladimir Torchilin, Northeastern University, with the CRS Founders Award.

Gopi Venkatesh and Mark Tracy present Krish Roy, University of Texas-Austin, with the CRS Young Investigator's Award, co-sponsored by Eurand Pharmaceutical Technologies.

Tsuneji Nagai and Mark Tracy present Sang Kyoon Kim and his advisor, Leaf Huang, University of North Carolina, with the CRS/T. Nagai Postdoctoral Research Achievement Award, co-sponsored by The Nagai Foundation Tokyo.

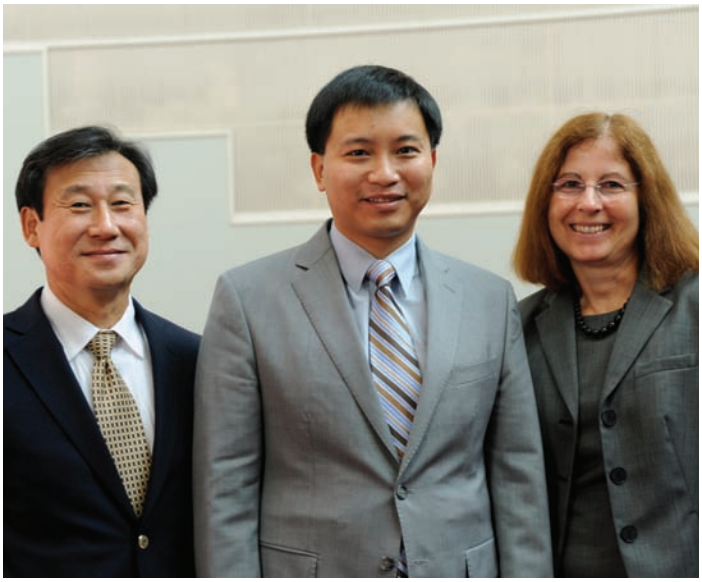
Jaap van Harten and Mark Tracy present Jörg Kreuter, University of Frankfurt, and Larisa Mihoreanu, King's College London, with the CRS Jorge Heller Journal of Controlled Release *Outstanding Paper Award, co-sponsored by Elsevier. Recipients not pictured: Anja Zensi, David J. Begley, Charles C. Pontikis, Celine Legros, Sylvia Wagner, Claudia Büchel, and Hagen von Briesen.*

Scott Wilson, Georgia Institute of Technology, receives the CRS Outstanding Oral Drug Delivery Paper Award, co-sponsored by Banner, from Tim Doran and Mark Tracy.

Kashappa-Goud Desai, University of Michigan, receives the CRS Outstanding Consumer & Diversified Products Paper Award, co-sponsored by Givaudan, from Robert Wieland and Mark Tracy.

Mark Tracy presents Thierry Vandamme, University of Strasbourg, with the CRS Outstanding Veterinary Paper Award, co-sponsored by Intervet.

Mark Tracy presents Oleh Taratula, Rutgers University, with the CRS Outstanding Pharmaceutical Paper Award, co-sponsored by Elan Drug Technologies.



Kinam Park and Susan Cady with Qun Wang, University of Kansas, the first recipient of the CRS Foundation Jorge Heller Postdoctoral Fellowship.

The inaugural CRS College of Fellows in attendance.

Who Will Be CRS Keynote Speakers in 2017?
Who Will Be CRS President in 2022, 2050, and Beyond?
Who Will Inspire Scientists of the Next Generation?

Future leaders need a strong foundation. CRS Foundation fellowships are designed to identify and acknowledge the future leaders of CRS, while honoring individuals who have made notable contributions to the Society and delivery technologies. By providing a catalytic amount of funding as well as recognition, the CRS Foundation's goal is to accelerate these outstanding scientists in their careers in delivery science and to create a long-term home for them within CRS.

Kinam Park, CRS Foundation Selection Committee Chair (left), and Susan Cady, CRS Foundation Board Chair (right), celebrate with David Nhu Nguyen, Joseph R. Robinson Postdoctoral Fellow, and Qun Wang, Jorge Heller Postdoctoral Fellow (center).

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Future fellowships will honor past and present leaders, ProfessorsTsuneji Nagai and Sung Wan Kim.

CRS Foundation Recognizes Two Postdoctoral Fellowships at 2010 CRS Annual Meeting

Qun Wang Selected for Prestigious Award Jorge Heller Postdoctoral Fellowship 2010

Susan Cady, CRS Foundation Chair, presents Jorge Heller Postdoctoral Fellowship to Qun Wang.

Qun Wang was honored with the Jorge Heller Postdoctoral Fellowship during the Awards Showcase at the 37th CRS Annual Meeting & Exposition. Acknowledging the support of his advisor, Prof. Cory Berkland (University of Kansas), and thanking the Selection Committee and CRS Foundation, Qun Wang accepted the $30,000 award that will support advanced research and travel for his fellowship year. He also met with attendees to discuss the poster he co-authored that highlights his research, "Injectable Colloidal Gels Offer Zero-Order Dexamethasone Release and Cranial Defect Filing" (poster 209, co-authored by Q. Wang, J. Wang, Q. Lu, M. Detamore, and C. Berkland).

Qun Wang

Selected for the second CRS Foundation fellowship from a pool of outstanding candidates, Qun Wang obtained a Ph.D. degree in environmental science from Wuhan University in 2007 and will soon complete another doctoral degree in chemical engineering, under the supervision of Dr. Cory Berkland, joint professor in the Department of Pharmaceutical Chemistry and the Department of Chemical Engineering, University of Kansas. Qun is interning at Cephalon Inc. as a formula scientist in orally disintegrating tablet, oral transmucosal, and oral powder drug delivery technologies. Qun's research focuses on the interface of engineering and pharmaceutics in the areas of polymer science and engineering, drug delivery systems, biomaterials, nanotechnology, tissue engineering, and "green" materials. He has created many novel materials for drug delivery systems and tissue engineering, including films, fibers, self-assembling colloids, gels, nano- and micro-particles. His recent research is in the use of biodegradable materials to make injectable 3D porous nano-colloidal scaffolds for tissue engineering and drug release systems. He has published 17 papers in well-known referred journals, including *Advanced Materials*, *Biomaterials*, *Journal of Membrane Science*, *European Journal of Pharmaceutics and Biopharmaceutics*, and *International Journal of Pharmaceutics*. He holds seven patent licenses in the United States and China.

David Nhu Nguyen Presents Research from Fellowship Year Joseph R. Robinson Postdoctoral Fellowship 2009

David Nhu Nguyen presents his research during the CRS Awards Showcase.

The CRS Foundation welcomed back 2009 fellowship awardee David Nhu Nguyen to reflect on his work over the past year, made possible by the Joseph R. Robinson Postdoctoral Fellowship. With thanks to colleagues and mentors, as well as the CRS Foundation donors and Board of Directors, David presented "Delivering Innate Immune Signals for Vaccine Adjuvants" (co-authored by D. Nguyen, G. Chikh, D. Anderson, R. Langer, and D. Lewis), which focused on understanding the major role that drug delivery plays in activating nucleic acid receptors in order to engineer vaccine adjuvants. Two projects undertaken during his fellowship year were the semi-rational, combinatorial design of lipidoid nanoparticles for the delivery of immunostimulatory RNA (isRNA) and the use of novel cationic lipid DNA complexes (CLDCs) currently in human clinical trials as an adjuvant for influenza vaccines. The research team is currently exploring both TLR-related and intracellular receptors as the potential mechanism of CLDC-mediated adjuvant activity.

David Nhu Nguyen

David has extended his work on vaccines and vaccine adjuvants through postdoctoral fellowships in the Langer laboratory at MIT and now in the laboratory of Dr. David Lewis at Stanford University. Currently at the Stanford University School of Medicine, where he is conducting research while pursuing a medical degree, David's interests are in combating infectious diseases through novel technologies for vaccination, vaccine adjuvants, and antiviral therapies. With undergraduate degrees in biology and chemical engineering from MIT in 2002, David completed a doctorate in 2008 in materials science and medical engineering through MIT and the Harvard-MIT Division of Health Sciences and Technology. At MIT he worked in the laboratory of Prof. Robert Langer on a variety of nucleic acid delivery applications, including biomaterials for delivering DNA vaccines, RNA interference of viruses such as influenza and hepatitis C, and immunostimulatory RNA drug delivery. At MIT he was also heavily involved in undergraduate education and mentorship.

The 2010 and 2009 fellowships honor CRS Past Presidents Jorge Heller and Joseph R. Robinson, whose passion for the Society and the science have provided past, present, and future leadership.

Magnetic Aerosol Droplets as Drug Carriers

R. Baumann,[1] G. Glöckl, and W. Weitschies
Institute of Pharmacy, Ernst-Moritz-Arndt-University, Greifswald, Germany

Introduction

Lung cancer is one of the most common types of cancer, and non-small cell lung cancer is especially difficult to treat, with poor prognosis for patient survival. Although there are established drugs, these do not show any effect in more than 50% of the patient population. It is our goal to accumulate effective drug doses in diseased lung regions using inhalative magnetic drug targeting (MDT).

Aerosols offer the possibility of loco-regional drug delivery, allowing for far smaller doses of chemotherapeutic agents and reduction of systemic exposure. Major handicaps associated with inhalation are the deposition of large droplets in the upper airways, which are associated with therapy-limiting adverse reactions and the loss of chemotherapeutic drugs due to exhalation of droplets smaller than 1 µm. To avoid adverse reactions and deposition of aerosol droplets loaded with cytostatic drug in regions of the lung that are not diseased, we attempted to reduce the droplet size to less than 1 µm. In this case, magnetic retention forces acting on the aerosol droplets may increase deposition probability in the diseased lung.

MDT Concept

For MDT a suspension of magnetic nanoparticles in water (ferrofluid) containing cytostatic drug is atomized and inhaled (Figure 1). A magnetic field is arranged close to the lung in the region of the lung cancer. In magnetic fields the dipoles of magnetic nanoparticles tend to align in the direction of the magnetic flux. A net magnetic movement of the solution is generated, and the aerosol droplets are moved to the magnetic poles. Magnetic nanoparticles in the diseased lung are deposited due to the magnetic gradient field. Magnetic aerosol droplets that are inhaled in the other lung lobe are exhaled because they are too small to be deposited on their own.

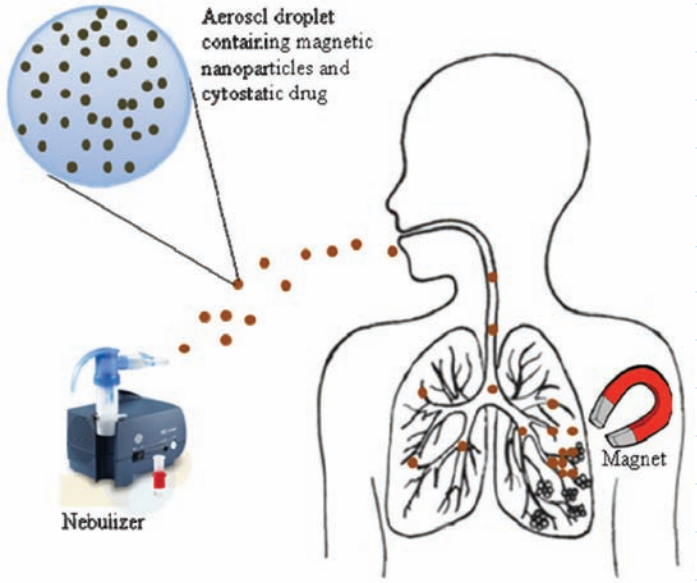

Figure 1. *Concept for magnetic drug targeting, modified according to C. Planck (1).*

Materials and Methods

To synthesize the ferrofluid, $FeCl_2$ and $FeCl_3$ were dissolved in water. Ammonium hydroxide was added to precipitate magnetic nanoparticles (MNP) consisting of Fe_3O_4 (magnetite). The resulting suspension was stirred, heated, and washed. Citric acid was added to coat the MNP in order to prevent aggregation and sedimentation. The hydrodynamic diameter of magnetite nanoparticles determined by photon correlation spectroscopy was approx. 100 nm.

Two different nebulizers were used to atomize the ferrofluid to vary the median mass diameter (MMD) of the droplets. The aerosol droplet size was measured by laser diffraction (MasterSizer MS30, Malvern Instruments, UK). The eFlow (Pari GmbH, Germany) generated aerosols using a vibrating membrane and created a MMD of 3 to 8 µm. The pneumatic nebulizer (Pari Boy SX, Pari GmbH, Germany) generated aerosol droplets of 3 µm. Cremophor RH 40, ethanol, and sodium chloride were used as additives to vary the surface tension and density of the ferrofluid and to reduce the droplet size.

The deflection of magnetic droplets was investigated in the magnetic field of two opposing circular disc permanent magnets (r = 25 mm, l = 15 mm) with a magnetic remanence of 1,450 mT at a distance of 20 and 40 mm between the magnets. The resulting magnetic field gradients were calculated with Mathematica®.

Approximately 50 mg of iron was sprayed into a square tube (5 × 2 cm) that was placed centrally between the two opposing magnets. The walls of the magnets were covered with paper. The paper with the deposited MNP was decomposed, and the iron content was quantified by flame atomic absorption spectrometry.

Results and Discussion

The strongest magnetic field gradients were generated at the edges of the opposing circular disc magnets. The gradients near the pole surface were up to 120 T/m. At a distance of 20 mm between the magnets, a nearly homogeneous gradient of 15 to 20

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Scientifically Speaking Baumann continued on page 12

Scientifically Speaking Baumann continued from page 11

T/m was achieved. The gradients decreased with increasing distance.

Atomization by the pneumatic nebulizer (Pari Boy SX) was robust and nearly unaffected by external conditions. In contrast, high fluctuations in aerosol droplet size created by eFlow that did not relate to surface tension or density were observed. Ethanol, sodium chloride, and cremophor RH 40 reduced the MMD of the droplets generated by Pari Boy SX. The droplet size of eFlow increased with the addition of adjuvants (Table 1).

Table 1. Aerosol droplet size of 0.5 and 1*M* ferrofluid with additives

	Pariboy SX		eFlow	
	0.5*M*	**1*M***	**0.5*M***	**1*M***
Ferrofluid	2.68	2.57	5.05	4.53
+ Ethanol 10%	2.60	2.53	6.25	5.24
+ NaCl 0.9%	2.39	2.44	5.06	4.77
+ Cremophor RH40 0.1%	2.58	2.47	6.35	5.55

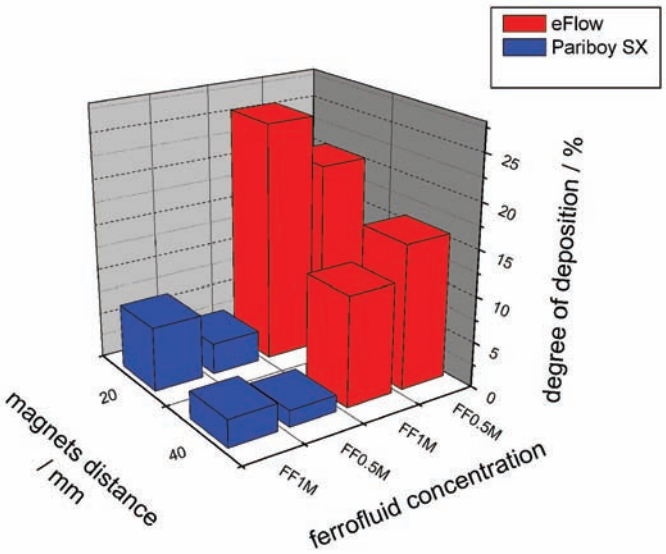

Figure 2. *Degree of deposition of 0.5 and 1*M *ferrofluid using different nebulizers and varying distances between magnets.*

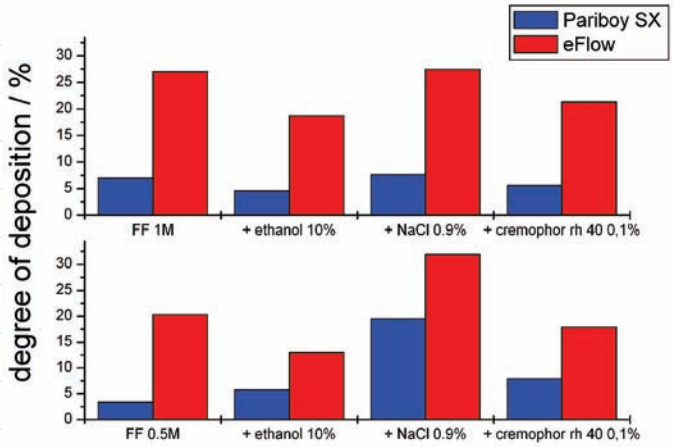

Figure 3. *Degree of aerosol deposition of 1*M *(top) and 0.5*M *(bottom) ferrofluid and influence of ethanol, sodium chloride, and cremophor RH 40 at 20 mm between magnetic poles.*

Atomic absorption spectrometry showed that up to 26% of iron was intercepted on the paper (Figure 2). The deposition of ferrofluid decreased considerably with decreasing magnetic field gradients (increasing distance between the magnetic poles). The best deposition was achieved by eFlow. This was most likely due to a slow droplet velocity and large droplet size of up to 6.5 µm generated by the vibrating membrane. Big droplets contained more MNP and were deflected more easily. This high deposition was not applicable for MDT, however. Aerosol droplets of this size only reached the upper airways and led to adverse reactions due to high deposition in the mouth and trachea.

The addition of sodium chloride increased the deposition of ferrofluid. In contrast, ethanol and cremophor RH 40 decreased ferrofluid deposition (Figure 3). The highest degree of deposition was reached using eFlow, which generated large aerosol droplets that were not applicable for MDT. Future efforts will be directed toward the generation of smaller droplets with diameters between 0.5 and 1 µm.

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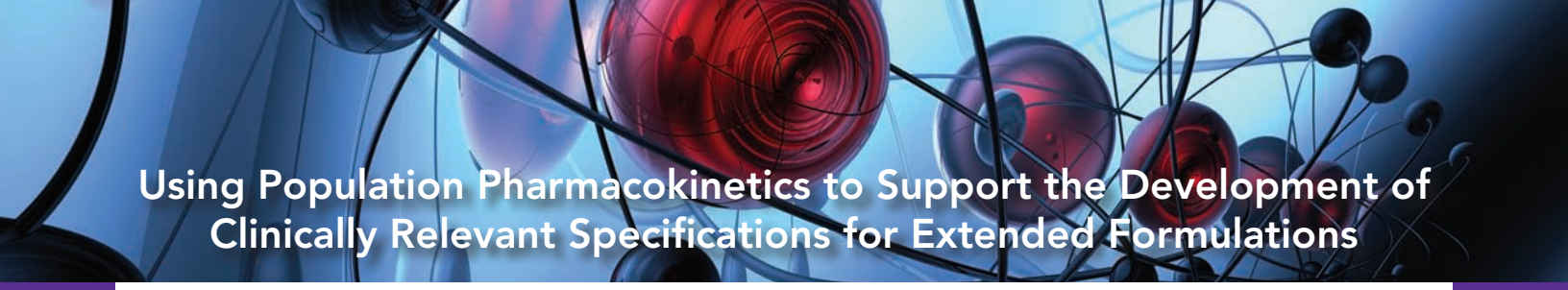

Using Population Pharmacokinetics to Support the Development of Clinically Relevant Specifications for Extended Formulations

A workshop co-sponsored by the American Association of Pharmaceutical Scientists and the Controlled Release Society.

Saturday, November 13, 2010 • 8:30 a.m. – 5:00 p.m.
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The Quality by Design (QbD) paradigm is ushering in new approaches for achieving a streamlined, knowledge-based process for generating products optimized to meet patient needs. Development of a Quality Target Product Profile (QTPP) can help maximize the likelihood of achieving the therapeutic objective by linking critical product quality attributes (CQAs) to the desired *in vivo* performance. In this workshop, we will discuss developing a QTPP through PK/PD modeling and simulation approaches that will enable linking CQAs to clinical outcome. Through the integration of population PK/PD models established on the basis of clinical trial data, this integrative approach could ensure the establishment of *in vitro* drug dissolution/release methods that link to the desired *in vivo* product performance, thereby providing dissolution/release criteria that are consistently informative and clinically relevant.

Who should attend?

Bench and clinical scientists involved in the development or regulation of modified release formulations and the optimization of dosing strategies.

Speakers include:

Introduction and objectives. *Marilyn Martinez, FDA*
Quality by Design: Impact on drug development and its global applications. *Moheb Nasr, FDA*
Design space and product specifications: A risk assessment approach. *Raafat Fahmy, FDA*
Quality Product Target Profile: Integrating product *in vivo* performance in a patient population with product design. *Arzu Selen, FDA*
Development of oral drug delivery platforms based upon patient GI characteristics. *Kevin Johnson, Intellipharm, LLC, and John Crison, Bristol-Myers Squibb*
A nonlinear mixed effects IVIVC model for multi-release drug delivery systems. *Adrian Dunne, Johnson & Johnson and University College Dublin*
The use of therapeutic drug monitoring to identify the relationships between optimized dosing strategies (input function) versus patient characteristics (covariates): Using this information to develop a target for *in vivo* product release characteristics. *Roger Jelliffe, University of Southern California*
The development of mechanistic population pharmacokinetic models to support the development of targeted release characteristics from modified release dosage forms. *William Jusko, University at Buffalo*
The use of modeling and simulation to target dosing strategies and predict optimal *in vivo* product release characteristics in a pediatric population. *Jeffrey Barrett, Children's Hospital of Philadelphia*
Integrating target *in vivo* performance characteristics into product design and specifications. *Maria T. Cruanes, Merck & Co., Inc.*

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SMEDDS as a Delivery System for Simvastatin: A Rational Formulation Approach

A. Sprunk,[1,2] C. J. Strachan,[1,3] T. Rades,[1] and A. Graf[1]

Why Choose SMEDDS as a Drug Delivery System?
SMEDDS (self-microemulsifying drug delivery system) has received considerable attention in the oral delivery of lipophilic and poorly water-soluble drugs to overcome poor and erratic bioavailability (1). Oral administration of SMEDDS results in the formation of a microemulsion by dispersion in gastric fluids, which is facilitated by the gentle agitation of the gastrointestinal tract. The large number of small droplets containing solubilised drug leads to a considerable increase in surface area and, hence, improved bioabsorption (1). The composition of these systems is usually complex and involves multiple components (e.g., drug, surfactant mixture, cosurfactant, and lipids). There are a number of requirements that these formulations must simultaneously meet for pharmaceutical applications, such as biocompatibility of the excipients and dilutability without phase separation even under drug load. Furthermore, the drug must remain dissolved upon dilution until it can be absorbed from the GIT (2).

Why Employ a Mixture Experimental Design for SMEDDS Development?
In most cases, development of SMEDDS has not been systematic. Researchers have generally used model systems previously found to be suitable for specific drugs. Therefore, it is difficult to extract general concepts or conclusions from these formulations that could make the development of these systems more feasible (1).

One might take a systematic approach by changing only the amount of one mixture component at a time. This would result in the performance of multiple experiments from which, subsequently, a more or less optimized formulation could be chosen. This "one-factor-at-a-time" approach might provide systematic comparisons among formulations and reveal the effects of individual components, but it is rather inefficient and unreliable in finding the optimal formulation. Specifically, when non-linear interactions between components take place, the optimum region can no longer be found by calculating linear sums of component factors and their effects on the formulation. In addition, the multiple requirements a formulation must meet for pharmaceutical administration might conflict, thus imposing even more difficulties.

With the help of an experimental design, however, the experimenter is able to consider multiple requirements. Multiple variables are changed simultaneously in a strategic way, resulting in fewer experiments and more meaningful results. The established model is able to pick up on non-linearities. Effects of and interactions between variables can be revealed and regions of desirable formulation compositions identified (3).

In this work experimental design was employed to determine appropriate experimental points for fitting quadratic models based on partial least squares (PLS) analysis. For model interpretation and formulation optimization, response surface methodology (RSM) was used.

Preparation and Characterization of Phase Diagrams
To compare the phase behaviour of the different combinations of surfactants and oil, ternary and quaternary phase diagrams were constructed and examined for the largest microemulsion area. The systems solubilising the highest amounts of simulated gastric fluid (SGF) in the continuous microemulsion area were selected for further study (Table 1; Figure 1).

Combinations of high HLB surfactants (labrasol [Lab] and polysorbate 80 [PS80]) with a cosurfactant showed that systems with high HLB values (14–15) produce larger microemulsion regions than those with low HLB values. The addition of a low HLB cosurfactant did not result in an increase in incorporable amount of SGF in the microemulsion. The hypothesis that the combination of non-ionic surfactants with a high HLB (12–16) can lead to an enlarged isotropic region and a stabilised microemulsion system (4) could be confirmed by the results in this study.

Solubility Studies
Simvastatin (SIM) was added as a lipophilic and poorly water-soluble (0.0014 mg/L) model drug to system N for solubility studies. Surfactant-oil mixtures were prepared, and excess SIM was added and partly dissolved by ultrasonication. After adding SGF, the mixtures were stirred for 60 min at 37°C. The samples were centrifuged, and phase clarity and separation were visually determined. Quantitative analysis of SIM in the supernatant was performed by a modified HPLC assay.

Mixture experimental designs using D-optimal response surface modelling were set up to determine the solubility of SIM in the SMEDDS and in the SMEDDS diluted with SGF. The experimental ranges were set by the existence of isotropic oil-surfactant mixtures and microemulsion area (Figure 2). The solubility in each mixture region was analyzed by fitting quadratic models based on PLS analysis (MODDE 7.0, Umetrics, Sweden).

Solubility of SIM in the SMEDDS
The solubility study of SIM in the formulation itself revealed that the quadratic model with two PLS factors was valid (data

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not shown), and a minimum of 44 mg of SIM per g was soluble in all mixtures, with a maximum amount of 30% ethyl oleate (EO) (Figure 3). Hence, all mixtures in the examined area would be suitable for a formulation containing a dose of 40 mg SIM per g.

Solubility of SIM upon SMEDDS Dilution

The response surface contour plots at a constant amount of EO (Figure 4) illustrate that solubility decreased markedly with increasing SGF percentage. Therefore, the microemulsion concentration appeared to be a major factor affecting drug solubility. Solubility decreased more slowly with a higher ratio of Lab/PS80.

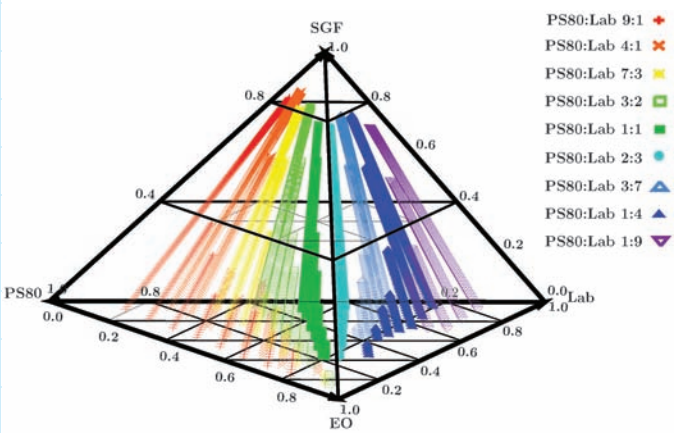

Figure 1. *Quaternary phase diagram of system N—labrasol (Lab), polysorbate 80 (PS80), and ethyl oleate (EO) mixtures titrated with simulated gastric fluid (SGF). Coloured areas indicate microemulsion area; each colour represents samples at distinct surfactant/cosurfactant ratios.*

The effect of the SMEDDS formulation mixture on the solubility at a constant amount of SGF is depicted in Figure 5. A high ratio of Lab to the other two components had a positive effect on solubility (Figure 5A). Increasing the amount of oil in the formulation had a negative effect (Figure 5A), and when the amount of SGF in the system was increased, the ratio of Lab/PS80 became less important (Figure 5B).

An optimized formulation with regard to the solubility of SIM using RSM was determined. The solubility predicted by the

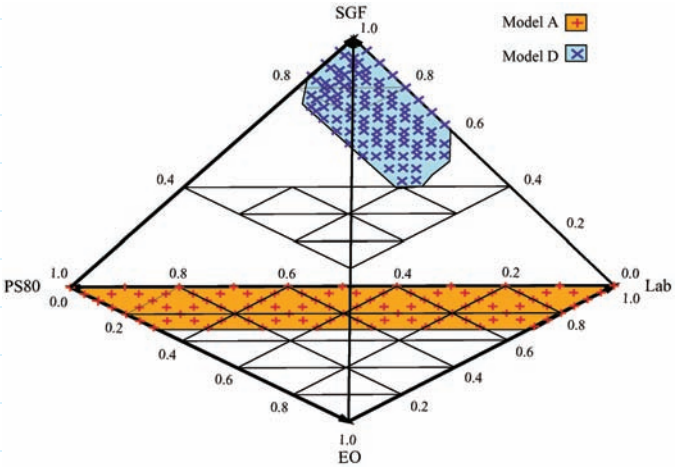

Figure 2. *Regions used in experimental designs. Model A (red): solubility in SMEDDS, in which labrasol (Lab) and polysorbate 80 (PS80) were varied from 0 to 100% and the oil component (ethyl oleate [EO]) was varied from 0 to 30%. Model D (blue): solubility upon SMEDDS dilution, in which the experimental ranges consisted of 0.2–35% Lab, 0–15% PS80, 0.2–8% EO, and 55–99.5% SGF (simulated gastric fluid).*

Table 1. Ternary and quaternary systems studied

System	Surfactant	Cosurfactant	Oil	SGF (%)[a]
Ternary phase diagrams				
A	Labrasol	–	Ethyl oleate	50
B	Labrasol	–	Crodamol GTCC	30
C	Labrasol	–	Olive oil	–
D	Labrasol	–	Ethyl caprylate	10
E	Polysorbate 80	–	Ethyl oleate	20
F	Polysorbate 80	–	Olive oil	10
G	Polysorbate 80	–	Crodamol GTCC	30
H	Polysorbate 80	–	Ethyl caprylate	30
I	Labrafil M 1944 CS	–	Ethyl oleate	–
Quaternary phase diagrams				
J	Labrasol	Labrafil M 1944 CS	Ethyl oleate	40
K	Labrasol	Labrafil M 1944 CS	Crodamol GTCC	27
L	Polysorbate 80	Labrafil M 1944 CS	Ethyl oleate	30
M	Polysorbate 80	Labrafil M 1944 CS	Crodamol GTCC	40
N	Polysorbate 80	Labrasol	Ethyl oleate	85
O	Polysorbate 80	Labrasol	Crodamol GTCC	71

[a] The aqueous medium was simulated gastric fluid (SGF). The percentage is the maximum amount of SGF in the continuous microemulsion region.

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Scientifically Speaking Sprunk continued from page 15

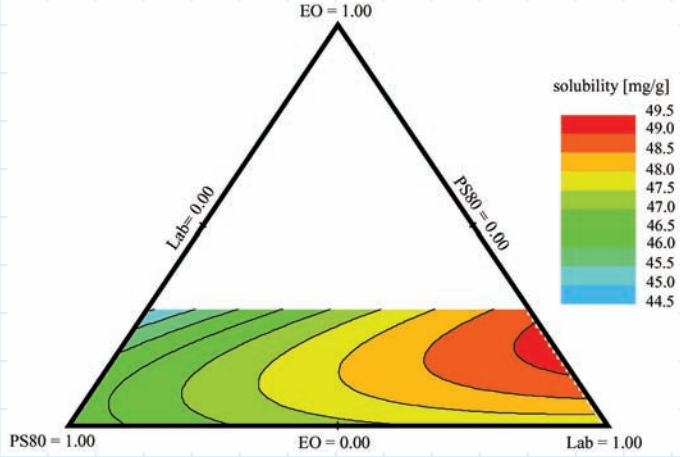

Figure 3. *Response surface contour plot of model A: predicted solubility of simvastatin (SIM) in SMEDDS formulations.*

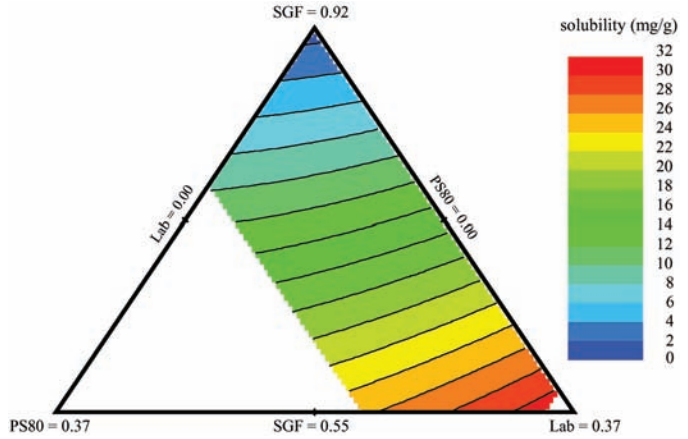

Figure 4. *Response surface contour plot of model D: predicted solubility of simvastatin (SIM) in SMEDDS upon dilution at a constant amount of ethyl oleate (EO) = 8%.*

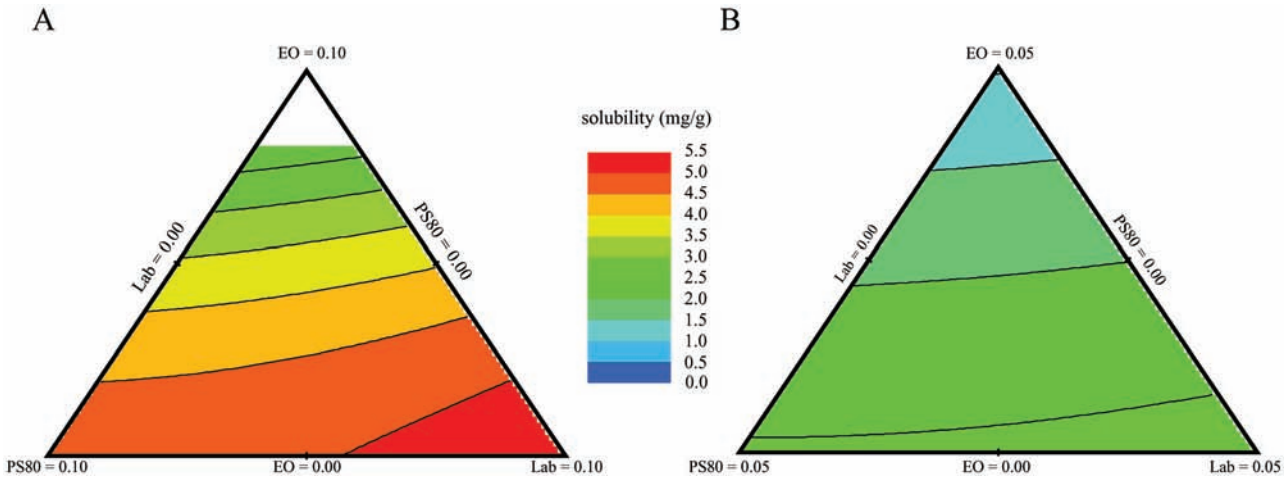

Figure 5. *Response surface contour plot of model D: predicted solubility of simvastatin (SIM) in SMEDDS upon dilution at a constant amount of simulated gastric fluid (SGF) = 90% (**A**) or 95% (**B**).*

model suggested that with a formulation of 40 mg SIM/g no drug precipitation would be expected upon dilution to 99.5% SGF. Phase behaviour revealed the necessity of PS80 for the development of a microemulsion. Without PS80, coarse emulsions and phase separation occurred upon dilution.

Conclusions and Future Directions

This study demonstrates that the development of complex formulations could be made more feasible with the use of an experimental design. It was possible to predict the quantitative influence of each component on the solubility of SIM and to derive an optimized formulation area according to RSM. A lack of drug precipitation in the stomach could be anticipated for optimized formulations after oral administration, which must be confirmed by further *in vitro* studies.

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Back to Basics: Dissolution Testing 3: The Rotating Paddle Method (Apparatus 2)

G. Bryan Crist[1] and R. B. Walker[2]

This series of articles introduces the basics of aspects of research techniques that may be required for the development and evaluation of controlled release technologies.

Introduction

This is the third in a series of articles covering the basic principles of operation required for various dissolution apparatus configurations. The rotating paddle method, commonly called "Apparatus 2," is the topic of this article, which focuses on the proper execution of the dissolution test to ensure the generation of accurate, reproducible, and reliable results.

As mentioned in the first article in the series (1), the dissolution test consists of two primary components: 1) sample preparation on the dissolution apparatus; and 2) analytical finish performed primarily with spectrophotometric or liquid chromatographic analytical instrumentation. This article concentrates on the paddle dissolution apparatus, its evolution and compendial requirements, the use of sinkers, and the rotating paddle testing procedure. The qualification requirements, chemical versus mechanical, were described in the previous "Back to Basics" article on the rotating basket (2) and, therefore, are not included in this article.

The paddle method has evolved from a variety of stirring mechanisms fitted with propellers and blades. The fixed blade design we know today was primarily credited to Poole and utilized a round-bottom organic synthesis flask that was later refined and adopted as a cylindrical, hemispheric-bottom vessel. The rotating paddle method was incorporated into the USP in 1978. Later that year, two tablets were identified as the first USP calibrator tablets: prednisone and salicylic acid. During the 1970s, the primary issue with dissolution testing was variability from laboratory to laboratory, which essentially ended with the introduction of the USP calibrator tablets and refining of dissolution apparatus in general (3). Presently, the term performance verification test (PVT) is used in place of calibrator tablets, and the requirement for salicylic acid tablets was dropped at the end of 2009.

The paddle apparatus proved to be a more robust system than the basket apparatus and provided an improvement in agitation characteristics. It has gained in popularity and is presently the most widely used of all the dissolution apparatus. It has been successfully used for tablets, capsules with sinkers, beads, powders, suppositories, and a wide range of modified release formulations.

The Rotating Paddle Apparatus

The rotating paddle apparatus is constructed of stainless steel and consists of a blade attached perpendicularly to a shaft (Figure 1). The paddle is set at a height of 25 mm above the bottom of the hemispheric-bottom vessel and typically is rotated at speeds of 50 rpm. The paddle may be coated with Teflon as an

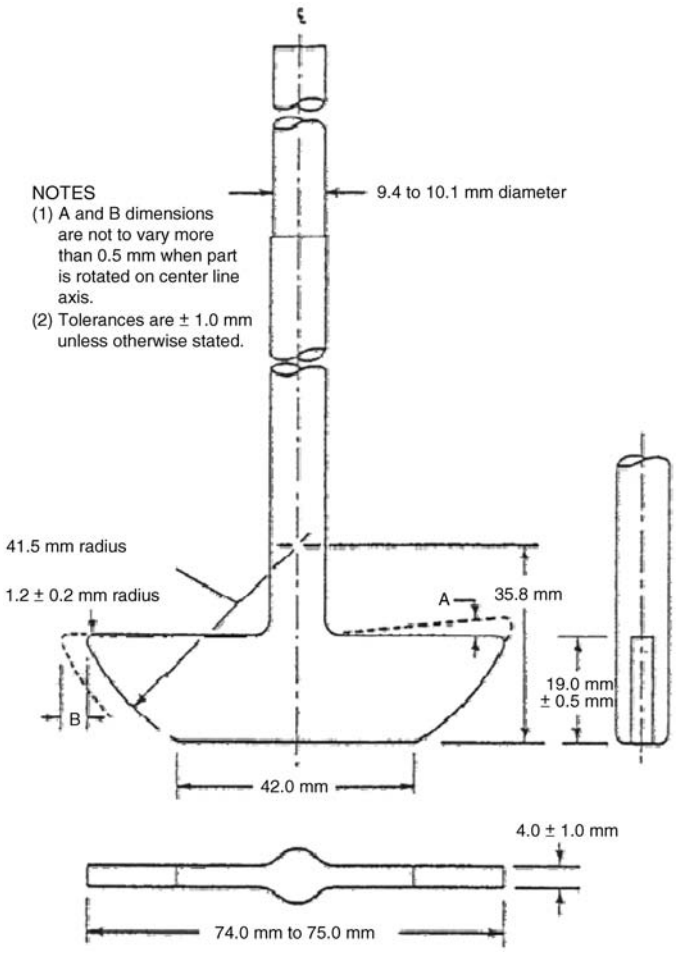

Figure 1. *USP <711> Dissolution paddle stirring element.*

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Creators continued from page 17

allowable variation, which prevents some products from sticking or binding to the surface of the stainless steel. The coating also allows for simple and effective cleaning. Teflon coating may be easily damaged, however, and should be stored properly to avoid scratching. The mishandling of these paddles can eventually cause the coating to peel away and possibly introduce additional turbulence due to the increase in surface area and, ultimately, an increase in dissolution rate. Scratches and pits in the Teflon may also become difficult to clean and possibly result in carryover of the active drug into a subsequent test. Coated paddles will last many years if properly handled and stored.

Stirring rates as low as 25 rpm have been used for rapidly dissolving formulations, like suspensions, and stirring rates as high as 75 rpm have been used for poorly soluble formulations and to overcome excessive coning. Stirring rates outside the 25–75 rpm range are discouraged due to variable hydrodynamics below 25 rpm and the loss of discriminatory power above 75 rpm. However, when dissolution profiles exhibit inappropriately dissolving drug substance during method development, adjustments outside the normal rotational speeds may be warranted and justified.

The paddle apparatus has been adapted to test numerous encapsulated formulations with the aid of a sinker. This is due to the requirement that the dosage form must settle to the bottom of the vessel at the beginning of the test. The sinker is described in the USP as a small, loose piece of nonreactive material, such as not more than a few turns of wire helix (4) (Figure 2). As a result of the International Conference on Harmonization (ICH) of the Dissolution Chapter, an alternate sinker, which originated in the Japanese *Pharmacopeia*, is now listed as an alternative. The helix sinker and the alternate sinker often provide different dissolution results due to their shape, size, and influence on fluid hydrodynamics between the paddle and base of the vessel. The construction of plain wire helix sinkers should be refined beyond the USP description because variations in construction from analyst to analyst can result in considerable variability. A unique method of sinker construction is offered by the USP in the new

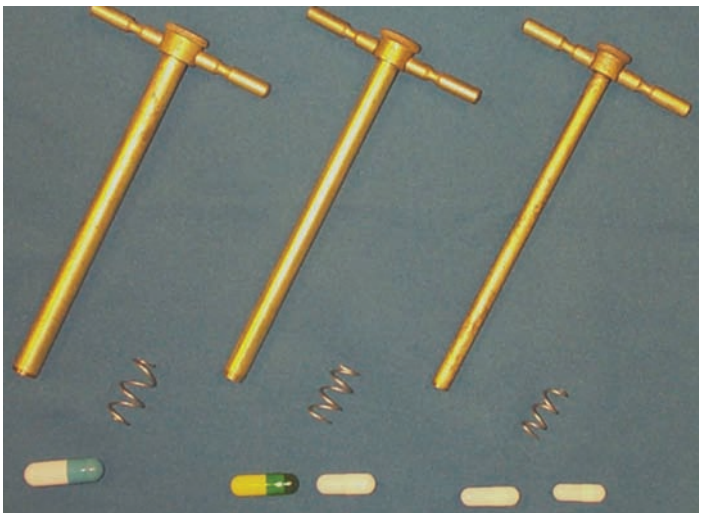

Figure 2. *USP <1092> Sinker construction examples for capsule sizes. Left to right: 0, 1, 2, 3, and 4.*

"General Information" chapter (<1092> Dissolution Procedure). It recommends that specific gauge stainless-steel wire be wrapped around various cork borers to standardize construction and minimize variability (5). Other sinkers may be justified and validated, but they must be specifically described in the dissolution method.

Due to the abundance of high-potency, low-dose formulations, small-volume vessels and paddles are available. Although they are not recognized by the harmonized pharmacopeias, they may be justified due to the extremely low analytical concentration of low-dose formulations if the low concentration cannot be compensated for through analytical techniques such as large HPLC injection volumes. Conversely, large-volume vessels (2 and 4 L) are included in the USP for poorly soluble dosage forms or bolus formulations, as required for veterinary products. Due to the increased capacity of media in large-volume vessels, the paddle apparatus is more efficient with the paddle stirring element rather than the basket.

The Rotating Paddle Procedure

When executing the rotating paddle dissolution test, a series of steps should be routinely performed during each test. These steps may be included in a general dissolution standard operating procedure (SOP), as they are often not included in a specific test method for a particular product.

- Prior to the start of the test, the analyst should evaluate the dissolution apparatus, vessels, and paddle shafts to ensure they are clean and dry.
- The analyst is responsible for the verification of physical parameters prior to the start of a test, especially if vessel, shaft, or paddle components were moved or exchanged.
- Media must be properly prepared according to the method and thoroughly deaerated. Dissolved gasses that are not removed will form as bubbles along the wall of the vessel, and they will also cover the surface of the paddle shaft. This increases the effective surface area of the paddle, which then increases the turbulence and dissolution rate for most disintegrating dosage forms.
- Media must be delivered to the vessel while maintaining a volumetric accuracy of ±1%. For a typical dissolution test with 900 mL and a required volumetric accuracy of ±9 mL, appropriate class A volumetric glassware is required, which may exclude most graduated cylinders.
- The media must reach 37.0°C in each vessel prior to the start of the test. Gentle stirring of the media with the paddles lowered to operating height is acceptable; however, high-speed stirring to rapidly heat media generally may introduce more air.
- Media temperature must be measured and recorded for each vessel at a minimum before and at the end of each dissolution test to verify that the temperature of the media has been maintained properly.
- The paddles must be stopped prior to introducing the dosage forms.
- Prepare all sampling materials if sampling manually or automatically, including fresh filters and measuring

equipment that is clean and dry. Prepare fresh, clean, dry, and properly labeled vials or test tubes for each sample time point.

- Handle all dosage units with gloved hands or protective tweezers to avoid scratching or cracking the capsules or the coating on tablets. Moisture and oils on the skin will affect the performance of many dosage forms prior to the start of the dissolution test.
- If weights are required for documentation, expose the dosage forms to as little humidity as possible. Some dosage forms can change considerably when exposed to humidity, and their integrity should be protected.
- Dosage units should not be placed on the evaporation covers prior to the start of the test due to excessive humidity above the dissolution vessel.
- Have all documentation materials nearby to record temperatures, times, and note visual observations taken during the test.
- Record times that the tablets are introduced into the non-rotating dissolution medium. Times may be staggered to allow for adequate sampling time, but the rotation of the paddle cannot begin until the dosage form settles to the bottom of the vessel, per USP.
- Visually inspect the location of the dosage forms in the lower portion of the vessel and record any unusual observations, such as the tablet sticking to the heel or wall of the vessel. The dosage form should not be floating.
- The proper sampling height is the halfway point between the top of the paddle blade and the surface of the dissolution medium.
- Samples should be pulled within 2% of the time that the test begins. In other words, samples must be pulled for a 30-min time point within ±36 sec of the 30-min time point. If all six samples are started at the same time, then all six samples must be pulled and filtered within this window of time. Automated sampling equipment is often used to obtain, filter, and document sampling accuracy.
- The filter stops the dissolution process and clarifies the sample for analytical measurement. Only validated filters should be used that remove all undissolved particles from the sample and do not bind drug substance after conditioning with a specified amount of sample containing media.
- The dissolution samples are ready for analytical measurement once they have cooled to room temperature.

All dissolution apparatus used for testing within a cGMP environment should be properly qualified and calibrated prior to use. Dissolution qualification and calibration methods are mentioned in a previous article in the "Back to Basics" series (2).

In the next article in the "Back to Basics" series on dissolution testing, we will cover the reciprocating cylinder, "Apparatus 3."

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Pharmacogenetics in Veterinary Medicine

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As is the case with human patients, a great deal of individual variation exists in a veterinary patient's response to drug therapy. While much of this variation can result from species differences in drug absorption, distribution, metabolism, and/or excretion (see articles by Marilyn Martinez in *CRS Newsletter*, Vol. 25, Nos. 2 and 3), differences within a given species can also exist. These differences are often the result of pharmacogenetics—genetically determined differences in drug disposition.

Arguably the most dramatic example of pharmacogenetics in veterinary patients is the ABCB1 (MDR1) deletion mutation in herding breed dogs, designated ABCB1-1Δ (1). P-Glycoprotein (P-gp), which is encoded by the MDR1 gene, has been fairly well characterized in dogs. P-gp is expressed on brain capillary epithelial cells, where it contributes to the blood brain barrier; on renal tubular cells and biliary canalicular cells, where it functions to excrete xenobiotics into urine and bile, respectively; and on enterocytes, where it prevents absorption of xenobiotics (2). As a result, alteration of P-gp function can dramatically influence drug disposition by affecting absorption, distribution, and excretion of substrate drugs.

A polymorphism in the ABCB1 gene consisting of a four base-pair deletion mutation was identified in several breeds of dogs nearly a decade ago. This deletion results in a shift of the reading frame that generates several premature stop codons (1). Because protein synthesis is terminated before even 10% of the P-gp protein product is synthesized, dogs with two mutant alleles exhibit a P-gp null phenotype, similar to *mdr*1 (–/–) knockout mice. Affected dogs include many herding breeds. For example, roughly 75% of Collies in the United States, Europe, and Australia have at least one mutant allele (3,4). Other affected breeds include Australian Shepherds, Shetland Sheepdogs, English Shepherds, Old English Sheepdogs, Border Collies, German Shepherds, Silken Windhounds, McNabs, and Long-haired Whippets. Affected dogs are highly sensitive to a number of drugs, including anthelmintics (ivermectin, milbemycin, selamectin, etc.), anticancer agents (vincristine, doxorubicin, and others), the antidiarrheal agent loperamide, and other drugs (5,6).

Evidence for P-gp's role in the blood brain barrier is apparent when one considers that dogs homozygous for ABCB1-1Δ (MDR1 mutant/mutant) experience adverse neurological effects after a single dose of ivermectin (>120 µg/kg). As a point of reference, the dose of ivermectin recommended for treating mange in dogs is 300–600 µg/kg. This dose can be fatal for MDR1 mutant/mutant dogs. Heterozygous (MDR1 wildtype/mutant) or homozygous wildtype dogs are not sensitive to ivermectin neurotoxicity at the 120 µg/kg dose, but heterozygote dogs may experience neurotoxicity at ivermectin doses >300 µg/kg, particularly if daily doses are administered (i.e., protocols for treatment of demodectic mange). By comparison, dogs homozygous for the wildtype MDR1 allele can receive 2,000 µg/kg of ivermectin in a single dose without signs of toxicity, and can receive 600 µg/kg/day for months without signs of toxicity. MDR1 mutant/mutant dogs also have increased susceptibility to neurologic adverse effects of other avermectins, including milbemycin, selamectin, and moxidectin.

Lack of functional P-gp at the blood brain barrier in MDR1 mutant/mutant dogs also results in extreme sensitivity to the antidiarrheal drug loperamide. Loperamide is an opioid that is generally devoid of CNS activity because it is excluded from the brain by P-gp (7). Loperamide neurotoxicity has been reported in Collies that have received routinely recommended doses of loperamide (0.14 mg/kg orally). In a prospective study, MDR1mutant/mutant dogs developed neurological toxicity (stupor, ataxia, etc.) after loperamide administration, while MDR1 wildtype dogs remained neurologically normal (8). In fact, homozygous wildtype dogs do not exhibit neurologic symptoms after receiving even higher doses of loperamide, indicating that P-gp plays a key role in modulating distribution of substrates such as loperamide to canine brain tissue. Use of a radiolabeled P-gp substrate drug, ^{99m}Tc-sestamibi, dramatically illustrates the effect of P-gp on the blood brain barrier in MDR1 mutant/mutant versus MDR1 wildtype dogs (Figure 1).

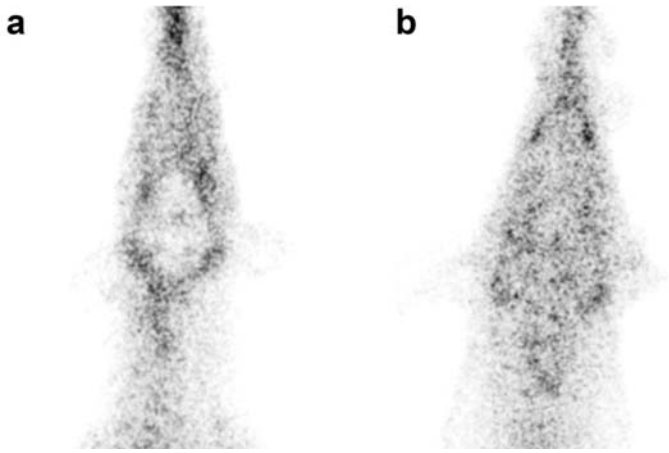

Figure 1. *Nuclear scintographic imaging of the heads of an MDR1 wildtype (**A**) and MDR1 mutant/mutant (**B**) dog acquired 1 hr after injection of the radiolabeled P-gp substrate sestamibi (^{99m}Tc-sestamibi). For orientation, the dogs' noses are at the top of the figure. A void of ^{99m}Tc-sestamibi uptake within the brain indicates functional P-gp in the MDR1 wildtype dog (**A**), while similar activity in the brain and surrounding tissue indicates lack of functional P-gp in the blood brain barrier of the MDR1 mutant/mutant dog (**B**). (Mealey et al. Drug Metab. Dispos. 2008: 1073-1079)*

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P-gp also contributes to renal and biliary excretion of P-gp substrate drugs. Concurrent administration of a P-gp inhibitor decreases the biliary and renal clearance of doxorubicin in rats (9,10). In a separate study, biliary and renal excretion of digoxin and vincristine were increased in rats after treatment with a P-gp inhibitor (9). Evidence for altered biliary excretion of P-gp substrate drugs in MDR1 mutant/mutant dogs compared with wildtype dogs is shown in Figure 2. In this study, MDR1 mutant/mutant dogs had significantly decreased biliary excretion of ^{99m}Tc-sestamibi compared with ABCB1 wild/wild dogs (11).

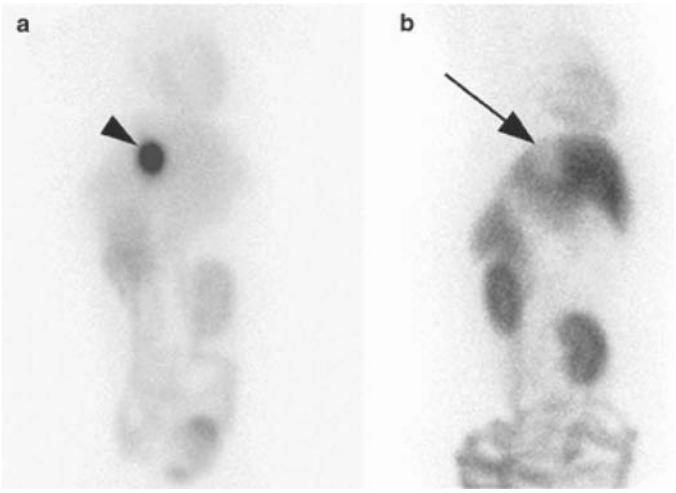

Figure 2. *Nuclear scintographic imaging of the abdominal areas of an MDR1 wildtype (**A**) and MDR1 mutant/mutant (**B**) dog acquired 2 hr after injection of the radiolabeled P-gp substrate sestamibi (^{99m}Tc-sestamibi). Intense gallbladder ^{99m}Tc-sestamibi uptake (arrow head) is present in the MDR1 wildtype dog (**A**), indicating the presence of functional P-gp actively pumping ^{99m}Tc-sestamibi into the bile. Conversely, a void of ^{99m}Tc-sestamibi activity in the location of the gallbladder (arrow) is present in the MDR1 mutant/mutant dog (**B**), indicating a lack of P-gp biliary excretion. (Coelho et al. J. Vet. Pharmacol. Ther. 2009: 417–421)*

Clinically, this appears to manifest as enhanced sensitivity to the toxicities of P-gp substrate drugs that rely on biliary excretion (e.g., vincristine and doxorubicin). Dogs that are heterozygous (MDR1 mutant/wildtype) or homozygous (MDR1 mutant/mutant) for the ABCB1 deletion mutation are significantly more likely to develop hematologic toxicity, specifically neutropenia (P = 0.0005) and thrombocytopenia (P = 0.0001), after treatment with vincristine than are ABCB1 wildtype dogs (12). Similar results have been documented with doxorubicin. Current recommendations for canine cancer patients are to assess the MDR1 genotype before vincristine or doxorubicin administration. Thus, vincristine and/or doxorubicin dosages can be reduced to prevent toxicity and treatment delays resulting from neutropenia or thrombocytopenia.

Pharmacogenetics of Drug Metabolism

Presently the greatest body of knowledge with regard to pharmacogenetics in human patients appears to involve genetic variation in drug metabolism. Pharmacogenetic variation can affect both phase I and phase II metabolic enzyme activity. Relatively few polymorphisms in drug-metabolizing enzymes have been described in veterinary patients, although this is likely to change as research in this area is currently in progress. Variation in metabolism of some drugs has been documented in dogs. CYP2B11 has been shown to have at least a 14-fold variation in activity in mixed-breed dogs. Greyhounds have been shown to have particularly low CYP2B11 activity, which results in sustained plasma concentrations of propofol and delayed recovery compared with mixed-breed dogs (13). The specific genetic alteration responsible for reduced CYP2B11 in Greyhounds compared with other canine breeds has not been determined. There is some evidence to suggest that CYP2D15 may also be polymorphic in dogs. The NSAID celecoxib is metabolized to a large degree by CYP2D15. Clearance of celecoxib in Beagles is polymorphic, with about half the population being extensive metabolizers and the remainder being poor metabolizers. Celecoxib has a 1.5- to 2-hr half-life in extensive metabolizers and a 5-hr half-life in poor metabolizers (14). One pharmacogenetic variant that has been identified in the canine CYP2D15 gene, a deletion of exon 3, results in undetectable celecoxib metabolism. The frequency and breed distribution of this polymorphism has not yet been determined. However, it is likely to have clinical significance for other drugs that are CYP2D15 substrates, including dextromethorphan, imipramine, and others.

A number of other mutations in drug-metabolizing enzymes have been described in animals, but the clinical relevance of these mutations, if any, has yet to be determined. For example, 10% of Beagles in one study were deficient in CYP1A2 because of a mutation that resulted in premature termination of protein synthesis (15). CYP1A2 does not appear to be responsible for metabolizing clinically used drugs in veterinary medicine, but CYP1A2 is studied frequently in people with regard to susceptibility to certain types of cancers. A feline hepatic CYP2E polymorphism has been identified, but the clinical relevance of this polymorphism has not been described. Similarly, polymorphisms have been described in several drug-metabolizing enzymes in cattle, but these single nucleotide polymorphisms are used as molecular markers in cattle for linkage analysis, testing of parentage, and distinction of breeds, rather than for predicting response to drug therapy (16,17).

With respect to phase II metabolic enzymes, a pharmacogenetic variation exists for the thiopurine methyltransferase (TPMT) enzyme. TPMT is a phase II enzyme that is responsible for metabolizing azathioprine and its active metabolites to their inactive forms. A ninefold range in TMPT activity exists in dogs, and enzyme activity level appears to be breed related (18). Giant Schnauzers tended to have lower TPMT activity, while Alaskan Malamutes had high TMT activity. Decreased TPMT activity has been documented to be associated with increased susceptibility to azathioprine-induced bone marrow suppression.

Pharmacogenetics in Clinical Veterinary Practice

It may be surprising to many physicians and pharmacologists that a commercial veterinary pharmacogenetics laboratory

From the Vet Group continued on page 22

From the Vet Group continued from page 21

(www.vetmed.wsu.edu/vcpl) is regularly performing canine MDR1 genotyping for practicing veterinarians. Important reasons that commercial pharmacogenetic testing for the MDR1 gene is readily available for canine patients, and not for human patients, include the fact that the MDR1 mutation in dogs has a very high allelic frequency (75% in Collies, 50% in Long-haired Whippets, and roughly 50% in Australian Shepherds) and the polymorphism is highly predictive for serious adverse drug events, not just for one drug class but for several drug classes. Table 1 provides a partial list of drugs that are substrates for P-gp.

Future Directions

The field of pharmacogenetics, particularly in veterinary medicine, is still in its infancy. However, we have an ever-increasing arsenal of molecular tools that can be used to expand our knowledge of pharmacogenetics. Furthermore, with the recent completion of genome projects for many veterinary species (canine, feline, bovine, equine), we may soon know the sequences of virtually all genes encoding drug-metabolizing enzymes, drug transporters, receptors, and other drug targets. While the ultimate goal of modern pharmacogenomics, individualization of drug therapy, may not be achieved for all drugs, it certainly has the potential to increase both safety and efficacy of many drugs for veterinary patients.

Table 1. Selected P-gp substrates[a]

Anticancer Agents	Opioids
Doxorubicin	Loperamide
Docetaxel*	Morphine
Vincristine*	Cardiac Drugs
Vinblastine*	Digoxin
Etoposide*	Diltiazem*
Mitoxantrone	Verapamil*
Actinomycin D	Talinolol
Steroid Hormones	Immunosuppressants
Aldosterone	Cyclosporine*
Cortisol*	Tacrolimus*
Dexamethasone*	Miscellaneous
Methylprednisolone	Ivermectin
Antimicrobial Agents	Amitriptyline
Erythromycin*	Terfenadine*
Ketoconazole	Ondansetron
Itraconazole*	Domperidon
Tetracycline	Phenothiazines
Doxycycline	Vecuronium
Levofloxacin	
Sparfloxacin	

[a] Substrate followed by an asterisk is a substrate of CYP3A.

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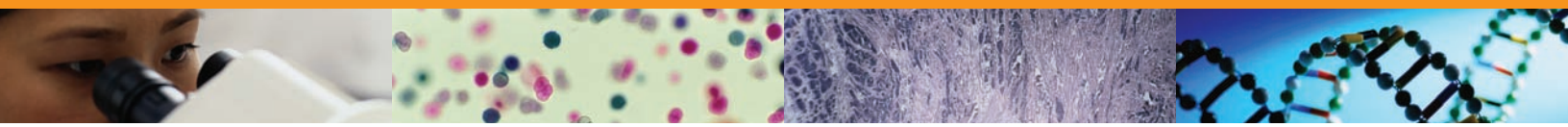


Research and Development Resources: Southwest Research Institute

Charles Frey
Coating Place, Inc., Verona, WI, U.S.A.

Southwest Research Institute (SwRI), a non-profit contract research organization headquartered in San Antonio, TX, has a long history of research and development support for varied industries. One niche of the organization is focused on micro- and nano-encapsulation. A series of questions were presented to Dr. James Oxley, a senior research scientist in the Micro- and Nano-encapsulation group at SwRI, to probe the motivations of and services offered by SwRI. Dr. Oxley's answers provide a brief overview of SwRI and outline the scope of controlled release services that have been realized at SwRI or that could be realized in the future.

Q ***Every organization builds from circumstance or a core charter. What motivations started SwRI, and when did the start occur?***

A Southwest Research Institute is the realization of a Texas wildcatter's dream. Thomas Baker Slick, Jr., an oilman-rancher-philanthropist, founded SwRI in 1947. Slick's vision of an internationally known scientific research center in San Antonio, Texas, took root with his donation of a ranchland site west of the city—where institute operations are still carried out. Slick challenged a group of pioneer scientists and engineers from around the nation to move to the new center to seek revolutionary advancements in many areas by developing and applying technology.

Q ***Do the initial motivations still hold today, and have they expanded in any way?***

A Yes. In addition to providing our clients with a wide variety of contract R&D services, we maintain an internal research and development program to allow employees to pursue their own research interests.

Q ***What is the mission statement of SwRI?***

A Benefiting government, industry, and the public through innovative science and technology.

Q ***From an overview perspective, describe the current department layout of SwRI?***

A SwRI is composed of 12 different operating divisions covering most major physical and engineering science disciplines, including space sciences, automotive engineering, and applied physics.

Q ***Where does the Micro- and Nano-encapsulation group lie?***

A The Department of Microencapsulation and Nanomaterials is within the Chemistry and Chemical Engineering Division and is appropriately referred to as Division 01.

Q ***Is there much interaction between the Micro- and Nano-encapsulation group and other groups in SwRI?***

A Absolutely. There is frequent collaboration within the institute on many levels for both internally and externally funded projects. Divisions that we frequently collaborate with include Mechanical Engineering, Automation & Data Systems, Applied Physics, and Fuels & Lubricants Research.

Q ***Innovation often develops out of the melding of needs, technologies, and ideas from unrelated areas. Do you feel there is untapped potential for such innovation within the organizational structure of SwRI?***

A I would describe it as tapped potential. Many of our projects emerge from unique requests that can only be fulfilled by an organization with such a broad scientific and engineering base. For encapsulation, this started in 1949 with our first project: encapsulating fuel for the French government, which was an innovation that started with what is now our Fuels & Lubricants Division.

Q ***Are there potential expansion areas that might foster controlled release research either directly or through collaboration with other departments?***

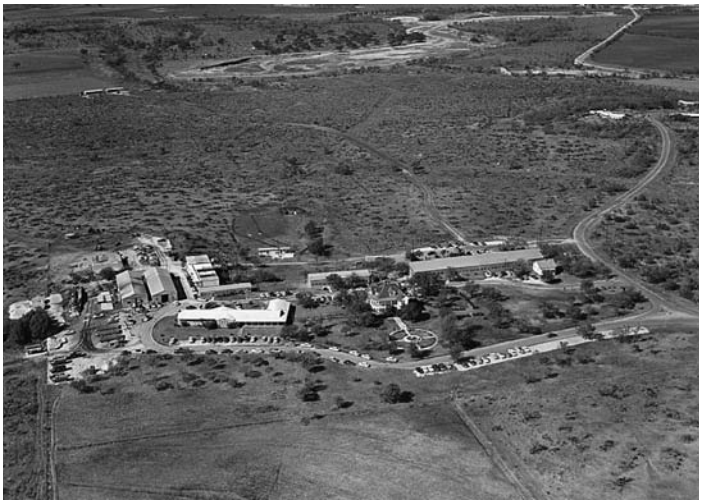
A Always. The structure at SwRI is dynamic and allows scientists and engineers to build and grow new areas of expertise to fit the needs of government, industry, and the public. In order to remain viable, it is important that we either change with or, preferably, lead advancements in new areas. There are several industry-specific areas that are expanding in collaboration with other departments. An example is the recent consolidation of our institute-wide capabilities from three different divisions related to food technology, including analysis (chemical and structural), formulation (encapsulation and controlled release), and engineering (manufacturing).

Consumer and Diversified Products continued on page 24

Consumer and Diversified Products continued from page 23

Q ***Describe the current technologies at SwRI that may be related to controlled release technology? Consider this both from traditional controlled release perspectives of payload delivery and also from broader perspectives that might encompass less traditional or marginal controlled release application.***

A Most of our controlled release technologies are based on micro- and nano-encapsulation. Part of what makes us unique is our breadth of capabilities, over two dozen different encapsulation techniques on a lab to pilot scale. This includes physical encapsulation techniques, such as spray drying or fluid bed coating, and chemical techniques, including solvent evaporation and complex coacervation. Our technologies are also a mix of custom equipment/processes and commercially available equipment. Examples of our custom processes include our rotating disc atomization and submerged nozzle co-extrusion processes, which were developed at SwRI in the 1950s and 60s. On the commercial side, we try to maintain an inventory of modern encapsulation equipment, such as benchtop spray driers or spheronization units that can readily be scaled up at a contract manufacturing facility. Furthermore, we have a versatile set of facilities, including cGMP capabilities, to support the preparation of materials for clinical trials in the pharmaceutical industry or product testing in the food industry.



Southwest Research Institute in 1949. (Photo courtesy of the Southwest Research Institute)

Southwest Research Institute in 2009. (Photo courtesy of the Southwest Research Institute)

Q ***What has historically made up your client base either by name, industry, or sector (government, academia, private industry, etc.)?***

A For the entire institute, funding is approximately 60:40 government to industry. For our encapsulation work, that balance is closer to 20:80. The government funding includes academic collaborations, since most (if not all) academic collaborations are tied to a government grant. With regard to industry, our client base has historically been spread out amongst all industries that use or consider using encapsulation. This includes pharmaceuticals, nutraceuticals, food, beverage, cosmetics, consumer products, oil/gas, agriculture, and many other industrial applications.

Q ***Are you bound by confidential disclosure agreements? Do these agreements limit what you can share about specific applications?***

A Yes. A majority of our clients prefer confidentiality agreements. So, unfortunately, this prevents us from discussing or disclosing some of our most exciting research and results. This is part of the reason we frequently use our internal R&D funding to generate results that are not covered by confidentiality agreements. It then allows us to have results for presenting at meetings or publishing in journals.

Q ***Describe some novel applications developed within the Micro- and Nano-encapsulation group that you are able to share.***

A While there are many examples to share, here are the first two that come to mind and are more related to consumer and diversified products. The first is the encapsulation of water. It is well known that this is a very difficult, if not impossible in some cases, task to accomplish. SwRI succeeded in encapsulating water in the 1970s for use in mining applications, specifically for mechanical release of water to cure adhesives used with mine shaft support rods. A second example is a controlled release form of chloride dioxide that can be formulated to trigger release by exposure to light or water.

Q ***Select a few key pieces of SwRI research and development that can be shared and provide a brief synopsis of each.***

A Two of the most significant pieces of research were carried out in the late 1950s and early 1960s with the development of the spinning disc atomization technology and early development of co-extrusion (annular jet) technology for encapsulating liquids with a physical process. This work built a solid foundation and reputation for SwRI and our encapsulation expertise. An example of a more recent key piece of research is work with multifunctional coatings, including impact indication and self-healing. We initially worked with impact indicating paints and coatings in the 1980s. This work experienced a resurgence recently with an increased interest in self-healing coatings.

Q ***Other than the actual research and development work results, what intangible benefits might be provided to clients through interaction with SwRI?***

A A few intangible benefits to highlight are the knowledge base of the workforce, breadth of services, and breadth of industries served. First, because SwRI is a very stable organization many of our employees within the department have been with the institute for over 30 years. This experience in the lab with hundreds to thousands of different encapsulation projects and experiments offers unmatched expertise to clients. Second, the breadth of divisions at SwRI offers a "one-stop-shop" for very complex projects, allowing clients to present a problem that would often take multiple organizations to solve. Finally, because we serve multiple industries that utilize encapsulation we have a unique perspective on how and when certain processes or materials should be used to solve a controlled release problem. We often pull ideas and solutions from other industrial applications that might otherwise be overlooked; outside the box thinking is standard practice.

Q ***Is there any other information about SwRI or the Micro- and Nano-encapsulation group that you feel would be of interest to readers?***

A Let me first thank you for the opportunity to share part of the SwRI story. It truly is a unique environment for research and development. ■

Erratum

CRS Newsletter
Volume 27, Number 3, 2010

In the Chapter News article "Misuk Bae Receives Student Service and Leadership Award" (page 33), the photo caption is incorrect. The correct caption is provided below.

Misuk Bae and Dr. Barrett Rabinow (Baxter Healthcare).

Welcome New Members

Sreedhara Alavattam
Carter R. Anderson
Koide Aya
Mimi V. Bach
Stefan Baier
Patrick Ballmer
Aaron Barkley
Jamie Beggs
Elias Belmonte
Brian Carlin
Ron Casey
Boram Chae
Jerry Chang
Kanad Das
Tim Daynard
Louis Demers
Michelle Deutsch De Montes
Garrett Ebersole
Miriam K. Franchini
Rahul S. Gawande
Solmaz Ghaffari
Itzik Goldwaser
Ryan Gordon
Florence Guimberteau
Damian Hajduk
Henry A. Havel
Douglas B. Hecker
Molly Hemmeter
Michel Hubert
Margit M. Janat-Amsbury
Dudley Jayasinghe
Masao Kamimura
Michail Kastellorizios
Raghu R. Kasu, Sr.
Donald Kelemen
Ji-Seon Kim
Sang W. Kim
Yu-Han Kim
Karl Kolter
Mary B. Kossuth
Johannes Kraemer
Vijaya K. Kuruganti
Burrhus Lang
Glenn Larsen
Eliot Lazar
Seungjae Lee
Qun Lu
Wuyuan Lu
Andrew Luk
Claudia Matos
Tetsuya Matsuura
Jei C. McKinney
Liliana A. Miinea
Paul Missel
Jong J. Na
Hyeonwood Park
Srinivasa R. Paruchuri
Clay Pearson
Conrad Raab
Cody Reynolds
Sunil B. Roy
Louis F. Ruocco
Ana C. Santos
Marina Sokolsky-Papkov
Jill M. Steinbach
Erika Stippler
Peter W. Swaan
Ennio Tasciotti
Ramachandran Thirucote
Lu Tian
Rajan K. Verma
Jin G. Wang
Kristin Wiederholt
Abraham Woldu
Xiao-Bing Xiong
Yasuo Yamaguchi, Sr.
Alpaslan Yaman
Hiroyuki Yamazaki
Jake Yu
Lawrence M. Zaccaro
Jinying Zhao
Natalia Zisman

CRS Delivering Bioactives

The Science that Is Beer—As Learned at the BridgePort Brewery in Portland!

Sarah Eccleston[1]

Yes, the formulation science of beer is a fascinating area. Indeed, budding brewers can now complete an M.S. degree in this subject at the University of Nottingham in the United Kingdom—although common sense tells me that learning on the job is much more fun…. Disclaimer 1: I (and CRS) encourage those who do choose a self-imposed lab-rat status to consume their beer responsibly!

I quote from an interesting article published in 1900 on "the influence of science in modern beer brewing":

> …and it is a fact which I am proud to place on record, that there is no more welcome or honoured guest in the brewery of to-day than the chemist and biologist. If the theories that are worked out in the laboratory are at first regarded with doubt and suspicion, they are eventually put to the test in the brewery on the industrial scale: and as they thus carry conviction, every advance in scientific discovery is accompanied by a corresponding movement in the industry whose welfare we are working to promote. On the other hand, it is quite obvious that with every step forward that is taken by the practical industry itself, fresh fields for investigation are opened up for the scientist; and thus the growth of the science and the industry are made dependent upon each other; and they must consequently be ever wedded and pass on happily, in the paths of progress, hand in hand (1).

There are some parallels here with our CRS community and the science and industries we represent. Academia and industry are interdependent, CRS provides a great forum for this interaction to take place, and what better imagery than Mr. CEO and Mrs. Professor "hand in hand," "wedded" and united in "the paths of progress."

One thing is certain—CRS members were welcomed very warmly into the BridgePort Brewery in Portland, OR, on the evening of Monday, July 12. We sampled some great Oregon beers, ate lots of (much-needed and very tasty) food, and learned some "formulation and processing" from our fantastic tour guide Todd—he was warned this might be a tough crowd….
The Young Scientist Committee arranged this event with two things in mind: 1) create an inexpensive event that is easily accessible to our young scientists, and 2) create an environment where "networking" and meeting new people is easy and again accessible to young scientists. It is very important that our more experienced members are on hand and willing to interact with the next generations.

[1] Senior Formulation & Process Development Scientist, Encap Drug Delivery, and CRS Young Scientist Committee member.

Just like any big happy family (have I brought a sentimental tear to any glass eyes yet?), we played a game together…. Well, this is where the very competitive nature of our group became apparent: each person was given a piece of a photo that had been divided into six and tasked with finding the other five pieces. This involved a lot of energetic "elbows-out" rushing around and most definitely saw strangers unite over the Eiffel tower, the Sydney opera house, Edinburgh castle, and, of course, the Sphinx. The Sphinx was the winning team—congratulations again to them. I like to think their motivation was simply recognition, glory, and the respect of their peers, but in reality the beer token prizes were very enthusiastically received…. This game really helped with introductions too—I would like to say hi to the woman with the middle piece of the Bay of Islands and hi to the person with the top left corner of the Taj Majal…what were their names again?

I think that we on the Young Scientist Committee met our objectives and hosted a successful event that has set the standard for meetings to come. All of the staff at the BridgePort Brewery were great, so thanks to them, and thanks also to our generous sponsors: Encap Drug Delivery and Diurnal Ltd.

Disclaimer 2: This article was penned after a very enjoyable night in the BridgePort Brewery. Cheers everyone, and here's to next year!

P.S. To keep up-to-date with other young scientist events, join our LinkedIn group by clicking on the subgroup tab on the main CRS group page.

Reference

1. Wyatt, F. The influence of science in modern beer brewing, J. Franklin Inst. 150(4): 299-320 (1900). ■

Mentors, Protégés, Mentoring, and the CRS Mentorship Program

Padma V. Devarajan[1] and Michael J. Rathbone[2]

Understanding Mentoring

Throughout our professional lives all of us will experience interactions with many teachers; however, some will experience an association with that "one GREAT teacher" who will walk into our life, touch our hearts, encourage us, awaken in us the spark that will open up new vistas, and shape and make us achieve our full potential. The CRS Mentorship Program was initiated to facilitate young scientists meeting that special person!

Triggering the process of development and growth is the hallmark of mentoring. It is an ability that stimulates and motivates gifted young professionals to take the path of personal and professional development. "Mentors" are those special people who possess the ability and who can make this happen.

Mentoring is an age-old practice. In fact, the genesis of the word "mentor" can be traced to the historic Golden Age of Greece. Mentor was a character in Homer's *Odyssey* who took care of and groomed Telemachus, the son of Odysseus, when he was away at war. What Mentor then did for Telemachus is today labeled as "mentoring."

Mentoring involves a partnership between the mentor and the protégé, i.e., the one who is mentored (sometimes called a "mentee"). The goal of the mentor is to identify the latent potential in protégés and to groom their special strengths into areas for growth. This process may entail some of the following activities:

Coaching	Protecting
Counseling	Helping
Guiding	Motivating
Advising	Acting as a role
Sponsoring	model

A person inclined to be a mentor must first and foremost be willing to invest time and energy to help the protégé. In addition they must have the necessary skills to be capable of providing support according to the specific needs of their protégé. On the other hand, young professionals who are eager to benefit from mentoring—from the knowledge and experience of senior, eminent professionals—must be willing to commit their time and efforts to establish and nurture the relationship in order to absorb and learn from whatever their mentor has to offer. Making and maintaining contact (initiating interactions, organizing meetings, and defining agendas) are the major requirement of a protégé.

Benefits to Mentor and Protégé

The mentorship program CRS offers to its young scientists is a 12-month opportunity for the protégé to interact with and be mentored by one of the Society's established members. Both mentors and protégés benefit from the program. For mentors who volunteer their time to mentor young promising minds on the path of progress and growth, the program provides them with the opportunity to relate to a person, perhaps on the other side of the world, who they may never have otherwise met; to develop their awareness of the requirements of young scientists across the globe; to cater to a young scientist's needs; and to spot the potential in a young scientist and contribute to their professional growth. Mentors involved in the CRS Mentorship Program often say that the experience provided them with immense personal satisfaction that arose out of the giving, grooming, and resultant growth of their protégé over the 12 months of their interaction.

What do the protégés get out of it? Contact with eminent, senior professionals and the resultant advice that these people provide on technical and professional matters; a potentially life-changing experience; the benefits of accelerated professional progress; the opportunity to have a supporter in times of need; and, of course, an international networking opportunity. But, in order for the protégé to benefit from this process, commitment is key. Indeed, the relationship will fail if the protégé is not committed to the program. Commitment by the protégé is the key factor in ensuring the success of the mentor-protégé relationship.

"The Mentor-Protégé relationship if wedded in a Golden Handshake, could result in a quantum leap forward, both for the Protégé and the Mentor." ■

1 Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, Mumbai, India.
2 School of Pharmacy, Griffith University, Queensland, Australia.

Innovation in Medicines: From Development to Production

Paolo Caliceti
CRS Italian Chapter

Traditionally, the CRS Italian Chapter organizes the scientific session of the annual AFI (Italian Pharmaceutical Association) Symposium, the main national meeting for people working in the pharmaceutical industry, academia and public institutions. This event is also a milestone for the CRS Italian Chapter because it represents an important occasion to present the mission and activities of the Society to the Italian pharmaceutical community. The session organized by the CRS Italian Chapter ends with the annual assembly for CRS members.

The AFI Symposium program includes several parallel sessions, workshops, minisymposia, roundtables, and activities that cover topics ranging from research and development to regulatory affairs. The meeting is completed with an exposition of international pharmaceutical companies and a poster session.

The 50th AFI Symposium was held in Rimini, Italy, on June 9–11, 2010, making it a special event with more than 1,000 delegates and a wide array of activities. For this special anniversary, Dr. Massimo Pedrani, member of the CRS Italian Chapter Committee, coordinated the CRS Italian Chapter session by organizing a miniexposition of the know-how and expertise of private and academic research groups: Innovation in Medicines: From Development to Production. The sessions were chaired by Dr. Massimo Pedrani (CRS), Prof. Bice Conti (CRS), Dr. Roberto De Luca (AFI), Dr. Elena Vidali (AFI), and Prof. Paolo Caliceti (CRS). The event attracted an unexpected number of participants from both academia and industry, with 16 contributions from industry and 24 from public institutions. Based on a soap-box formula, the speakers had 10 minutes to highlight the excellence of their know-how and development process. The minisymposium provided a window on the Italian technological scene, disclosing the opportunities offered for innovation in drug delivery and production processes, which may be attractive for collaborations and industrial development.

The scientific program was enriched by a poster session, and awards were assigned to four outstanding scientific contributions. The session ended with the annual CRS Italian Chapter member assembly, during which the president provided information on past and upcoming activities and updates about the member and financial situations.

CRS Italian Chapter wishes to thank Prof. Alessandro Rigamonti, AFI president and symposium chair, for strongly supporting the chapter and offering the privilege of organizing the scientific session.

Following is a list of presentations. Full abstracts are available on the CRS website under the Italian Chapter section.

Biological drugs come back, P. Ciana, University of Milan
V*itro–vivo* mathematical model correlation, M. Grassi, University of Trieste
Chitosan-based polyelectronic complexes for nasal drug delivery, B. Luppi, University of Bologna
New devices for dispensing ophthalmic treatments may be the key to managing the life-cycle of established products with low investments in filling technology, M. Birkhoff, Pfeiffer-Valois
Omega-3 and antioxidant-rich liposomes for nasal administration of anti-Alzheimer drugs, G. Corace, University of Bologna
Microemulsions for ophthalmic applications, F. Carli, Azad Pharmaceuticals
Development of squalene nanoparticles for anticancer therapy, F. Dosio, University of Turin
Filmable pharmaceutical formulations: From transdermal to oral delivery, M. Di Grigoli, Bouty
Characterisation of propinate beclometasone particles sprayed form pressurized inhalers, F. Buttini, University of Parma
Rational and viable: The future of drug delivery, T. Schmierer, Capsugel
Sub-unit vaccines: Design of a new adjuvant generation, C. Colonna, University of Pavia
A novel approach to medical treatment chewing: 3Tabgum, A. Salini, Flarer
Chronocap delivery platform, A. Gazzaniga, University of Milan
Combination of prilling and dielectric treatments for controlled drug release, P. Del Gaudio, University of Salerno
Pressurised metered dose inhaler: The Chiesi modulite, S. Bonelli, Chiesi Farmaceutici
Formulation and production of polymeric systems for the intestinal release of probiotics, B. Albertini, University of Bologna
Ethylcellulose mol wt variation effect on coacervation processes for microencapsulation, F. Fabiani, Eurand International
Polymer and lipid nanoparticles for oral administration of sodium diclofenac: *In vitro* and *ex vivo* studies, G. Rassu, University of Sassari
Modular assemblies for oral multi drug and multi drug release in Parkinson disease treatment, S. Mercuri, University of Parma
MMx therapeutic system, L. Moro, Cosmo Pharmaceuticals
Cubosome, a new delivery system, E. Esposito, University of Ferrara
Dry technology for powder inhalation: Half breathability, half dose, G. Caponetti, Eratech
Design of synthetic and semisynthetic bone tissues for tissue regeneration, R. Dorati, University of Pavia
W.A.S. Eudragit: More easy to use system, F. Roversi, Rofarma

Albumin-loaded solid lipid microparticles fabricated by spray congealing and spray freeze drying, M. Di Sabatino, University of Bologna

Continuous microgranulation, L. Rabaglia, IMA

Hemoderivatives in bioadhesive compositions for the prevention and the treatment of mucositis, G. Sandri, University of Pavia

Innovative and multifunctional excipients for immediate and sustained release oral forms: Cellets delivery system, P. Tschopp, Pharmatrans Sanaq

Polymer and gold nanoparticles: Applications in innovative formulations, S. Salmaso, University of Padova

Pharmaceutical application of a novel CO_2-based technology, P. Esposito, SiTec Pharmabio

Novel vascular systems for dermal and transdermal drug delivery, A. M. Fadda, University of Cagliari

Mal-o-fast: An oral dispersible film, F. Cilurzo, Pharmafilm spin-off University of Milan

Microemulsion system for oral administration, C. Ciocca, Accelera

SNL from hot microemulsions: New applications, P. Gasco, Nanovector

Advances in polymer conjugation for the delivery of proteins and drugs, A. Mero, University of Padova

Evaluation of suitable methodologies for *in vitro* characterisation of controlled release microparticles for pulmonary drug delivery, S. Scalia, University of Ferrara

Mucosadh: Un collutorio a rilascio prolungato, C. Gennari, Pharmafilm spin-off University of Milan

Thermal conductivity measurement: A promising tool for the study of drug skin penetration, L. Giovannelli, DISCAFF, University of Piemonte Orientale

Nanotechnologies for using zoledronic acid in cancer treatment, G. De Rosa, University "Federico II" of Naples ■

2010 Membership Application

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In the News

Compiled by Steven Giannos
Industrial Editor

July 2010

FDA Approves Strativa Pharmaceuticals' Zuplenz (Ondansetron) Oral Soluble Film for Prevention of Chemotherapy-induced, Radiotherapy-induced, and Postoperative Nausea and Vomiting

PRNewswire: July 2, 2010 – WOODCLIFF LAKE, NJ – Strativa Pharmaceuticals has announced that the U.S. Food and Drug Administration (FDA) has approved Zuplenz (ondansetron) oral soluble film for the prevention of postoperative, highly and moderately emetogenic cancer chemotherapy-induced, and radiotherapy-induced nausea and vomiting. Zuplenz, a unique formulation of ondansetron, is the first oral soluble film approved by the FDA as a prescription medication.

FDA approval was granted based on clinical study data comparing the bioequivalence of 8 mg of Zuplenz to 8 mg of Zofran ODT (orally dissolving tablet). The pharmacokinetic results of these studies demonstrated that a single dose of Zuplenz, taken with or without water and under fed and fasting conditions, was comparable to Zofran ODT.

"The FDA approval of Zuplenz marks an important milestone for Strativa as it reinforces our commitment to enhancing prescription products to meet the different needs of patients," said John A. MacPhee, president of Strativa Pharmaceuticals. "Zuplenz offers an innovative and convenient, easy-to-take formulation for patients who have trouble swallowing tablets, while providing the trusted efficacy expected from ondansetron."

Zuplenz uses proprietary PharmFilm oral soluble film technology from MonoSol Rx to rapidly dissolve on the tongue without the need for water, which can cause additional discomfort for some patients suffering from nausea and vomiting. Zuplenz will be offered in 4- and 8-mg dosage strengths and is expected to be available in retail pharmacies in the third quarter of 2010.

Nausea and vomiting is a common side effect associated with chemotherapy, radiotherapy, and surgery. Left untreated, nausea and vomiting can have serious consequences, such as exhaustion, dehydration, and undernourishment, which can interfere with treatment and healing. For more information about Strativa, visit www.strativapharma.com.

Lupin Receives FDA Approval for Famotidine for Oral Suspension

PRNewswire: July 1, 2010 – BALTIMORE, MD – Lupin Pharmaceuticals, Inc. (LPI) has received final approval from the U.S. Food and Drug Administration (FDA) for its Famotidine for oral suspension (40 mg/5 mL). Commercial shipments of the product have already commenced.

Lupin's Famotidine for oral suspension is the AB-rated generic equivalent of Merck's Pepcid, which is indicated for the short-term treatment of active duodenal ulcer, active benign gastric ulcer, and gastroesophageal reflux disease (GERD). Pepcid for oral suspension had annual sales of approx. $29 million for the 12 months ending March 2010 based on IMS Health sales data.

Headquartered in Mumbai, India, Lupin Limited is an innovation-led transnational pharmaceutical company producing a wide range of quality, affordable, generic and branded formulations and APIs for the developed and developing markets of the world. Lupin Pharmaceuticals, Inc. is the U.S. wholly owned subsidiary of Lupin Limited, with sales and marketing headquarters in Baltimore, MD. For more information, visit www.lupinpharmaceuticals.com.

FUISZ Announces Advances in Devices and Solid Dosage Form

PRNewswire: July 1, 2010 – MIAMI, FL – FUISZ has announced two medical technology advances. First, FUISZ announced that it has received a notice of issuance from the U.S. Patent and Trademark Office for patent claims that cover a direct connection between prescribing physicians and blood analysis devices. The invention allows the healthcare provider to set the parameters of allowable analyte levels for each patient and enables simple notifications for any variance out of a predetermined range. Joseph Fuisz, managing member of FUISZ stated, "These patent claims represents a quantum leap in the use of portable blood analyzers to provide a higher level of care for patients while reducing burdens on healthcare providers. We are in discussions with the blood analyzer industry for the licensing of this technology."

FUISZ also announced that it has filed a new patent in the field of solid oral bioactive dosage forms. This novel system works to enhance or retard drug absorption. It is particularly well suited to buccal, sublinqual, and other forms of mucosal delivery, including nanoparticles. Joseph Fuisz commented, "This innovation can be readily adapted for use with existing products to improve control of drug absorption. It will be particularly well received in the opiate market where controlling relative absorption of opiates and agonists is so critical. This technology draws upon our deep

In the News continued on page 32

In the News continued from page 31

knowledge of quick dissolve dosage forms and applies that knowledge in a broad manner to all solid dosage forms."

FUISZ is a family owned company. Fuisz principals Richard Fuisz, M.D., and Joseph Fuisz, Esq., are named inventors on or owners of hundreds of patents and patent applications. These patents span several fields: drug delivery, quick dissolve dosage forms, including quick dissolve tablets, thin films, slow dissolve sheets, conventional oral dosage units, opiate abuse resistance, women's health, electronic mail, e-commerce, and tobacco. The company is based in Miami, FL (www.fuisz.com).

June 2010

ULURU Inc. Announces Licensing Agreement for Altrazeal™ in China

PRNewswire-FirstCall: June 30, 2010 – ADDISON, TX – ULURU Inc. (NYSE Alternext: ULU) has signed a licensing and supply agreement with Jiangxi Aiqilin Pharmaceuticals Group (Aiqilin) for the marketing of Altrazea™ in China, including Hong Kong, Macau, and Taiwan. Under the terms of the licensing and supply agreement ULURU will receive an upfront licensing payment, milestone payments based on regulatory approvals and sales performance, and a royalty on product sales. Aiqilin has also been granted certain manufacturing rights. The license agreement covers Altrazeal™, Altrazeal™ Silver, and Altrazeal™ Collagen.

Commenting on the agreement, Chunhua Hu, president and CEO of Aiqilin, stated, "There are more than 20 million wound patients annually in China. The wound care market segment is a rapidly growing area in the Chinese market. Aiqilin is well connected and has strong support from the clinical experts and researchers, extensive marketing and sales channels to effectively promote, sell and further develop Altrazeal™ in China."

The Chinese market is rapidly becoming a major healthcare market, where it is projected that sales will grow from $25 billion in 2009 to $220 billion in 2020, making it the second largest market in the world. It is anticipated that Altrazeal™ could be approved by the Chinese regulatory authorities in early 2011.

Kerry P. Gray, president and CEO of ULURU, stated; "We are very pleased to have formed this strategic relationship with Aiqilin. China is an extremely important market where we anticipate Altrazeal™ can rapidly establish a significant market presence. This represents the first step in our plan to have Altrazeal™ marketed globally and provides external commercial validation of Altrazeal™ and our proposed product line extensions."

Aiqilin is a specialty pharmaceutical company specializing in the development and commercialization of drug delivery products with a major focus in wound care. ULURU Inc. is a specialty pharmaceutical company focused on the development of a portfolio of wound management and oral care products to provide patients and consumers improved clinical outcomes utilizing its innovative Nanoflex™ aggregate technology and OraDisc™ transmucosal delivery system. For further information about ULURU Inc., please visit www.uluruinc.com. For further information about Altrazeal™, please visit www.Altrazeal.com.

Using Nanotechnology to Improve a Cancer Treatment: Drug Delivery System Hits Tumors but Spares Kidneys

Nannotechnology Now: June 26, 2010 – CAMBRIDGE, MA – The research, conducted in laboratory animals, marries chemistry and nanotechnology to deliver toxic platinum atoms to tumors while almost entirely blocking the platinum from accumulating in the kidney, according to Shiladitya Sengupta, a Harvard assistant professor of medicine and health sciences and technology, whose Laboratory for Nanomedicine at Harvard-affiliated Brigham and Women's Hospital conducted the work.

Sengupta has focused his research for three years on cisplatin, a powerful anti-cancer drug used in first-line chemotherapy. Sengupta said the drug, discovered about 40 years ago, has many positive aspects. It is relatively inexpensive and effective against many cancers. Its toxicity, however, limits its use. "Even if you can see amazing results as an anti-tumor therapy, you can't give more," Sengupta said.

Despite several attempts, cisplatin hasn't been improved upon. Two similar drugs that also incorporate platinum are on the market, but while they are less toxic to the kidney, they are also less active against tumors. Although the chemistry involved is complex, the key to cisplatin's effectiveness—and its toxicity—lies in how easily it releases platinum, both at the tumor site and, undesirably, in the kidneys. Manufacturers of the two alternative drugs have reduced the toxicity of the drugs by making them hold onto their platinum more tightly.

Sengupta's work took a different track. Understanding that particles greater than 5 nm in size would not be absorbed by the kidney, he set out to engineer a super-sized cisplatin. Understanding the chemical properties of the cisplatin molecule and the laws that govern molecular folding, his team designed a polymer that would bind to cisplatin, much as a thread runs through a bead's central hole. By stringing together enough cisplatin, the whole molecule wrapped itself into a ball 100 nm in size, which is too large to enter the kidney. It took a couple of tries to get the molecular design right. Although the initial design proved nontoxic to the kidneys, it wasn't as effective as the original cisplatin. Sengupta and colleagues tweaked the chemical formula so the molecule didn't hold quite so tightly to the platinum atoms.

Studies conducted by Basar Bilgicer, assistant professor at the University of Notre Dame, showed that the molecule accumulated in tumor tissue, whose leaky blood vessels allowed it to pass out of the capillaries that feed the tumor. The molecule is too large to pass into other tissues, such as the kidney, lungs, liver, and spleen. Once lodged in the tumor, the higher acidity there caused the molecule to fall apart, dumping its toxic load on the cancerous tissue. "It showed absolutely minimal toxicity to the kidney," Sengupta said.

The new compound has been found to be effective against lung and breast cancers. Instructor in pathology Daniela Dinulescu at Brigham and Women's Hospital also demonstrated that the nano-compound outperformed cisplatin in a transgenic ovarian cancer model that mimics the disease in humans.

The research, which received funding from the National Institutes of Health and the Defense Department's Breast Cancer Research Program, has not been tried in humans and would require potentially lengthy testing before being ready for patient care.

Described in the *Proceedings of the National Academy of Sciences*, the project also included researchers at the University of Notre Dame, the Harvard-MIT Division of Health Sciences and Technology, the Dana-Farber Cancer Institute, the National Chemical Laboratory in Pune, India, and the Translational Health Science and Technology Institute in New Delhi. Sengupta praised the work and creativity of fellows Abhimanyu Paraskar and Shivani Soni on the project.

Soligenix Announces Publication of Positive Data Describing Protection from Mucosal and Systemic Ricin Intoxication by Intradermal RiVax™ Administration

PRNewswire-FirstCall: June 25, 2010 – PRINCETON, NJ – Soligenix, Inc. (OTC Bulletin Board: SNGX), a late-stage biopharmaceutical company, has announced the publication of an article in the June 2010 edition of *Vaccine* that describes protection from mucosal and systemic ricin intoxication by intradermal administration of RiVax™, the company's vaccine against ricin toxin. The article was authored by the company's collaborators at the University of Texas Southwestern Medical Center at Dallas (UT Southwestern) where the vaccine originated. RiVax™ is currently being evaluated in Phase I human safety and immunogenicity trials, as well as non-human primate trials, for efficacy.

The purpose of the study was to determine whether RiVax™ administered by intradermal (ID) injection would be more immunogenic and protective at lower doses. ID vaccination has several practical advantages in protecting humans due to the ease of administration, especially when using an ID gun, thereby eliminating the need for needles and subsequent needle disposal. In this publication, a comparison of ID and intramuscular (IM) vaccination with or without an aluminum salt adjuvant at several dose levels was investigated. The levels of anti-RiVax™ antibodies generated in serum, as well as the ability of the vaccine to protect mice against ricin intoxication following systemic, gastric gavage, or aerosol challenges, were determined.

The major findings to emerge from this study are as follows. ID versus IM administration of RiVax™ without adjuvant conferred equal protection. RiVax™ adsorbed to aluminum adjuvant was significantly better than RiVax™ alone in eliciting specific antibodies, resulting in both systemic and mucosal protection when 90–99% less vaccine was used. Vaccination with RiVax™ adsorbed to aluminum adjuvant via the ID route was significantly better than vaccination via the IM route at protecting animals from ricin challenge; hence, smaller doses of vaccine may be required when ID vaccination is used. In comparing IM versus ID vaccination with RiVax™ adsorbed to aluminum adjuvant at low doses, the latter was more effective at protecting mice from ricin-induced lung damage. Finally, RiVax™ specific antibody levels correlated with post-challenge survival.

"There have been many attempts to develop a prophylactic ricin vaccine, using different preparations of the ricin holotoxin with and without various adjuvants," stated Dr. Ellen Vitetta, director of the Cancer Immunobiology Center at UT Southwestern and senior author of the study. "But none of these have been as extensively studied as RiVax™, and none have looked at the ID vaccination route."

"Since it is likely that a ricin vaccine would be used in an emergency setting or by the military, the ease of ID vaccination with jet injectors or similar devices with lower doses of vaccine is rather important," stated Robert N. Brey, Ph.D., chief scientific officer of Soligenix. "It should also be noted that ID vaccination was highly effective at protecting the lungs of the mice from ricin aerosols, a likely route of delivery in the setting of bioterrorism."

The article, entitled "Intradermal Administration of RiVax™ Protects Mice from Mucosal and Systemic Ricin Intoxication," was authored by Drs. Marconescu, Smallshaw, Pop, Ruback, and Vitetta at UT Southwestern. The research was funded directly by an NIH grant to UT Southwestern and complements the NIH funding to Soligenix for the development of RiVax™. The full article is available online at http://dx.doi.org/10.1016/j.vaccine.2010.05.045.

Archimedes Pharma Receives CHMP Positive Opinion for PecFent for the Treatment of Breakthrough Cancer Pain

PRNewswire: June 25, 2010 – READING, England – Archimedes Pharma, a leading specialty pharma company, has announced that its lead product, PecFent, has received a positive opinion from the Committee for Human Medicinal Products (CHMP) of the European Medicines Agency (EMA). CHMP is recommending PecFent, an innovative fentanyl nasal spray, be authorized for marketing in European Union countries for the treatment of breakthrough cancer pain (BTCP)—sudden, unpredictable episodes of intense pain that occur despite background pain medication.

Jeffrey H. Buchalter, president and chief executive officer of Archimedes Pharma, commented, "This is a defining moment for Archimedes Pharma. Breakthrough cancer pain is a poorly served indication and affects up to 95% of all cancer patients with pain. Today's announcement by the CHMP is an important step towards bringing a new treatment option to these patients in Europe. It also marks a step change in scale for Archimedes Pharma's already successful European commercial operations and

In the News continued on page 34

In the News continued from page 33

an important landmark in our development as a leading global specialty pharma company. Our clinical development programme delivered excellent results and we look forward to delivering this new option for patients in Europe as soon as we can following the grant of the Marketing Authorisation."

PecFent is an aqueous fentanyl citrate solution using Archimedes Pharma's proprietary PecSys™ technology to allow fentanyl to be retained on the nasal mucosa and is designed to produce rapid but controlled absorption into systemic circulation. The positive opinion is based on the results of Archimedes Pharma's comprehensive clinical development program for PecFent, which comprised three Phase III studies, including an active comparator study and a large long-term safety and acceptability study. The program included more than 650 patients and more than 100 investigational sites from the United States, United Kingdom, Germany, France, Spain, and Italy—in total, 13 countries across 4 continents.

Archimedes Pharma submitted a New Drug Application (NDA) for PecFent with the U.S. Food and Drug Administration (FDA) in August 2009 and is in the process of establishing its own U.S. commercial organization to market the drug in the United States once approved. PecFent was previously known as NasalFent.

MonoSol Rx Expands Collaboration with Midatech to Deliver Peptides Utilizing Its PharmFilm® Drug Delivery Technology

PRNewswire: June 24, 2010 – WARREN, NJ – MonoSol Rx, the developer of PharmFilm® drug delivery technology has announced the expansion of its agreement with Midatech Group (Oxford, U.K.) to develop nanoparticle-based proteins and peptides for therapeutic delivery utilizing pharmaceutical films. Under the terms of the expanded agreement, MonoSol Rx has made an equity investment in Midatech, and Keith Kendall, executive vice president and chief financial officer of MonoSol Rx, will join the Midatech Board of Directors.

Commenting on the agreement, A. Mark Schobel, president and CEO of MonoSol Rx, said, "We have strengthened our collaboration with Midatech on the heels of positive data indicating the successful delivery of a 6000 Dalton polypeptide in a pre-clinical model. Having demonstrated that the size and chemical composition of Midatech's biocompatible nanocarriers are ideally suited for oral delivery using our PharmFilm® technology, we are continuing to jointly research and develop nanoparticle-based oral film formulations of certain peptides and proteins that are currently limited by their need to be injected or infused."

Prof. Tom Rademacher, chair of Midatech Group said, "We believe that MonoSol Rx's PharmFilm® technology is a stable and effective vehicle for delivering a therapeutic dose of our peptide carrying nanoparticles buccally or sublingually for specific indications, thereby eliminating the need for injection or more invasive delivery. The synergy of our two technologies is particularly valuable in indications that can only be treated with injectables, as well as for certain proteins and peptides competing with small molecules for market share."

Since 2008, MonoSol Rx and Midatech have been leveraging the self-assembling glyconanoparticle and PharmFilm® technologies to formulate large molecules for oral bioavailability on film. PharmFilm® formulations under the collaboration have the potential to provide an easy-to-use, noninvasive delivery alternative to many of today's injectable and intravenous therapeutics.

STMicroelectronics and Debiotech Debut Disposable Insulin Jewel Pump at ADA Congress

PRNewswire-FirstCall: June 23, 2010 – LAUSANNE and GENEVA, SWITZERLAND – Debiotech and STMicroelectronics (NYSE: STM) publicly showcased their novel insulin "Jewel Pump" at the Debiotech stand at the American Diabetes Association 70th Scientific Sessions (June 25–29) in Orlando, FL. Representing the most advanced use of microfluidic MEMS (micro-electro-mechanical systems) technology in diabetes treatment, the tiny device, for which FDA clearance is now pending, can be mounted on a disposable skin patch to provide continuous insulin infusion, enabling substantial improvements in the treatment efficiency and quality of life of diabetic patients.

The highly miniaturized disposable insulin pump combines Debiotech's expertise in insulin delivery systems with ST's strengths in manufacturing high-volume silicon-based microfluidic devices. The Jewel Pump is smaller, thinner, and lighter than currently available insulin pumps and can be worn as a nearly invisible patch on the skin that provides 4.5 mL of insulin, suitable for a 6-day treatment. Microfluidic technology also provides better control of the administered insulin doses, more closely imitating the natural secretion of insulin from the pancreas, while detecting potential malfunctions of the pump to further protect patients. As a disposable device manufactured using high-volume semiconductor processing technologies, the MEMS-based Jewel Pump is also much more affordable, allowing the patient or healthcare system to avoid the substantial upfront investment typically associated with current pump solutions.

"The collaboration with ST has produced key contributions to the industrialization success of this very innovative MEMS technology for the treatment of diabetes," said Dr. Frederic Neftel, president and CEO of Debiotech. "We are now able to demonstrate a real breakthrough in insulin delivery that combines the highest level of reliability and performance, while enhancing the safety for the patient and improving overall Quality of Life."

Insulin pump therapy, or continuous subcutaneous insulin infusion (CSII), is an increasingly attractive alternative to individual insulin injections that must be administered several times a day. With CSII, the patient is connected to a programmable pump, including a storage reservoir, from which

insulin is infused into the tissue under the skin throughout day and night according to the specific needs of the patient.

"The success of the cooperation with Debiotech to bring their visionary concept to a high performance and affordable commercial product underlines the enormous contribution that semiconductor companies can make in the areas of healthcare and well being," said Benedetto Vigna, group vice president and general manager of ST's MEMS, Sensor and High Performance Analog Division. "Working with partners such as Debiotech, we are able to deploy our world-leading MEMS design and manufacturing strengths to improve the health and well being of millions of people around the world."

Michael J. Fox Foundation Awards $4.6 Million to Help Advance Neurotrophic Factors as Transformative Parkinson's Treatments

PRNewswire-USNewswire: June 22, 2010 – NEW YORK, NY – The Michael J. Fox Foundation for Parkinson's Research (MJFF) has announced $4.6 million in awards to support two promising studies of neurotrophic factor therapies for Parkinson's disease (PD). The projects, funded under a directed LEAPS (Linked Efforts to Accelerate Parkinson's Solutions) initiative, bring together leading investigators to build on the knowledge and experience gained from previous trials of neurotrophic factors to help speed this avenue of research toward better treatments for people living with PD.

Neurotrophic factors (also known as trophic factors or growth factors) are specialized proteins that protect and nourish neurons in the brain, including the dopamine neurons that die in Parkinson's disease. Preclinical studies and several early-phase clinical trials of trophic factors have shown the potential to slow or stop the progression of Parkinson's—a key unmet need for PD patients. However, the results from Phase II clinical trials have yet to demonstrate the efficacy of neurotrophic factor therapies. A complication in developing trophic-based therapies is the inability of these large proteins to cross directly into the brain, requiring innovative methods for drug delivery.

"MJFF continues to believe in the potential of neurotrophic factors as transformative therapies for people living with Parkinson's disease," said Todd Sherer, Ph.D., vice president of research programs at MJFF. "The Foundation's new approach to this area of research is to develop better methods to deliver trophic factors to the appropriate brain regions at the appropriate doses. And that's exactly the focus of the two projects that MJFF is supporting."

One of the awardees, the biopharmaceutical company Ceregene, Inc. will be conducting a Phase II clinical study evaluating CERE-120, a gene therapy product that aims to deliver the neurotrophic factor neurturin to dying dopamine neurons in the brain. Ceregene's new clinical study follows an earlier Phase II trial, also supported by MJFF, which failed to show a benefit of CERE-120 over placebo on the primary endpoint (unified Parkinson's disease rating scale) after 12 months. However, continued follow up of blinded data from the trial participants showed a statistically significant treatment effect for CERE-120 at 18 months and, at that time, MJFF partnered with Ceregene to further analyze trial data. Based on the findings that suggested inadequate distribution of CERE-120 to the area of the brain affected by PD, Ceregene has enhanced the method of delivery and dosing regimen of its gene therapy for use in continuing clinical studies.

The second award supports a collaborative effort between Biovail Laboratories International SRL and MedGenesis Therapeutix, Inc. to develop a different neurotrophic factor, GDNF (glial cell line-derived neurotrophic factor), as a potential PD therapeutic. Although earlier clinical studies of GDNF have shown promise, no trial has conclusively demonstrated the safety and efficacy of this trophic factor as a Parkinson's treatment. Biovail and MedGenesis are working on an effective method of delivering GDNF to targeted areas of the brain, addressing a key limitation of previous studies. MJFF's support will help advance this work, bringing the potential benefits of GDNF closer to patient relevance.

Neurotrophic factors are a high-priority therapeutic target for MJFF, which has committed approx. $20 million to their development to date. For more information about these projects, including grant abstracts and researcher bios, visit www.michaeljfox.org.

Probactive Biotech, Inc. Announces an Agreement to Co-develop Novel Biopharmaceuticals for Cancer with Dalat Nuclear Research Institute of Vietnam

PRNewswire: June 22, 2010 – GARDEN GROVE, CA – Probactive Biotech, Inc., a Garden Grove, California-based corporation, has entered into an agreement with the Dalat Nuclear Research Institute to co-develop a number of cancer drugs, utilizing combinations of antitumor antibodies and antitumor radioactive compounds. Antitumor antibodies have the ability to take antitumor compounds directly to tumor sites within the body.

"We are extremely pleased with this opportunity," said Mr. Ngo, president and CEO of St. Paul Biotech. "There is a thriving pharmaceutical industry in Vietnam, and the Dalat Nuclear Research Institute has been producing radionuclides for medical use for over 30 years. My company in the U.S. has been engaged in developing antitumor antibodies, so this is a natural fit to co-develop these novel drugs."

Probactive Biotech has combined medical-grade iodine-131 and yttrium-90 with antitumor antibodies, producing remarkable and targeted anticancer activity. Targeted drug delivery means that healthy cells have little or no exposure to the drug product. Parts of the research and development program will be completed at the Dalat Nuclear Research Institute in Vietnam. The later human clinical trials will be conducted in Vietnam under the regulatory guidelines of the Ministry of Health and also in compliance with U.S. FDA regulations.

In the News continued on page 36

In the News continued from page 35

"The competitive landscape for the pharmaceutical industry has changed," added Ngo. "We can now utilize recognized international science and technological resources to develop advanced biopharmaceuticals for a fraction of the cost usually associated with drug development. The medical and economic benefit from this type of strategic alliance will be significant."

Pain Startup Incline Therapeutics Grabs $43 million and Could Be Acquired by Cadence Pharmaceuticals

San Francisco Business Times: June 21, 2010 – SAN FRANCISCO, CA – Cadence Pharmaceuticals Inc. could buy Redwood City startup Incline Therapeutics Inc., which has secured $43 million in financing and an FDA-approved needle-free pain medication system, for as much as $285 million.

An acquisition by San Diego, California-based Cadence (NASDAQ: CADX) would be a windfall for Frazier Healthcare and other venture capital firms that backed Incline's series A round. The cash will pay for further development of Ionsys, a needle-free, pre-programmed system applied to the upper arm or chest and designed to deliver levels of the opioid fentanyl to patients following surgery.

Ionsys was developed by Johnson & Johnson-controlled Alza Corp. of Mountain View, CA, and approved in 2006 by the U.S. Food and Drug Administration and the European Medicines Agency. The system, however, is not on the market. Incline will seek approval from both agencies for new patient safety features that are being developed for Ionsys. FDA approval of the add-ons requires a strategy to deal with fentanyl, which is contained in Ionsys and can be abused by opioid addicts or misused by patients. Other VCs participating in Incline's financing round were 5AM Ventures, Technology Partners, Adams Street Partners, Saints Capital Partners, and Emergent Medical Partners.

Savara Selected as Texas Emerging Technology Fund Recipient

PRNewswire: June 14, 2010 – AUSTIN, TX – Savara, Inc., an inhalation drug delivery company, has been chosen by the state of Texas as the recipient of a commercialization award funded through the Texas Emerging Technology Fund (ETF). The company, which produces novel respiratory therapeutics, will receive a $1.9 million award for the commercialization of its products. "Savara's dry-powder technology holds great potential for treating asthma, lung cancer, and other lung-based diseases," said Jack McDonald, chair of Perficient, Inc. and of the Central Texas Regional Center of Innovation and Commercialization (RCIC). "This investment by the ETF will not only help grow our biotech industry in central Texas but may result in new therapies that save lives."

Savara is an inhalation drug development company developing next-generation respiratory therapeutics utilizing its proprietary NanoCluster dry-powder formulation technology. NanoCluster's unique features can produce numerous patient benefits, including reduced dosage, enhanced efficacy, improved safety, and increased tolerability, as well as greater patient convenience.

"Texas is a leader in cutting-edge biotechnologies thanks to investments from the Texas Emerging Technology Fund that have attracted companies and top researchers to our state," said Governor Rick Perry. "Savara's technology will help identify and treat lung cancer more quickly and efficiently, saving lives and bringing us one step closer to eliminating this deadly disease." This award will be used to advance the development of Savara's lead project toward investigational new drug (IND) approval.

Angiotech's Licensee, Cook Medical, Files PMA Submission for FDA Approval of Zilver PTX Drug-eluting Stent Platform

PRNewswire-FirstCall: June 11, 2010 – VANCOUVER, CA – Angiotech Pharmaceuticals, Inc. (NASDAQ: ANPI, TSX: ANP) has announced that Cook Medical, a license holder of Angiotech's paclitaxel technology, has submitted its pre-market approval (PMA) application to the U.S. Food and Drug Administration (FDA) for the company's unique polymer-free Zilver PTX drug-eluting peripheral stent. Intended for use in patients with peripheral arterial disease (PAD) in the superficial femoral artery (SFA), Zilver PTX is a self-expanding, highly durable nitinol stent that uses a proprietary, polymer-free technology to deliver a locally therapeutic dose of paclitaxel, an anti-proliferative drug, to the target lesion.

Cook's PMA submission includes data from the randomized portion of the ongoing Zilver PTX clinical trial, the largest study of its kind for the endovascular treatment of PAD in the SFA. Encompassing a global single-arm registry and a randomized study involving 1,276 total patients, including diabetics, symptomatic patients, and those with complex lesions, the 479 patients enrolled in the randomized study and the 787 in the single-arm study are experiencing clinical improvement, excellent stent durability (i.e., fracture resistance), high rates of event-free survival, and freedom from target lesion revascularization. Patency data from the single-arm study was reported at 86.2% at 12 months at EuroPCR in May.

"PAD currently affects approximately eight million men and women over the age of 40 in the United States," said Michael Dake, M.D., professor in the Department of Cardiothoracic Surgery at Stanford University Medical School, medical director of the Cath/Angio Laboratories at Stanford University Medical Center, and the trial's principal investigator. "The medical community considers percutaneous transluminal angioplasty to be the treatment of choice for patients with PAD, but Zilver PTX shows promise for being a superior method for improving the quality of life of these individuals."

"Filing for pre-market approval with the FDA is an exciting step forward for us in bringing Zilver PTX to market in the United States," said Rob Lyles, vice president and global leader of Cook Medical's Peripheral Intervention division. "Cook is committed to continually improving the efficacy and safety of our products with the overall aim of improving patient outcomes."

Nautilus Neurosciences Announces U.S. Launch of CAMBIA (Diclofenac Potassium for Oral Solution) for the Treatment of Migraine

PRNewswire: June 8, 2010 – BRIDGEWATER, NJ – Nautilus Neurosciences, Inc., a neurology-focused specialty pharmaceutical company headquartered in New Jersey, has announced that CAMBIA (diclofenac potassium for oral solution) is now available in the United States for the acute treatment of migraine with or without aura. CAMBIA was approved by the U.S. Food and Drug Administration in June 2009.

"The approval and subsequent commercialization of CAMBIA as a unique formulation of diclofenac offers an important treatment option for the millions of people who suffer from migraines," said Alan M. Rapoport, M.D., clinical professor of neurology at the David Geffen School of Medicine at UCLA and founder and director-emeritus of the New England Center for Headache in Stamford, CT. "With a simple, quick administration that can be used at any time during a migraine attack, CAMBIA offers rapid onset of pain relief with an established safety profile."

Migraine affects more than 36 million people in the United States, 75% of them women. According to a survey published in the *Journal of the American Board of Family Medicine*, many migraineurs still hope to find a better treatment for their migraines, with more than a quarter dissatisfied with their treatment and fewer than a fifth of migraineurs describing themselves as "very satisfied" with their treatment.

A novel, water-soluble, buffered diclofenac potassium powder, CAMBIA is the only prescription non-steroidal anti-inflammatory drug (NSAID) available for the acute treatment of migraine. Engineered using Dynamic Buffering Technology (DBT), a patented absorption-enhancing technology developed by APR Applied Pharma Research S.A., CAMBIA is specifically designed for fast, effective relief from the symptoms of migraine. CAMBIA enters the bloodstream quickly and readily achieves peak plasma concentrations, providing rapid onset of pain relief via oral therapy without increasing the patient's total exposure to diclofenac.

"The U.S. availability of CAMBIA represents an important milestone for Nautilus and an important new product for the millions of Americans who suffer from migraines," said James Fares, chair and CEO of Nautilus Neurosciences. "The launch of CAMBIA further establishes our corporate commitment to bringing unique products to those in need and being a true partner with the migraine community. The unique formulation of CAMBIA provides a new treatment option that can reduce key migraine symptoms quickly, effectively and safely."

The FDA approval of CAMBIA was based on two Phase III placebo-controlled trials showing that CAMBIA was superior to placebo in all four FDA-mandated co-primary end points for migraine—pain, nausea, photophobia, and phonophobia. Both studies also showed that reduction in pain intensity was significantly greater in the CAMBIA group than in the placebo group as early as 15 minutes following treatment, and headache response rates were superior to placebo for up to 24 hours.

Avista Capital Partners Commits $48.5 million to OptiNose to Develop an Innovative Nasal Drug Delivery Technology Slated to Begin Phase III Trials

PRNewswire: June 7, 2010 – NEW YORK, NY – Avista Capital Partners (Avista), a leading private equity firm has committed to invest $48.5 million in OptiNose. OptiNose has developed an innovative nasal drug delivery technology that enables administration of drugs deep in the nasal cavity, enabling the treatment of both local and systemic disease. In conjunction with this investment, OptiNose will reincorporate in the United States and move its headquarters from Oslo, Norway, to Yardley, PA.

OptiNose, which was founded by Dr. Per Djupesland in 2000, has extensively tested its nasal drug delivery device under the leadership of the current CEO, Helena Kyttari Djupesland. The company recently completed Phase II clinical studies for chronic rhinosinusitis with polyposis, chronic rhinosinusitis without polyposis, and migraine therapies with positive results. Avista's investment will support Phase III trials and enable OptiNose to build out its clinical development and commercialization infrastructure. WFD Ventures, a New York-based venture capital firm specializing in medical technology investing, will also maintain a significant stake in the company and continue to actively support the development program.

Peter Miller, the president and former chief executive officer of Take Care Health Systems, a business Miller co-founded and sold to Walgreens, has been appointed the new chief executive officer of the company and will serve on the OptiNose Board of Directors. Prior to joining Take Care Health Systems, Miller spent more than a decade at Johnson & Johnson in senior executive positions.

Larry Pickering, an Avista healthcare industry executive who will become the new chair of OptiNose, said, "OptiNose's technology is extremely promising for the indications slated to begin Phase III trials and for a wide variety of other applications. We look forward to supporting the Company as it enters these trials with a low risk development pathway. I have known Peter since his time at Johnson & Johnson and am convinced he is the ideal executive to lead this Company."

Miller stated, "I am very excited about the opportunity to lead a company that has core technology with such strong potential and to work with the talented OptiNose team and a group of investors with such a history of success. OptiNose's devices deliver intranasal drugs in a completely new way to targeted regions of the nasal cavity, including the sinuses and the olfactory region, without lung deposition. I believe this technology provides a broad platform for delivering significant value to patients, physicians, and payers, with potential applications in pharmaceuticals, vaccines, and OTC products."

In the News continued on page 38

In the News continued from page 37

CEO Helena Djupesland and Dr. Per Djupesland said, "We are delighted to welcome Peter Miller and Avista Capital Partners to the OptiNose team. We strongly believe in our technology, which solves many of the common problems associated with current nasal drug delivery techniques. With Peter's leadership and healthcare background, and the support and deep healthcare experience offered by Avista and WFD Ventures, we are confident in our ability to leverage our device's potential with many compounds."

Bill Doyle, managing partner of WFD Ventures, stated, "We at WFD continue to be strong supporters of OptiNose and are excited about working with Avista and Peter Miller to assist the Company in executing…its growth plan."

Philips and RXi Partner to Research RNAi Delivery

in-PharmaTechnologist.com: June 7, 2010 – Philips and RXi Pharmaceuticals have formed a research agreement to investigate combining their technologies for delivery of RNA interference (RNAi). Research into the delivery of RNAi has focused on ensuring the molecule's stability and ability to target relevant organs and tissues. Philips and RXi believe the combination of their respective technologies could fulfill both of these requirements.

In preclinical studies the companies will investigate the use of RXi's self-delivering rxRNA (sd-rxRNA) alongside Philips' ultrasound technology. sd-rxRNA is designed to enable administration and spontaneous cellular uptake without the use of a delivery vehicle. These capabilities are achieved by chemically modifying the compound to give it stability in biological fluids, a low stimulatory effect on the immune system, and high target specificity. "By combining RXi's proprietary sd-rxRNA molecules, which have unique properties of 'self delivery,' and Philips' ultrasound technologies, we will be working together to achieve targeted and specific delivery to relevant organs and tissues," said Noah Beerman, president and CEO of RXi.

Under the terms of the agreement sd-rxRNA will be investigated in conjunction with Philips' image-guided ultrasound-mediated drug delivery platform. Philips' tool allows the investigation of delivery of therapeutics across blood vessel barriers and facilitates uptake into cells. "The development of ultrasound techniques that could non-invasively trigger the delivery of new drug formats such as RNAi therapeutics at a targeted location opens up exciting possibilities for advancing personalized medicine," said Henk van Houten, senior vice president of Philips Research.

Researchers will investigate the use of these technologies at Philips' facilities in Eindhoven, The Netherlands, and RXi's operations in Worcester, MA. Both companies will contribute proprietary technologies, resources and expertise to the project.

Oramed Pharmaceuticals Forms Joint Venture and Launches Entera Bio Ltd.

PRNewswire-FirstCall: June 2, 2010 – JERUSALEM, IL – Oramed Pharmaceuticals Inc. (OTCBB: ORMP), a developer of oral drug delivery systems, has announced that its subsidiary Oramed Ltd. has entered into a joint venture agreement with Laser Detect Systems Ltd., an Israeli company listed on the Tel Aviv Stock Exchange, for the establishment of a new company to be called Entera Bio Ltd. Under the terms of the agreement, Oramed will out-license technology to Entera for the development of oral delivery drugs for certain indications. The out-licensed technology differs from Oramed's main delivery technology that is used for oral insulin and is subject to a different patent application. Entera's initial development effort will be an oral formulation for the treatment of osteoporosis.

Dr. Phillip Schwartz will serve as Entera's chief executive officer. Schwartz has more than 10 years of experience in the pharmaceutical and biotech industries and served as a lecturer at Harvard Medical School. Prior to joining Entera, Schwartz served as the scientific and medical development manager for Endo Pharmaceuticals.

Nadav Kidron, chief executive officer of Oramed Pharmaceuticals, commented, "This joint venture affords an opportunity to explore a technology with different characteristics from Oramed's main technology, which has the potential to make a significant contribution in the oral drug delivery arena. We look forward to a successful relationship with Laser Detect and Entera."

According to the agreement, Laser Detect will invest $600,000 in Entera, and Entera will be owned in equal parts by Oramed and Laser Detect. Entera's chief executive officer will be granted options to purchase ordinary shares of Entera, reflecting 9.9% of Entera's share capital, immediately following the dilution by these options. Entera's Board of Directors will be composed of four members—one director designated by each of Oramed and Laser Detect, Dr. Schwartz, and Kenneth Abramowitz, co-founder and managing general partner of NGN Capital. For more information about Oramed's clinical development programs, please visit www.oramed.com.

May 2010

Alexza Secures $25 million Committed Equity Financing Facility with Azimuth Opportunity, Ltd.

PRNewswire-FirstCall: May 26, 2010 – MOUNTAIN VIEW, CA – Alexza Pharmaceuticals, Inc. (Nasdaq: ALXA) has obtained a committed equity financing facility under which it may sell up to $25 million of its registered common stock to Azimuth Opportunity, Ltd. over a 24-month period. Alexza is not obligated to utilize any of the $25 million facility and remains free to enter into and consummate other equity- and debt-financing transactions. This facility replaces a similar facility that was established in March 2008 and expired after its 24-month term.

"This flexible financing facility is an important component of our portfolio of financing options, giving us the potential ability to raise capital quickly, at a competitive cost, and it may allow us to manage dilution more effectively by issuing shares in multiple tranches at times of our choosing over the next 24 months," said August J. Moretti, senior vice president and chief financial officer of Alexza. "We believe these advantages could benefit Alexza and our stockholders as we continue to transition from the development stage to commercialization."

"This is an exciting time for Alexza. As our October 11, 2010, PDUFA goal date approaches, we continue to scale-up our commercial manufacturing, and we are working with Biovail for the expected launch of our lead program AZ-004 (Staccato® loxapine) in Q1 2011," said Thomas B. King, president and CEO of Alexza.

Oramed Pharmaceuticals Announces Publication of an Article on Its Oral Insulin Capsule ORMD-0801

PRNewswire-FirstCall: May 26, 2010 – JERUSALEM, IL – Oramed Pharmaceuticals Inc. (OTCBB: ORMP.OB) (www.oramed.com), a developer of alternative drug delivery systems, has announced that a paper entitled, "Open-Label Study to Assess the Safety and Pharmacodynamics of Five Oral Insulin Formulations in Healthy Subjects," authored by Drs. Roy Eldor, Miriam Kidron and Ehud Arbit, was accepted and published in the journal *Diabetes, Obesity and Metabolism* (DOM).

"Publication of our data in a prestigious journal such as DOM lends further credence to the importance of oral insulin as a potential drug in the management of diabetes. The data published on formulation optimization is an important milestone in the development of ORMD-0801 and provides… continued evidence of clinical safety and the foundation for the proof of concept study for our proprietary oral drug delivery platform," said Miriam Kidron, chief officer of Oramed.

Sanofi-aventis Establishes Strategic Alliance with MIT's Center for Biomedical Innovation

PRNewswire-FirstCall: May 26, 2010 – PARIS, FRANCE – Sanofi-aventis (EURONEXT: SAN and NYSE: SNY) has announced a strategic alliance agreement with the Massachusetts Institute of Technology (MIT) Center for Biomedical Innovation, which will be known as the sanofi-aventis Biomedical Innovation Program (SABIP). The goal of the strategic alliance is to advance knowledge in the area of human health through basic and applied research and to promote scientific exchange between MIT and sanofi-aventis. The alliance provides sanofi-aventis the opportunity to develop therapeutic, diagnostic, and prognostic applications based on discoveries made during the alliance.

Under the newly announced partnership, SABIP will support a number of activities over the next three years through the granting of Biomedical Innovation Funding Awards. These financial awards will provide MIT researchers with focused, flexible, and rapidly available support to enable innovative research projects for the development of potential healthcare solutions for patients.

"As sanofi-aventis continues to transform the focus beyond pharmaceuticals to patient healthcare integrated solutions, collaborations like SABIP that promote the exchange of scientific knowledge between academia and industry will play a key role," said Marc Cluzel, executive vice president, R&D, of sanofi-aventis. "By bringing together the talents and expertise of MIT researchers, who are leaders in engineering and biological sciences, with the resources of sanofi-aventis, this alliance has the potential to provide innovative solutions to patients such as new drug delivery devices and technologies."

"MIT and its Center for Biomedical Innovation are very excited about our collaborative research program with sanofi-aventis. MIT brings strengths in advanced science and engineering relevant to health care and welcomes the opportunity to work with sanofi-aventis on problems of common interest in biomanufacturing, nanotechnology and other areas," said Claude Canizares, vice president for research and associate provost at MIT.

Rapidly Biodegradable Plastic Announced by Tamarisk Technologies

PRNewswire: May 25, 2010 – WILKESBORO, NC – Tamarisk Technologies has developed a new plastic that biodegrades in about 60 days. Tests conducted by both Tamarisk Technologies and Intertek Labs, an independent third-party laboratory, have shown that this plastic technology may be the answer to the world's need for a biodegradable and compostable plastic. "This is a truly revolutionary breakthrough; it looks and feels like the plastic I have seen all my life, but the difference is that our plastic does not harm the environment and costs far less to produce," said Dean Crowell, president and chief operation officer of Tamarisk Technologies, LLC.

The biodegradable plastic is created from renewable sources of raw materials and uses much less energy to produce than current technologies. This new future friendly technology will also allow plastic producers to shortcut current manufacturing processes, creating a plastic that will cost significantly less to produce.

Some of the properties of the new rapidly biodegradable plastic from Tamarisk Technologies, LLC include high PSI strengths; water-proof matrix; biodegrades in 60 days; compostable, leaves only nitrogen and carbon dioxide in the soil when completely biodegraded; and the backbone structure of the plastic can be altered for any plastic application.

This plastic technology is another groundbreaking technology developed by Tamarisk Technologies, LLC. Additional technology provided by Tamarisk includes: serum specific micro-encapsulation, a drug delivery technology that delivers up to 95% of the therapeutic payload to the blood serum, and alginate-based building materials, a polymer technology for the building trades.

In the News continued on page 40

In the News continued from page 39

For more information, contact Dean Crowell, Tamarisk Technologies, LLC President & COO (Phone: +1.336.838.2033; E-mail: dcrowell@organicbalance.com).

Biomedical Structures Receives Growth Capital from Ampersand Ventures to Fund Ongoing Expansion

PRNewswire: May 24, 2010 – WARWICK, RI – Biomedical Structures LLC (BMS), a leading supplier of custom-designed biomaterials and textiles used in advanced clinical applications from orthopedics and reconstructive surgery to tissue engineering, has completed private equity financing with Ampersand Ventures. Biomedical Structures has delivered strong and profitable growth since its inception as an independent, privately held company in 2003. Ampersand's funding will enable BMS to meet the increasingly complex demands of the medical device industry with expanded capabilities in service, technology platforms, and breakthrough biomaterials. Terms of the transaction were not disclosed.

"Biomedical textiles are integral to the current and next-generation devices of some of the world's largest integrated medical device manufacturers. BMS has done a remarkable job positioning itself as a leader in the field, allowing it to capitalize on the industry's strong growth, particularly in exciting new areas such as tissue engineering," said Ampersand Partner, Todd Rainville. "Ampersand is thrilled to have invested in this promising business, and we look forward to working closely with the BMS management team."

BMS specializes in the design and manufacture of crafted, nonwoven fibers and biomaterials such as tissue scaffolds and woven vascular grafts for biomedical applications. BMS serves as a key partner to leading device companies to transform concepts into early prototypes, optimize them through development cycles, and, ultimately, to serve as the contract manufacturer for final products at all volume levels. Customer end products include a range of 510(k)-approved, implantable devices, components for surgical procedures, and drug delivery tools.

John Gray, president of BMS, commented, "The Ampersand investment comes at a critical time in our company's development when we are seeing increased demand for our expanding portfolio of products and services. The additional resources will enable us to grow even faster with new personnel, more advanced equipment, and increased manufacturing capacity. Ampersand's investment validates the growth strategy that we have been implementing since our inception, and allows us to focus intently on providing a distinct set of services to our customers."

Gray added, "I look forward to working with Ampersand partners, Todd Rainville and Herb Hooper, both of whom have joined our board of directors. Their counsel and strong industry relationships will be valuable assets to BMS as we continue to accelerate our longer term growth strategy by driving biomedical textiles into new therapeutic applications."

Isis Biopolymer, Inc. Announces SBANE Award

PRNewswire: May 19, 2010 – PROVIDENCE, RI – Isis Biopolymer has been awarded the 2010 Rising Star Award by SBANE (Smaller Business Association of New England). The Rising Star is a coveted annual award that honors innovative products and services offered by early-stage companies in New England.

SBANE recognizes the intrinsic value that innovation possesses in driving the New England economy. To that end, SBANE utilizes its highly competitive innovation awards program to showcase technology-driven enterprises that are potentially "game changers" in their markets. Innovation is at the heart of economic prosperity, and SBANE recognizes those companies that have transformed their innovative ideas into a product or service that delivers proven value to customers.

The IsisIQ™ patch is a fully programmable, multi-day, multi-drug, transdermal drug delivery patch. The patch is compact, non-invasive, and wireless, using a patented design offering advances in microprocessors, thin-film batteries, and polymer thick film.

"We are honored to have been recognized by SBANE for our innovation and game changing technology for transdermal delivery of prescription drugs and over the counter products," stated Shawna Gvazdauskas, chief commercial officer of Isis Biopolymer. "We are also proud of the fact that we develop and manufacture our patches in Providence, RI." ■

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CRS-IPTS Educational Workshop on Vaccine Development (Immediately prior to 15th International Pharmaceutical Technology Symposium)

September 11-12
Kervansaray Lara Hotel
Antalya, Turkey
http://ipts-hacettepe.org

Workshop Sponsored by CRS: Recent Advances in Controlled Release and Non-invasive Drug Delivery of Biopharmaceuticals

September 20-21
Sheraton Baltimore Inner Harbor
Baltimore, MD, U.S.A.
www.aapspharmaceutica.com/meetings/workshops/NIDD

8th International Nanomedicine and Drug Delivery Symposium (Presented by Center for Drug Delivery and Nanomedicine)

October 3-10
Hilton Omaha
Omaha, NE, U.S.A.
www.nanodds.org

2010 NanoMedicine Summit – NanoMedicine: Bridging the Gap from Basic Research to Clinical Application

October 18-19
InterContinental Hotel and Bank of America Conference Center
Cleveland, OH, U.S.A.
www.nanomedicinesummit.org

CRS Satellite Workshop: Novel Methods for Developing Clinically Relevant Product Specifications

November 13
Morial Convention Center
New Orleans, LA, U.S.A.
www.controlledreleasesociety.org/main/meetings

FIP Pharmaceutical Sciences 2010 World Congress (in association with the AAPS Annual Meeting and Exposition)

November 14-18
New Orleans, LA, U.S.A.
www.pswc2010.org/

2011

CRS Product Development Forum – Poorly Soluble Drugs

January 27-28
Doral Golf Resort and Spa
Miami, FL, U.S.A.
www.controlledreleasesociety.org

14th Industrial Symposium and 5th Trade Fair on Microencapsulation (organized by CRS, SwRI, and Bioencapsulation Research Group)

March 7-9
The Sheraton Gunter Hotel
San Antonio, TX, U.S.A.
http://impascience.eu/bioencapsulation/2011_San_Antonio

38th Annual Meeting & Exposition of the Controlled Release Society

July 30-August 3
Gaylord National Resort and Convention Center
National Harbor, Maryland, U.S.A.
www.controlledreleasesociety.org/main/meetings