CONTROLLED RELEASE SOCIETY

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NEWSLETTER

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inthisissue

On the cover –

A glimpse of the 33rd Annual Meeting & Exposition of the Controlled Release Society in Vienna, Austria.

Steven Giannos
Editor

Bozena Michniak
Editor

Yvonne Perrie
Editor

Randall Mrsny
President

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FROM THE Editors

By Yvonne Perrie

Yvonne Perrie

Dear Reader,

This issue brings reports and news from our CRS meeting in Vienna, which was an excellent conference. Indeed, we have managed to source many new contributors for the *Newsletter*, especially from the poster sessions where so many interesting studies were reported—the problem was catching up with all the authors. Our two sets of Scientifically Speaking contributors, Dr. Fatouros and Prof. Bourwstra who provided a nice article on skin drug delivery and Dr. Tseng who discussed some very interesting tissue fabrication work, were both collared at this meeting. Similarly, thanks to a session provided by the Education Committee we have a very informative article on "How To Write a Scientific Paper"—a must read for all new writers, so be sure to circulate the *Newsletter* or direct people to our website, where we have all the past issues online. Hopefully, this issue will give you a good flavour of the conference and an opportunity to catch up with some of the topics covered.

However, I don't want to dwell too much on how good the conference was, especially if you were not there, as I know it is getting harder these days to get away to conferences, either due to time constraints, cash constraints, or both. A good friend of mine, Dr. Hannah Batchelor (editor of the *Academy of Pharmaceutical Scientists Newsletter*) recently wrote a very nice editorial on the value of conferences. As an aside, we did recently ponder over whether the only people who read editorials are editors, but if you are not an editor and are reading this, then I am glad to say you have proven our theory wrong. Anyway, as we talked about conferences Hannah noted that there is no specific data on the number of meetings held each year, but, based on an analysis of her e-mail inbox, she estimated that there surely must be a conference held daily. In this case, how many should we attend and which do we go to? Obviously the CRS Annual Meeting for starters, but what others? There are so many, and when we are at a meeting, how do we make the most of it? Indeed, can you overdose on conferences—apparently there are recognised signs of conference fatigue: puffy eyes, dry mouth, and a longing for fresh air and your own cooking. Personally, I never yearn for my own cooking, but the rest of the symptoms I have experienced now and again, through no fault of the conference. Even if not suffering from conference fatigue, we also have to contend with e-distractions. I (like many I believe, judging from the queues) seem to have a strange addiction to e-mail: my compulsive need to e-communicate almost requires counselling. However, the e-ingress is not all bad. I am not so old as to have forgotten the "fun" of 35-mm slide presentations, with one slide in and 10 back to front, upside-down, or just jamming in the carousel. Has PowerPoint made life better, or coaxed us into leaving the writing of our presentations until even later? Also, many of us still choose to add an element of risk by putting in a few video clips, which may, or may not, run on the day of our presentation.

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Randall Mrsny

From the President

By Randall Mrsny
Welsh School of Pharmacy, University of Wales, Wales, U.K.; and Trinity BioSystems, Inc., Menlo Park, CA, U.S.A.

It is difficult to know where to start this letter. There are many points one could/should address at the initiation of their tenure as CRS president. This year, in particular, there are several points to be addressed that would not typically be in such a letter. Over the last year, as many of you now know, the society changed management staff—an event requiring lawyers, contract review, negotiations, etc. Thus, do I first thank individuals in the CRS leadership for their phenomenal dedication and efforts that made this transition a reality? What about the new staff who ran a very successful annual meeting in Vienna under very challenging circumstances? Do I thank the CRS members for their support that allowed me to attain this position? Then, of course, it is also important to provide some perspective on the state of the society and the goals one has for its near and more distant future. The following letter may seem disjointed as I attempt to weave all of these issues together in a way that hopefully resembles a tapestry, and not spaghetti spilled on the floor.

As was brought up at the Membership meeting in Vienna, the CRS has changed its support staff to the non-profit organization Scientific Societies run under the leadership of Steven Nelson. This new staff was not only instrumental in transition events, but they had to wait until February (when the transition could occur legally) to set in motion their efforts to run a CRS Annual Meeting in a venue approximately 5,000 miles from their home base in St. Paul, Minnesota. The fact that the Vienna meeting was one of our most successful yet is a testament to their monumental efforts. This outcome provides a strong sign that this management group was an excellent choice to provide the CRS with successful meetings in the future. Whilst this change in staff was the reason you may have noticed so many new faces helping to run the meeting in Vienna, one common thread did exist—we were lucky enough to get Ronda Thompson to follow the CRS from our previous management group to Scientific Societies. Her experience with CRS membership, its leadership, and the inner workings of the society's committees helped ensure a successful transition. Thus, I thank our staff for their remarkable job and exceptional devotion to the CRS.

Our transition to Scientific Societies was perceived to be critical for the long-term fiscal health of the CRS; an outcome that is anything but trivial. Over the last year Jennifer Dressman, Vladimir Torchilin, and Art Tipton were exceptionally busy making sure this transition occurred. A special thanks needs to be given in recognition of their tireless efforts, with have placed the society in the hands of an excellent, experienced staff who will work with the leadership of CRS to expand our activities and increase the benefits to our members. That this transition effort began during Jennifer Dressman's tenure as president and was completed during Vladimir Torchilin's time in that office highlights the important role played by the immediate past president of the society. The time scale of such a critical task, requiring more than one president's term, exemplifies the important change to the by-laws that was unanimously approved by the membership in Vienna—a change that allows the immediate past president to retain a voting role on the board of directors for one year following their presidency.

Continuity of efforts by the CRS leadership helps facilitate the natural evolution of the CRS that must occur for it to retain its position as the premier international forum for the many facets of controlled release. At the forefront of this effort is Martyn Davies, who delivers outstanding scientific programs year after year. Thanks need to be given to Martyn Davies and the Scientific Program chairs for the Vienna meeting (Maria Jose Alonso, Antonios Mikos, and Ali Rajabi-Siahboomi [Bioactive Materials Track]; Teresa Thomas Virgallito and Harlan Hall [Consumer and Diversified Products]; and David Brayden and Craig Bunt [Veterinary]) for making Vienna a very well attended, exciting annual meeting with more than 1,100 submitted abstracts! This is the primary focus of the CRS—the science. It is what makes the CRS a special organization and what will continue to define us if we wish to remain successful in the future.

It is up to the individuals participating in the four-year sequence of vice president → president-elect → president → immediate past president to mould a strategy to meet the needs of our membership; currently those individuals are Lisbeth Illum, Susan Cady, myself, and Vladimir Torchilin, respectively. In addition, it is up to our treasurer, Art Tipton, to provide the board with a financial perspective that keeps the society solvent. Our members-at-large (currently Clive Wilson and Ian Tucker) provide a perspective to the board that permits the needs of the membership to be at the forefront of our discussions. But, it is individual committees that provide actual outcomes for goals defined by the board to meet the needs of the membership and, thus, the society. A special thank you needs to be given to the individuals who have worked to make these committees successful. Susan Cady ran the Awards Coordinating Committee last year, with the role now passing to Lisbeth Illum. Jennifer Dressman ran the Nominating Committee last year, a role that has passed to Vladimir Torchilin. Martyn Davies continues to run the Meetings Committee, where he is looking at ways to

From the President continued on page 4

From the President continued from page 3

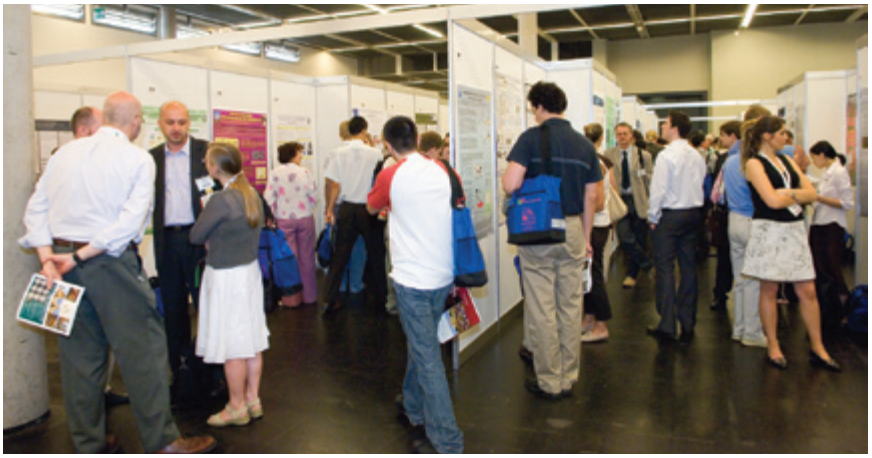
increase the global impact of the CRS while maintaining its scientific excellence. Mike Rathbone has done an amazing job as head of the Education Committee, which in many ways has similar goals of globalization and dissemination of CRS science.

With the completion of our management team transition, the board can now look forward to tackling a variety of issues that were prudently postponed during this time of flux. Once the final goals have been (re)validated by the board to ensure they are addressing the current and most important issues for the CRS, I will provide a more definitive set of action items that various committees will work to achieve during the next year. This is not to infer that the CRS is broken and needs to be fixed. The society is very healthy and fiscally sound and has an extremely bright future. Our goal is to provide maximum benefits to the diverse individuals who make up the CRS membership today and in the years to come. In general, our efforts will focus on defining ways to recruit an even broader base of individuals to the society to extend the applications of CRS sciences and to continue nurturing our younger members, for they define our future. Any and all activities undertaken over the next year must, first and foremost, not diminish our efforts to deliver the best possible annual meeting in Long Beach, California, in July 2007.

It is the membership of the CRS that makes it special for me. No other society can boast the breadth and depth of disciplines and expertise presented at our annual meeting. I look forward to working over the next year to maintain the quality and standards of the society and to explore ways to continually deliver benefits to our members. I welcome your ideas and thoughts concerning the CRS; I can be contacted at mrsnyr@cardiff.ac.uk.

Randall Mrsny
President

Highlights of the 2006 CRS Annual Meeting & Exposition



Meeting Round-up

Hot! That's the word that best describes the 33rd Annual Meeting & Exposition of the Controlled Release Society held in Vienna, Austria.

The exhibits, oral presentations, poster presentations, sessions, and debates were all hot because of the topics discussed and equipment on display. The Vienna meeting was also cool. It was cool to see old colleagues and friends and make new ones.

CRS offered three very successful and highly popular workshops on Saturday: CMC Regulatory Issues for Controlled Release Parenterals, chaired by Diane Burgess and Kinam Park; Drug-Device Combination Products: Novel Technologies and Regulatory Challenges, chaired by Tejal Desai and John Santini; and Role of Intestinal and Hepatic Transporters on Oral Bioavailabilities of Drugs chaired by Yuichi Sugiyama and Per Artursson.

The meeting's opening reception was one of grandeur. The kick-off event was held at the Vienna mayor's office, and attendees were awestruck by the elaborate setting and exquisite bubbly and nibbles. This special treat created a tremendous air of expectation that lasted until all of the presentations had been given on the final day.

CRS is honored to have extraordinary sponsors and exhibitors. These people and the companies they represent make things happen. Attendees got a taste of the CRS sponsors' valued participation at the Awards Ceremony. Together the sponsors and CRS are making a difference in recognizing industrial, academic, and student leaders.

The 33rd Annual Meeting & Exposition of the CRS proved once again that CRS is truly an international organization. The five plenary speakers were from five different countries: France, Israel, Japan, the United Kingdom, and the United States. A total of more than 50 nations and six continents were represented by attendees, exhibitors, speakers, and presenters. CRS strives to bring the latest science and innovative products to the forefront during an annual meeting, and in 2006, this was accomplished once again. Seven leaders in the controlled release and delivery industry hosted Releasing Technology Workshops. New start-up companies as well as well-known companies with new products, a total of 30 companies in all, packed the house during the Molecular Profiles sponsored Soapbox Sessions.

The exhibit hall was the place to be to find anything and everything needed to further research and make a researcher's life easier. Of course, the wine and cheese reception hosted by Altea Therapeutics Corporation in the exhibit hall caused a commotion too.

One exhibitor in particular, Banner, thought the annual meeting and exposition held in Vienna was the greatest CRS event ever. On Monday, Banner hosted the inaugural Industrial Insights Luncheon. This invitation-only luncheon gave Banner the audience, the floor, and the food for an uninterrupted hour.

All CRS participants are important to the success of a CRS Annual Meeting & Exposition—no one takes a back seat, especially students. CRS promotes student involvement and offers a variety of ways to reach them. One of the student mainstays at the meeting is the Highlights of Student Posters Session. Ten posters authored by students, from the hundreds received, were selected for oral presentations during this exciting session.

From the plenary speakers to the special sessions and everything in between, the break-out rooms were full of attendees eager to hear the latest in research findings and technologies. Selecting from 199 oral presentations was a daunting undertaking for most attendees, but somehow they made their choices and found the right rooms.

The morning and afternoon sessions Monday through Wednesday began with the plenary speakers. Topics of interest to the packed auditorium included supramolecular chemistry, signal transduction therapy, the future of nanomedicine, new technologies for *in vivo* and *in vitro* diagnostics, and drug transporters.

Monday was the day for CRS attendees who work or study in veterinary fields. The Vet Session Advances in Veterinary Controlled Release started the day off right with oral presentations selected from abstract submissions. On Monday afternoon, the Innovations in Veterinary Drug Delivery Mini-symposium was held. Four invited speakers held their audience captive for the two-hour symposium. Monday evening attendees enjoyed the Pfizer Animal Health sponsored Vet Get Together featuring Keith Ellis' lively and entertaining presentation.

Tuesday was a big day for Consumer & Diversified Products (C&DP) CRS attendees. In the morning, the Controlled Release in Foods and Beverages oral session was held, followed by the Controlled Release of Probiotics, Antioxidants, and Nutraceuticals oral session in the afternoon. In between these sessions, members of the C&DP Committee and those interested in joining the C&DP Committee attended their annual luncheon. To say the group came back to the Austria Center very happy is an understatement.

> *"The CRS meeting helps us to reinforce our relationships with our technical colleagues in the industry and find new opportunities."*
>
> – Richard Salzstein
> Aqualon, Global Industry Director—Pharmaceuticals

CRS was honored to host the Capsugel/Pfizer Special Session. This session is quite unique in that a grand prize winner is selected at the conclusion of the oral presentations. Jan Vertommen of Capsugel/Pfizer chaired the special session along with CRS President Vladimir Torchilin. After hearing the four award-winning students' presentations, the difficult task of selecting the final winner was tackled by Jan, Vladimir, and the three Capsugel/Pfizer Invited Speakers. After much debate, Frederic Mathot from the Universite Catholique de Louvain in Belgium was named the grand prize winner for his presentation, "Intestinal Transport Mechanisms and Biodistribution of Novel Polymeric Micelles After Oral Delivery."

The much anticipated closing party took place on Tuesday evening. One of the annual highlights during this party is witnessing the official changing of the guard. Outgoing President Vladimir Torchilin handed off the gavel to incoming President Randall Mrsny without skipping a beat, and attendees once again enjoyed one of Vienna's magnificent, historic buildings.

Wednesday afternoon 2006 Founders awardee Jorge Heller discussed his life's work with a few hundred of his closest friends and admirers. ALZA, the CRS Founders Award sponsor, was pleased to be a part of honoring Jorge Heller. Many attendees were surprised Jorge had not already won the Founders Award.

The CRS Young Investigator Award is highly coveted, so there was an air of anticipation as the audience walked into the Austria Center's auditorium to hear the presentation by 2006 Young Investigator winner Stefaan De Smedt from Ghent University in Belgium. Stefaan had them on the edge of their seats while he covered the research areas that brought him to the notice of the Young Investigator Award Committee.

At the 29th Annual Meeting & Exposition of the CRS in Seoul, Korea, Eurand and CRS collaborated in holding the first ever Eurand Special Session. in 2006 the Eurand Special Session continued its showcase of excellence. Stephen Perrett of Eurand and CRS Vice President Susan Cady chaired the special session. William Charman, winner of the 2006 CRS/Eurand Career Achievement Award in Commercialized Technology of Oral Delivery, was the special session invited speaker. Three CRS/Eurand Novel Approaches in Oral Drug Delivery Industrial Award recipients followed with their presentations. At the conclusion, it was the job of Stephen, Susan, and Bill to select one winner. Minutes turned into what seemed like hours for the three presenters who waited to hear the announcement. Finally, Tejal Desai from the University of California-San Francisco was chosen as the Eurand Special Session grand prize winner.

The Industrial Session was so popular in Miami that it was back in Vienna and even bigger. This two-day event sponsored by Pfizer was standing room only. Attendees appreciated the opportunity to learn from the 14 presenters and ask questions of the expert panel members at the end of the Monday and Tuesday sessions.

If you thought it sounded difficult to decide which oral presentations to attend, think of the monumental effort attendees made in selecting which of the more than 900 posters they would read during the two poster sessions. The isles were crowded with poster authors and their attentive audience. Many business cards were exchanged, along with thoughts on future collaborations.

As the saying goes, all good things must come to an end, and so it was with the 33rd Annual Meeting & Exposition of the CRS. It is with great anticipation that we all look forward to Long Beach, California, in 2007, where once again you'll hear, see, and experience the best in controlled release and delivery. ■

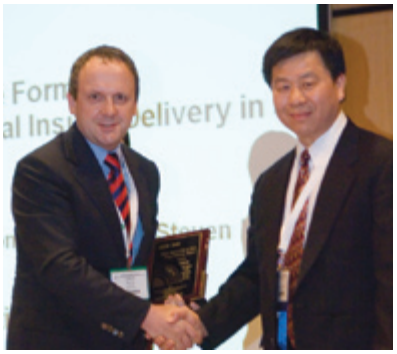
Recognizing Excellence

Congratulations 2006 CRS Awardees!

As part of a special awards ceremony held during the 33rd CRS Annual Meeting & Exposition in Vienna, Austria, the Controlled Release Society presented awards covering a wide range of disciplines to 19 scientists from around the globe in recognition of their contributions to the science of controlled release. The CRS thanks the sponsors who provided their time and financial support to promote the innovative science at the meeting and highlight these talented scientists. Congratulations to all the distinguished winners!

Amitava Mitra accepts the 2005 Outstanding Paper in Drug Delivery Award, co-sponsored by 3M Drug Delivery Systems, from Richard Beesley of 3M Drug Delivery Systems.

Ofra Benny receives the 2005 Outstanding Pharmaceutical Paper Award, co-sponsored by CyDex, Inc., from Jose Rodriguez, Jr., of CyDex.



Puchun Liu, Tae Kyoung Kim, and Tejal Desai are presented with the Novel Approaches in Industrial Oral Drug Delivery Awards, co-sponsored by Eurand, by Stephen Perrett of Eurand.

Sevda Senel is presented with the 2005 Outstanding Veterinary Paper Award, co-sponsored by Intervet, by Susan Cady of Intervet.

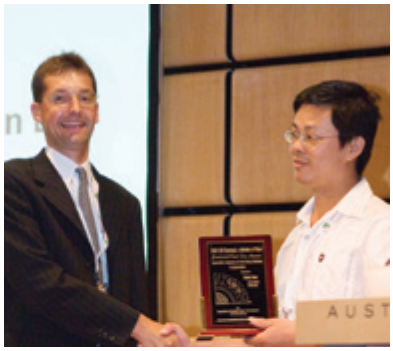
CRS President Vladimir Torchilin accepts the Outstanding Parenteral Drug Delivery Paper Award, co-sponsored by Baxter Healthcare, from Barrett Rabinow of Baxter Healthcare on behalf of Tamer Elbayoumi.

Nicolas Anton receives the Outstanding Consumer & Diversified Products Paper Award, co-sponsored by Firmenich, Inc., from Damien Berthier of Firmenich.

Bill Charman accepts the Career Achievement in Oral Drug Delivery Award, co-sponsored by Eurand, from Stephen Perrett of Eurand.

Giovanni Tosi accepts the 2005 Jorge Heller Journal of Controlled Release Outstanding Paper Award, co-sponsored by Elsevier, from Federica Rosetta of Elsevier on behalf of Maria Angela Vandelli.

Teruo Okano receives the Nagai Innovation Award, co-sponsored by The Nagai Foundation Tokyo, from Tsuneji Nagai of The Nagai Foundation Tokyo.



Eva-Maria Collnot, Kelly Marie Kitchens, Frédéric Mathot, and Zhiping Zhang are honored with the Innovative Aspects of Oral Drug Delivery and Absorption Graduate/Post-Doc Award, co-sponsored by Capsugel, a division of Pfizer, by Jan Vertommen of Pfizer.

Mohammad Najlah is honored with the CRS Outstanding Oral Drug Delivery Paper Award by CRS President Vladimir Torchilin.

Tsuneji Nagai accepts the Rainer Hoffmann Product Through Science Award, co-sponsored by Lohmann Therapie Systeme, from Hans Junginger, chair of the Rainer Hoffmann/CRS Awards Committee.

Stefaan De Smedt receives the CRS Young Investigator Award from CRS President Vladimir Torchilin.

Jorge Heller is honored with the Founders' Award, co-sponsored by ALZA, by Andrew Scott of ALZA.

The Controlled Release Society Thanks the 33rd Annual Meeting & Exposition Sponsors

Thank You to the Exhibitors of the 33rd Annual Meeting & Exposition of the Controlled Release Society!

More than 100 exhibiting companies, many of them first-time CRS exhibitors, offered the latest research, technology, products, and services for controlled release and delivery at the Vienna, Austria, meeting.

For 2007 exhibit information go to http://www.controlledreleasesociety.org/meeting/exhibitors/default.cfm or contact Debby Woodard at +1.651.994.3817 or dwoodard@scisoc.org.

"It's the perfect opportunity to connect with past, present, and future clients and stay connected with the marketplace."

— Martha Sloboda, Adhesives Research, Inc., Actives Business Manager

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ALTEA Therapeutics Corporation
Aptuit
Aqualon, A Business Unit of Hercules Incorporated
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Pharmaceutical Profiles Group
Pharmaceutical Technology
Pharmaceutical Technology Europe
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Scintipharma Inc.
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Simulations Plus, Inc.
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Spectral Dimensions, Inc.
Stable Micro Systems Ltd.
Surface Measurement Systems Ltd.
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Technology Catalysts International
TeraView, Ltd.
ThioMatriX
Travanti Pharma Inc.
Varian, Inc.
Wolters Kluwer Health
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What's on Board

By-law Changes Approved

During the CRS Members Meeting held July 26, 2006, in Vienna, CRS members voted in favor of changes to the society by-laws that will allow the Immediate Past President to serve a one-year term as a voting member of the Board of Directors (BOD). This requires the following changes in By-law Article III. Board of Directors, Officers and Committees:

Section 1. Board of Directors
The society shall have the following elected officers which will constitute the Board of Directors of the CRS: President, President-Elect, Vice President, Scientific Secretary, Treasurer, 2 Members-at-Large, Immediate Past President

Section 5. Term of Office
a. The President, President-Elect, Vice President and Immediate Past President shall each hold office for one (1) year.

New and Retiring Board Members

Two new board members began their terms at the annual meeting in Vienna: Vice President Lisbeth Illum and Member-at-Large Ian Tucker.

Professor Lisbeth Illum is Director of IDentity, a consultancy company, and is also associated with Nottingham University as a special professor. She was the founder and managing director of DanBioSyst UK Ltd. (now Archimedes Ltd.), a company specializing in drug delivery systems. Professor Illum was awarded her M. Pharm, Ph.D. and D.Sc. degrees from the Royal Danish School of Pharmacy. Her research expertise covers the area of novel drug delivery systems for difficult drugs such as polar small molecular weight compounds and peptide and protein. She has studied novel approaches to the delivery of such drugs. Professor Illum has published numerous scientific papers, co-edited four books, and filed nearly 50 patents. She is an elected Fellow of the AAPS, has lectured throughout the world at conferences and workshops, and is a member of the editorial boards of seven scientific journals.

Dr. Ian Tucker is Professor of Pharmaceutical Sciences and Dean of the School of Pharmacy, University of Otago, New Zealand. He received his Bachelor of Pharmacy and Ph.D. degrees from the University of Queensland, Australia. Dr. Tucker helped form the New Zealand Chapter of the Controlled Release Society, an active chapter that combines with the Formulation and Drug Delivery Research Theme, an association of researchers from diverse disciplines, to hold an annual conference attracting registrants from universities, government institutes, and industry. His research focuses on mechanistic understanding of controlled release delivery systems and pre-clinical assessment of new chemical entities. He is the author or co-author of numerous scientific articles in peer-reviewed journals. In addition to membership in the CRS and AAPS, Dr. Tucker is a member and past president of the Australasian Pharmaceutical Science Association (APSA). He is a former governor of the CRS and a member of the SCOTT committee, which is responsible for approval of human clinical trials in New Zealand.

The Controlled Release Society extends a special thank you to retiring Member-at-Large Jeffrey Cleland, Telik Inc., Palo Alto, CA, U.S.A., whose term ended during the annual meeting in Vienna.

2006–2007 CRS Board of Directors

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University of Strathclyde, Glasgow, U.K. ■

Scientifically Speaking

Timolol Maleate: A Promising Candidate for Electrically Assisted Skin Delivery

By Dimitrios G. Fatouros, Department of Pharmaceutics and Analytical Chemistry
The Danish University of Pharmaceutical Sciences, Copenhagen, Denmark; and
Joke A. Bouwstra, Department of Drug Delivery Technology
Leiden Amsterdam Center for Drug Research, Leiden, The Netherlands

Transdermal drug delivery offers several advantages over traditional drug delivery systems, including elimination of first-pass metabolism, sustained release of drugs, and accurate dosing on demand (1). However, transport of molecules across the skin is slow due to the low permeability of the stratum corneum, the uppermost layer of the skin. The stratum corneum consists of corneocytes embedded in lipid regions. The corneocytes are filled with keratin filaments and water. Many efforts have been made to overcome the stratum corneum barrier, which has resulted in various chemical and physical approaches to increase the transdermal permeation of topically applied drugs (2).

One of the methods, application of an electric current to the skin, has been shown to promote the transdermal transport of drugs by an additional driving force, namely an electrical potential gradient across the skin. One key advantage of iontophoresis is that it offers the possibility of externally controlled flux modulation, carefully adjusted to the needs of the patient (3). Several factors affect iontophoretic delivery of a drug, such as the drug concentration, electric current, and pH and ionic strength of the drug compartment. The physicochemical properties of a drug (charge, size, lipophilicity) influence its potential as a candidate (4).

Transdermal delivery of cardiovascular drugs, β-blockers, has been investigated, since they undergo extensive first-pass hepatic metabolism and can have adverse effects due to variable absorption profiles (5). The electrically assisted skin delivery of several β-blockers has been studied previously (6–13). In two recent reports the feasibility of transdermal iontophoretic delivery of timolol maleate and the possibility of delivering therapeutic doses of this drug were investigated (12,13).

In Vitro Iontophoretic Studies

Transdermal iontophoretic studies were conducted *in vitro* with human epidermis. A three-chambers continuous flow through diffusion cell mimicking *in vivo* conditions was used for the permeation experiments (14), and a protocol totaling 20 hr was applied. The total course of the diffusion experiments included three stages: 6 hr passive diffusion, 9 hr iontophoresis at constant current density, and 5 hr post-iontophoresis passive diffusion. The anodal chamber was filled with 40 mg/mL of timolol maleate in phosphate buffer saline (PBS) at pH 7.4; the cathodal chamber contained PBS at pH 7.4.

The current density varied from 0.125 mA/cm^2 to 0.250 and 0.500 mA/cm^2. The permeation profile of timolol across human epidermis is depicted in Figure 1. During the pre-iontophoresis period, the passive fluxes were negligible. By switching on the current at 6 hr, the fluxes rapidly increased, and when the current was switched off at 15 hr, the fluxes rapidly declined. This demonstrates the potential of iontophoresis to increase drug transport across the skin. A steady state flux of 441 ± 67 μg/cm^2·hr was achieved during the application of 9 hr of iontophoresis at a current density of 0.5 mA/cm^2. The influence of current density on the transport of timolol across human epidermis was investigated under the same anodal conditions with varying current density. A linear relationship between current density and steady state flux was observed (Figure 2) demonstrating the possibility that delivery of the drug can be adjusted by adjusting the current density.

The oral dose of timolol in humans varies between 10 mg/day and a maximum of 60 mg/day. Considering an oral bioavailability of 50% and a daily oral dose of 20 mg of timolol, a steady state flux of 125 μg/cm^2·hr is necessary, with a patch size of 20 cm^2, after application of 4 hr of iontophoresis. Using the relationship illustrated in Figure 2, the calculated current density for these conditions is only 0.137 mA/cm^2.

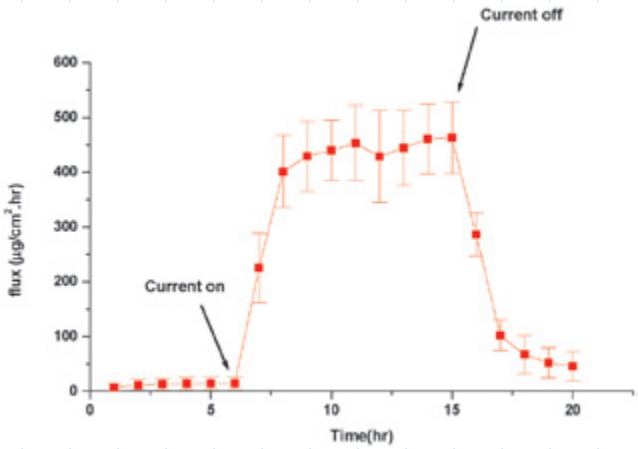

Figure 1. Permeation profile of timolol maleate across human epidermis during 6 hr passive diffusion, 9 hr iontophoresis at current density of 0.5 mA/cm^2 and 5 hr post-iontophoresis passive diffusion at 32°C. (Reprinted with permission from Fatouros and Bouwstra [12], www.tandf.co.uk/journals/, Taylor and Francis)

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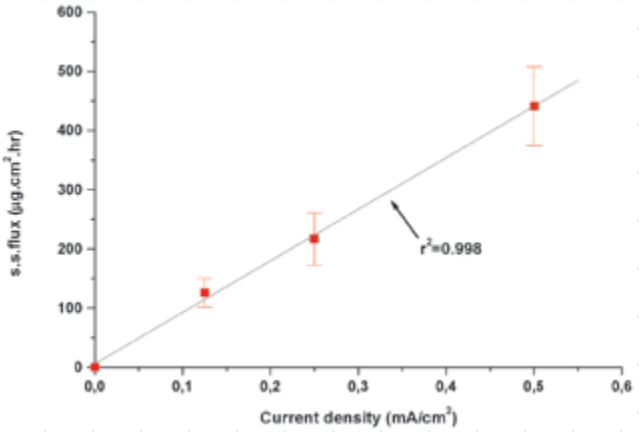

Figure 2. Iontophoretic flux of timolol maleate across human epidermis as a function of current density at 32°C. (Reprinted with permission from Fatouros and Bouwstra [12], www.tandf.co.uk/journals/, Taylor and Francis)

Since the maximum strength of the current that can be used is limited by patient safety and skin irritation, the upper limiting value of current density is often stated to be 0.5 mA/cm^2 (15). The results of timolol maleate are very promising, since it might be possible to achieve therapeutic levels assuming a similar flux *in vivo* as was obtained *in vitro* in terms of iontophoretic flux of timolol with low current densities.

However, the question that also needs to be answered is does iontophoresis induce changes in the structure of the skin? Several studies have been conducted to address this issue (16–18), and it was concluded that iontophoresis showed almost no changes in lipid organization in the stratum corneum. However, the water distribution *in vitro* and the corneodesmosome and lipid structure in the stratum corneum *in vivo* in humans after iontophoresis have not been studied yet.

To assess the changes in water distribution in the stratum corneum as a consequence of iontophoresis, cryo-scanning electron microscopy studies were conducted after iontophoresis under the same conditions (6 hr passive diffusion followed by 9 hr iontophoresis at a current density of 0.5 mA/cm^2) used for the timolol transport studies. In addition, *in vivo* studies were performed with 0.5 hr passive delivery followed by 3 hr iontophoresis at a current density of 0.25 mA/cm^2 (19). In a previous study, it was shown that these conditions only induced minimal skin irritation (20).

In vitro cryo-scanning electron microscopy studies revealed that an electric current induced changes in the water distribution in the stratum corneum. Figure 3A depicts a typical electron micrograph of human epidermis after 15 hr of passive diffusion. The corneocytes are swollen due to the uptake of water, not only in the central part of the stratum corneum, but also in the superficial layers. Non-swelling cells, distinguished by a lower contrast and, therefore, grey appearance in the image, are located at the interface between the stratum corneum and stratum

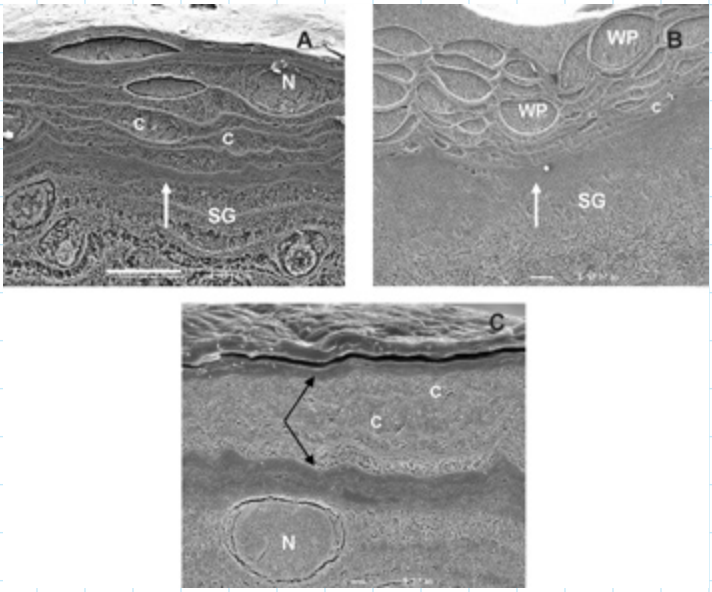

*Figure 3. **A**, Cryo-scanning electron micrograph of human abdomen dermatomed skin (200 µm thickness after 15 hr passive diffusion (anodal part). Corneocytes (C) are strongly swollen. The white mesh work in the interior of the corneocytes indicates the keratin filaments;, the dark regions between the keratin filaments represent the localization of the water. The circular regions in the stratum corneum represent remnants of cell nuclei (N). The non-swelling cells, indicated by a white arrow, are located in an interface between the stratum corneum and stratum granulosum (SG). Scale bar = 10 µm. **B**, Cryo-scanning electron micrograph of human abdomen dermatomed skin (200 µm thickness) after 6 hr passive diffusion and 9 hr iontophoresis with a current density of 0.5 mA/cm^2 (anodal part). Water pools (WP) are present in the intercellular regions. The non-swelling cells, indicated by a white arrow, are located in an interface between the stratum corneum and stratum granulosum (SG). Scale bar = 10 µm. **C**, Constant relative humidity was controlled using a saturated solution of Na_2CO_3 (40%, w/v) at 25°C for 15 hr (control). Low hydration areas are indicated by black arrows. Nuclei (N) are also present. Scale bar = 1 µm. (Reprinted with permission from Fatouros et al. [19], Elsevier)*

granulosum. These cells are often detected (21). These layers might reduce the water transport from the viable epidermis to the skin surface and prevent the body from dehydration. The circular regions in the corneocytes occasionally observed represent remnants of nuclei and water pools.

An image of human epidermis exposed to a current density of 0.5 mA/cm^2 obtained from the anodal site is depicted in Figure 3B. This image clearly shows a redistribution of the water in the stratum corneum after iontophoresis. Most importantly, an increased number of water pools in the intercellular regions at the anodal site after the application of the electric current is noticeable compared with passive diffusion (in the absence of current). Furthermore, the cells are less swollen after exposure to a current density of 0.5 mA/cm^2 for 9 hr. Freeze-fracture electron microscopy studies *in vivo* revealed a more frequent fracture across the desmosomes at the sixth tape-strip at the

anodal site after iontophoresis compared with the control (no iontophoresis), but the lipid organization in the stratum corneum, which is very important for the skin barrier, was not affected (19).

Our observations provide strong evidence that the appearance of intercellular waterpools (*in vitro*) is related to a reduced strength of the corneodesmosomes in the upper part of the stratum corneum, which might be a consequence of both the applied current and higher water content in the stratum corneum at the anodal site. Similar changes in the stratum corneum water distribution were observed by Warner et al. (22) after application of pure water onto the skin. Indeed, a lower hydration layer in the stratum corneum was observed close to the stratum corneum-stratum granulosum junction after exposure of the skin surface to a constant relative humidity of approximately 80% for 15 hr. The humidity was controlled with a saturated solution of Na_2CO_3 (Figure 3°C).

These data indicate that a 9-hr application of a 0.5 mA/cm^2 current *in vitro* and 3-hr application of a 0.25 mA/cm^2 current *in vivo* did not affect the skin architecture dramatically and that as far as structural changes in the stratum corneum are concerned, iontophoresis is a safe method.

Summary
Electrically assisted delivery of timolol across skin could be feasible, since therapeutic levels might be achieved with low current densities. Electron microscopy studies revealed that even at relatively high current densities, no drastic changes in the ultrastructure of the stratum corneum are observed, indicating that iontophoresis is a safe method under the experimental conditions we used.

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Scientifically Speaking

Fabrication and Cell Behavior of Micro- and Nano-fibrous Scaffolds of PBSA and PLLA Produced by Electrospinning

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The main goal of tissue engineering is to provide a two-dimensional (2D) or three-dimensional (3D) architecture for cells to grow or repair their own damaged part in the original structural and morphological entity and, ultimately, to restore their function. To accomplish this, biomaterials are utilized as a supporting and functional matrix for cell attachment, inducing cell proliferation and differentiation to a specific functional cell and multiplying into specific tissues and organs thereafter. It is well known that the extracellular matrix (ECM) plays an important role in controlling cell behavior. The ECM is composed of a basement membrane and interstitial complex that is a chemically and physically cross-linked network of proteins and glycosaminoglycans. All of these features are nano-sized. Although much smaller than the cells, which are mostly micro-sized, the ECM serves to organize cells in space, provide them with environmental signals to direct site-specific cellular regulation, and separate one tissue space from another (1).

To create an ideal scaffold that serves as a basement membrane or an artificial ECM for tissue engineering, it is important to replicate the dimension of the ECM. A unique technology, "electrospinning," can serve this purpose and be used to fabricate porous scaffolds with micro- and nano-sized fibrous structures (2). The potential application of bio-nanotechnology in tissue engineering is huge in that it can not only mimic the nano-sized dimension of the natural ECM, but can also form a defined architecture to guide cell growth and development as needed. The established "contact guidance" theory holds that a cell has the maximum probability of migrating in preferred directions that are associated with the chemical, structural, and/or mechanical properties of the substratum. It has been reported (5) that the arrangement of cells in 2D and 3D architecture has beneficial effects on cell differentiation, proliferation, and functional longevity.

In this article, poly(butylenes succinate-*co*-butylene adipate) (PBSA) and poly-L-lactide (PLLA) were used as samples to fabricate micro- and nano-fibrous membranes by electrospinning. The ability to fabricate micro- and nano-fibrous membranes by electrospinning will lead to a great improvement in pore size and porosity control of the membrane for tissue engineering use. In the experiment, PLLA or PBSA was dissolved. Electrospinning conditions were set as reported previously (3), and the morphology of the obtained fibrous membranes was observed under SEM. The pore size and pore size distribution of electrospun membranes were measured with a capillary flow porometer. The contact angle was determined with a contact angle analyzer. The influence of polymer concentration and applied voltage on the formation of electrospun membranes was examined.

SEM photographs of the resulting PBSA scaffolds are shown in Figure 1. The SEM photographs illustrate that an electrospun membrane with a fibrous architecture was not formable at a lower polymer concentration and lower applied voltage. With increasing PBSA concentration and applied voltage, a fibrous structure was successfully produced. It was concluded that within the range of applied voltages examined, a PBSA micro-fibrous scaffold (PBSA-ESM) was fabricated successfully only when a 20% concentration was employed, whereas a PLLA micro-fibrous scaffold (PLLA-ESM) was formed at 10, 15, or 20%. This might be attributed to the fact that the solubility parameter of PLLA (δ = 19.8) is closer than that of PBSA (δ = 23.8) to that of CH_2Cl_2 (δ = 20.0), resulting in the greater extent of intermolecular intertwining that forms the fibrous structure for PLLA than was seen for PBSA at the same concentration (4). At the concentration that produces a desirable level of intermolecular intertwining to form a fibrous structure, the applied voltage of electrospinning will determine the diameter of the resulting fibers.

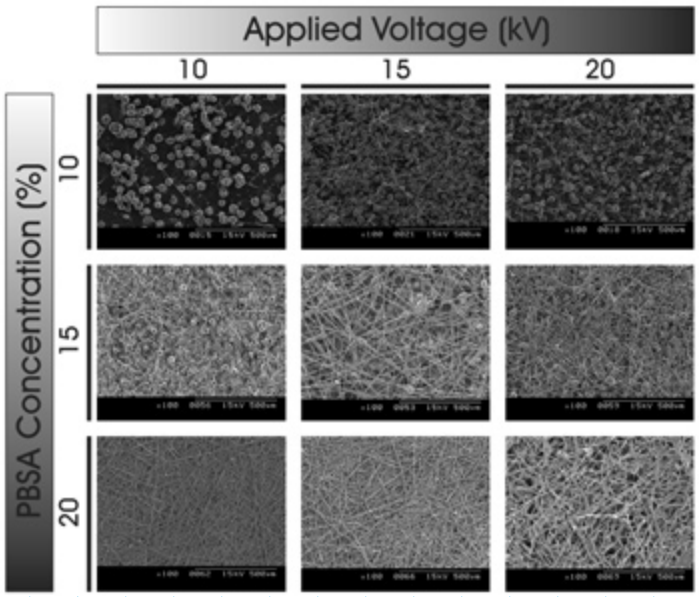

Figure 1. SEM photographs of PBSA electrospun fibrous membrane.

The influence of adding DMF in CH_2Cl_2 on the resulting properties of the electrospun membrane was examined; the results are listed in Table 1. The finest fiber diameter that could be produced was about 1 µm when PLLA was dissolved in CH_2Cl_2. The properties of electrospun membranes were improved when DMF/CH_2Cl_2 was used. Not only was the fiber diameter of both PLLA and PBSA reduced with the addition of DMF, the pore size of both scaffolds was also reduced. For those scaffolds with a pore size (4–5 µm) that was far smaller than the cell size, it might be the better choice for use as the tissue barrier. On the other hand, for those membranes with a larger pore size surrounded by a larger diameter fiber, it would be expected to be a better choice for use as a tissue regenerative matrix for cell proliferation.

DMF in CH_2Cl_2	Fiber diameter (µm)	Pore size (µm)	Porosity (%)
30%	0.4±2.91	4.4±2.27	45.4
20%	0.5±0.23	4.7±3.21	57.0
0%	5.8±4.06	29.2±9.14	67.7

Table 1. *Properties of PLLA membranes electrospun from various concentrations of DMF in CH_2Cl_2.*

To test cell adhesion and proliferation, the samples were cut into circles with 15-mm radii, which were then placed individually into culture wells. After the mats were set, NIH 3T3 fibroblast cells were seeded on top of the membrane. The media were composed of DMEM, sodium pyruvate, and pyridoxine HCl supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin. Once the media were added, culture wells were covered and placed in an incubator for 4 and 8 hr (cell adhesion) and 1, 3, and 5 days (cell proliferation). The WST-1 test was used to examine cell adhesion. With regards to cell adhesion and proliferation, more cells attached on the PBSA-ESM than on the PLLA-ESM as shown in Figure 2. This might be attributed to the lower contact angle (59.1°) of PBSA compared with PLLA (72.9°), which facilitated cells undergoing spreading. PLLA-ESM demonstrated a 60% increase in cell attachment compared with PLLA-CS (casting film), whereas it exhibited a 47% increase for PBSA-ESM compared with PBSA-CS.

These results further confirm that a 3D scaffold is able to facilitate cell attachment to a greater extent than a 2D membrane. The results shown in Figure 2 indicate that a PLLA-ESM scaffold promotes cell proliferation to a greater extent compared with PBSA-ESM and PLLA-ESM scaffolds.

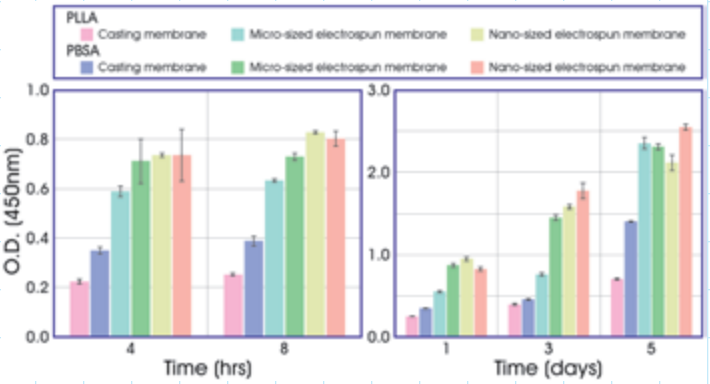

Figure 2. NIH 3T3 adhesion and proliferation of casting (2D) and electrospun (micro- and nano-sized) PLLA and PBSA membranes.

This might be due to the greater availability of space for cell proliferation resulting from the larger percentage of porosity in PLLA-ESM.

Conclusions

Electrospinning of PLLA or PBSA can be used in a DMF/CH_2Cl_2 binary solvent system to produce desired micro- and nano-fibrous scaffolds. The 3D structure and hydrophilic nature of scaffolds obtained through electrospinning promote cell attachment. Pore structure in the resulting scaffolds provides space for cell proliferation. The results suggest that a PBSA or PLLA nano-fibrous scaffold could be applied as a basement membrane.

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Industrial Applications for Uniform Controlled Release Particles

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Introduction
Most commercially available raw materials are sold as grains, flakes, blocks, or powders. As such, the handling of active agents becomes difficult. BRACE microspheres and microcapsules can solve these problems. Microspheres are solid spheres with a matrix-encapsulated active agent, whereas microcapsules consist of a solid shell and a liquid or solidified core (Figure 1, left and centre pictures, respectively).

Figure 1. Schematic drawing of microcapsules and microspheres. From left to right: Microcapsule with solution as core, microcapsule with cell suspension as core, and microsphere with matrix-encapsulated active agent.

The major difference between these two types of microgranules is the different release profiles obtained. Microspheres usually have a diffusion controlled release profile with a permanent release rate that is controlled kinetically by the particle size, whereas microcapsules expel their contents through either a single high burst as the shell breaks or (with special shell materials) extremely slow release of the contents (Figure 2).

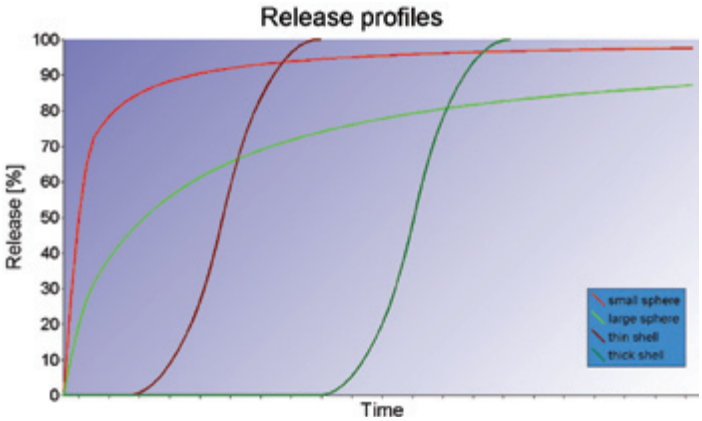

Figure 2. Release profiles of different types of microspheres and microcapsules. While small microspheres have a fast release profile (bright red), larger microspheres have slower release rates (bright green). The burst time of microcapsules depends on the thickness of their shell (dark red and dark green).

Because the patented BRACE processes for the production of microspheres and microcapsules use vibrating nozzles, the feed must be liquid. The processes produce fine droplets of the same diameter and volume. Due to surface tension, a spherical particle is formed that must be solidified. Solidification is accomplished by an appropriate means such as drying, chemical reaction, or cooling.

Using these processes it is possible to produce particles with a monomodal grain size distribution that have a single sharp maximum (d_{max}/d_{min}). Values lower than 1.10, 1.05, or even 1.01 are customary for spherical granules produced with a microsphere unit designed by BRACE (Figure 3). Additionally, it is possible to obtain microspheres or microcapsules with a diameter range of 50–6,000 µm. For the production of particles smaller or larger than this, BRACE manufactures special nozzles. A wide range of shell materials can be used in this highly scalable process.

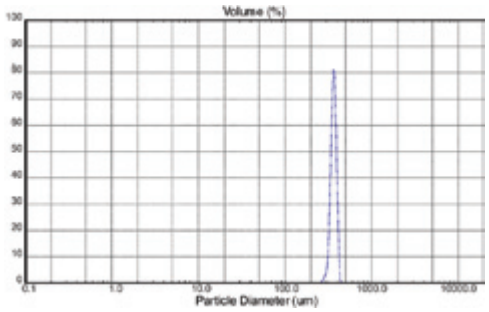

Figure 3. Size analysis of microspheres (Malvern mastersizer).

BRACE microsphere units are space as well as energy saving. The process itself can be easily scaled up to higher throughputs and can be used for a wide variety of different materials. All installations can be designed to match customer's needs, e.g., GMP/GLP, FDA or pharma, food, nuclear, chemistry, or other industrial standards. In the following, scalability in industrial applications is analyzed.

Experimental Method
The process itself can be described schematically (Figure 4) as follows. A liquid feed is pumped from a feed tank (point 3) to the nozzle head (point 5), exiting the vibrating device (point 2) induces break-up of the flow into uniform droplets. These are

formed into spheres by the surface tension of the liquid. The droplets are solidified during falling (point 8). This can be accomplished—depending on the materials and/or coagulation system used—by cooling, chemical reaction, or drying. The head of the microsphere unit can be placed inside a heating chamber for temperature-sensitive materials. Visual control of the process can be achieved either by a stroboscopic lamp (point 6) or a camera set (point 7) for remote control. The electronic cabinet (point 1) that controls the microsphere unit can be integrated into an already existing control system.

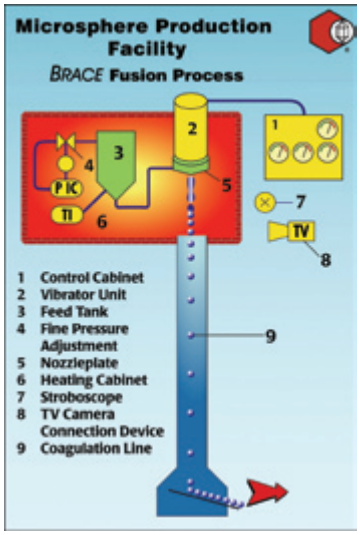

Figure 4. BRACE microsphere process (fusion process).

Results and Discussion

Tests have shown that the vibrating nozzle processes (laminar flow break-up) scale very well with Newtonian liquids. For industrial applications, it is possible to use multi-nozzle systems as well as high throughput settings, and a close correspondence to theoretical calculations is seen (Figure 5). For non-Newtonian liquids, scalability according to theoretical calculations is not possible. However, throughput can still be changed using a different number of nozzles.

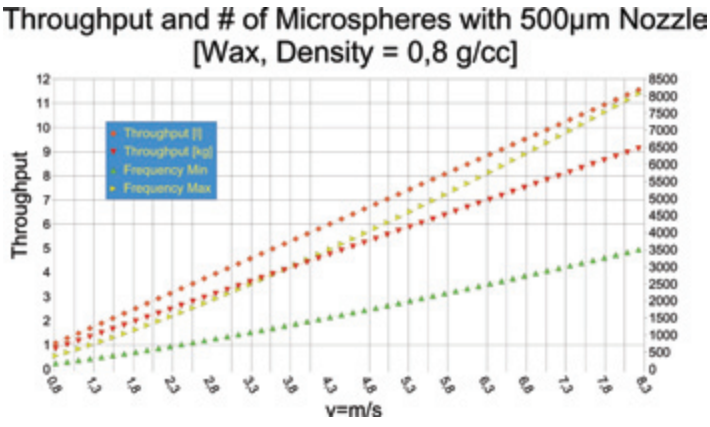

Figure 5. Development of theoretical throughput against flow speed.

Investigations of process stability demonstrate that the unit can run unattended for long periods without user interaction. With large-scale production units (>1,000 L/hr), uninterrupted production in three shifts on a 24 hr per day basis can be achieved. User interaction is reduced, with cleaning and maintenance cycles occurring every few months.

The production capacity of a BRACE microsphere installation ranges from about 10 mL/hr to more than 1,000 L/hr. With a 500-µm nozzle a throughput of 11 L/hr, with about 8,000 microspheres (1 mm diameter) per second, can be produced. With a 200-µm nozzle (resulting in about 400-µm microspheres) throughput is only about 2.8 L/hr with 30,000 microspheres per second.

Suitable Materials and Properties

There are few limitations for the materials that can be used in BRACE microsphere processes. The materials must be liquid, the viscosity has to be lower than 10,000 mPa·sec, emulsions and dispersions have to be stable over the duration of the process, dispersed particles should have diameters smaller than one-quarter of the nozzle size to be used, and presolidification should be a fast process so the particles are not deformed.

The resulting list of potential chemicals is very long and includes, among others, alginates, gelatines, agar, wax/thermoplastics, oxides as Si-, Al-, Ti-, Zr-, Hf-, Ce-, In-, and Y-oxides, PEG, PVA, polyacrylate, methacrylate, etc. Suitable active agents depend on the encapsulation technique. For matrix-encapsulation (microspheres) the active agent can be dispersed, dissolved, or emulsified into the shell material. For microcapsules the core material can consist of a liquid, like a solution, an emulsion, a dispersion, or a fusion/melt. The only restriction is that the core material should not react with the shell material (i.e., weaken it).

Examples

The BRACE processes are widely used in the chemical, pharmaceutical, and food industries (Figure 6). For example, waxes (Figure 6A) are used in cosmetics, dental applications, or as catalysts with active ingredients. Agar-agar (Figure 6B) is used to encapsulate oils or other volatile ingredients for cosmetic applications, whereas gelatine or alginates are used to encapsulate oils, fragrances, or flavours for food and feed technology applications. Polymer beads (Figure 6C) are used in combinatorial synthesis because the BRACE process produces monomodal grains of high-quality polystyrene microspheres with defined binding capacities. In the pharmaceutical industry, the BRACE process is used to encapsulate active agents either against the destructive forces in the digestive system or to mask the taste of very bitter materials (Figure 6D). The adjustable size of the microspheres is used to produce defined release profiles. Chemical and petrochemical industries use catalyst carriers (Figure 6E) and grinding balls produced by BRACE processes to obtain maximum performance and low wear and tear in process or as ball tip pens when made from silicon-carbide. Medical industries use inorganic microspheres in bone

C&DP continued on page 20

C&DP continued from page 19

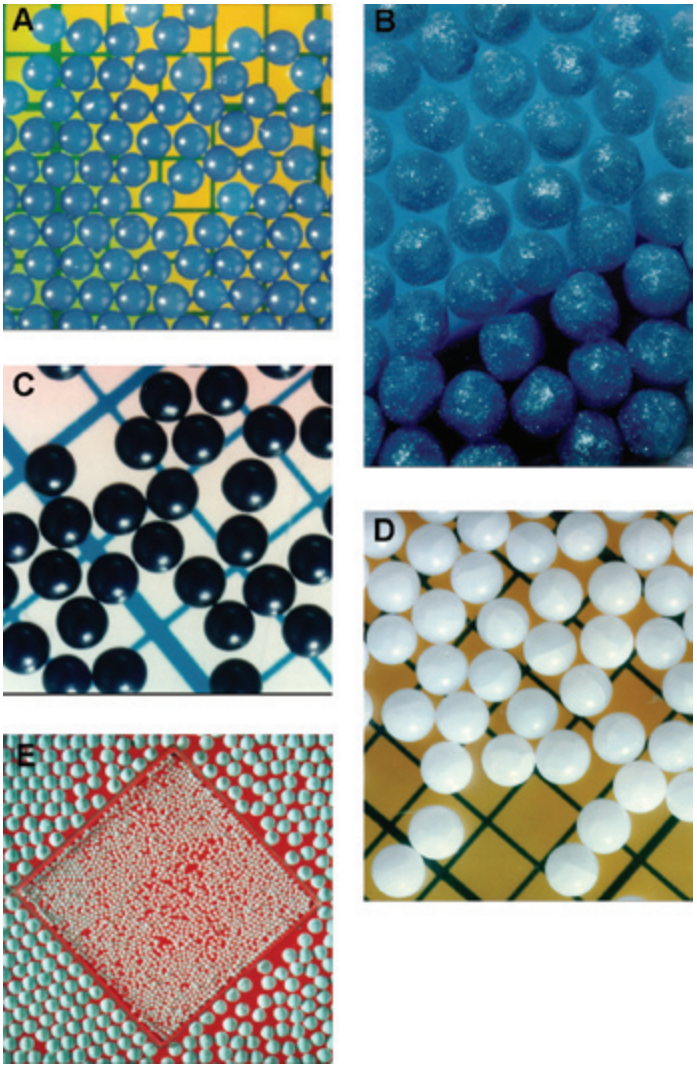

*Figure 6. Examples of Brace process applications. **A**, Waxes; **B**, Agar-agar; **C**, Polymer; **D**, Taste masking; **E**, Catalyst carriers.*

surgery applications, while food technologists prepare toothpaste with "crunch." In various industries the advantages of microencapsulated adhesives are used for gluing at assembly and thereby reducing costs on the assembly line.

Manufacturing Costs

Manufacturing costs depend on the material and the production capacities. For industrial-scale production, manufacturing costs start at 2.66 €/kg for production of 50 t/year and reach 0.31 €/kg at 1,000 t/year (Table 1). This calculation is based on a thermoplastic with a melting point of about 80°C, including a turn-key installation with building, storage, and packing facilities, quality control, and operator cost.

Thermoplaste, Wachse					
Investment, Description	Manufacturing Capacity, 1 shift, 2000 h/a				
Tons per year	50	100	300	500	1000
kg per hour	25	50	150	250	500
Nr of Nozzles	12	24	72	120	240
Feed preparation	20.000 €	25.000 €	40.000 €	50.000 €	80.000 €
Microsphere Unit	150.000 €	180.000 €	240.000 €	290.000 €	380.000 €
Storage and Packing	10.000 €	15.000 €	20.000 €	30.000 €	50.000 €
Total I	**180.000 €**	**220.000 €**	**300.000 €**	**370.000 €**	**510.000 €**
Laboratory, Quality control	10.000 €	12.000 €	16.000 €	24.000 €	30.000 €
Total II	**190.000 €**	**232.000 €**	**316.000 €**	**394.000 €**	**540.000 €**
Building (rent)	**15.000 €**	**15.000 €**	**20.000 €**	**20.000 €**	**25.000 €**
Raw material 1€/kg	**50.000 €**	**100.000 €**	**300.000 €**	**500.000 €**	**1.000.000 €**
Operators per shift	2	2	2	3	3
Operator cost per shift	80.000,00 €	80.000,00 €	80.000,00 €	120.000,00 €	120.000,00 €
Maintenance 5% of Total II	9.500,00 €	11.600,00 €	15.800,00 €	19.700,00 €	27.000,00 €
Amortisation 5a, 8% (0,2505)	**47.595 €**	**58.116 €**	**79.158 €**	**98.697 €**	**135.270 €**
Amortisation 10 a, 8 % (0,14903)	28.316 €	34.575 €	47.093 €	58.718 €	80.476 €
Manufacturing cost per kg (5a)	**3,04 €**	**1,65 €**	**0,65 €**	**0,52 €**	**0,31 €**
Cost including material	**4,04 €**	**2,65 €**	**1,65 €**	**1,52 €**	**1,31 €**

Table 1. *Manufacturing cost for different production scales (a thermoplastic with a melting point of about 80°C is assumed).*

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BMES Names Distinguished Scientist and Lecturer Award Recipient for 2007

Antonio G. Mikos

Antonios G. Mikos of Rice University has been named the BMES Distinguished Scientist and 2007 Lecturer Award recipient—the highest honor bestowed on a biomedical engineer by the Biomedical Engineering Society—in recognition of his pioneering and seminal contributions to tissue engineering and biomaterials research.

Antonios Mikos is the J. W. Cox Professor of Bioengineering and Professor of Chemical and Biomolecular Engineering at Rice University. He is also the director of the J.W. Cox Laboratory for Biomedical Engineering and the Rice Center for Excellence in Tissue Engineering. Tony joined the Rice faculty in 1992 as the T.N. Law Assistant Professor of Bioengineering and Chemical Engineering, earning promotions to associate professor in 1996 and professor in 1999.

At Rice, Tony has supervised 20 doctoral and 4 masters theses. He has trained 23 post-doctoral fellows and supervised the research of 60 undergraduate students. He is currently supervising the research of 16 doctoral students. Tony is also the author of more than 300 publications, 130 proceedings, 200 abstracts, and 20 patents. He is the editor of seven books, including *Frontiers in Tissue Engineering* (Elsevier Science, 1998) and nine journal special issues.

Tony is a founding editor of the journal *Tissue Engineering* and a member of the editorial boards of the journals *Biomaterials* (special issues editor), *Advanced Drug Delivery Reviews*, *Cell Transplantation*, *Journal of Biomaterials Science Polymer Edition*, *Journal of Biomedical Materials Research* (Part A and B), and *Journal of Controlled Release*. He is active in the American Institute of Chemical Engineers, Biomedical Engineering Society, Controlled Release Society, Society for Biomaterials, and Tissue Engineering Society International.

Tony's research has earned numerous professional honors and awards, including the 2005 Marshall R. Urist for Excellence in Tissue Regeneration Research of the Orthopaedic Research Society; 2003 Huygens Lectureship of the Netherlands Organization for Scientific Research; 2001 Clemson Award for Contributions to the Literature of the Society for Biomaterials; 2000 Phoenix Pharmazie-Wissenschaftspreis; 1998 Young Investigator Research Achievement Award of the Controlled Release Society; 1996 Outstanding Young Investigator Award of the Materials Research Society; 1994 Whitaker Young Investigator Award of the Biomedical Engineering Society; and 1991 Victor K. LaMer Award of the American Chemical Society. He was also the recipient of a FIRST Award of the National Institutes of Health in 1996 and was elected a Fellow of the International Union of Societies for Biomaterials Science and Engineering in 2000 and the American Institute for Medical and Biological Engineering in 1999.

Tony's research spans the areas of synthesis, processing, and evaluation of new biomaterials for tissue engineering, scaffolds for three-dimensional cell culture, conduits for guided tissue regeneration, substrates for targeted cell adhesion, carriers for controlled drug delivery, and non-viral vectors for gene therapy. His research has led to the development of novel orthopedic, cardiovascular, neurologic, and ophthalmologic biomaterials.

From the Editors continued from page 2

Setting e-distractions aside, here is some advice from my fellow editor's editorial on how to get the most out of a conference:

- **Sit at the front:** This helps you to feel more involved in the talk and aids concentration.
- **Take notes:** You will consider the most relevant information and have some thing to reflect upon after the event. This will also help the information stay with you for longer—listening is a weak learning style; digestion and interpretation into short notes is a much stronger technique, and you can share the information.
- **Catch up on the latest advances:** It is important to catch up on the latest advances in your field, but also try learning something from a new field with the aim of perhaps widening your research applications.
- **Break away:** Try to talk to someone who you don't already know. Going to a conference to talk to people you already know may be fun, but you should also try to get to know new people; you never know when you may need a contact at a company or information about a topic.
- **Be enthusiastic:** If you are interested in and excited about your work, then others will be too—this applies to talks, posters sessions, and general chit chat.
- **Intimacy:** Smaller conferences are generally better for networking; there is often a greater chance to meet the speakers and to interact within the sessions.
- **Rate the speakers:** At some point we all have to present our work—why not learn from the masters and see how they attract and maintain interest within a presentation; this also helps concentration.

Best regards,
Yvonne Perrie

Chapter News

Expand Your Local Network—Join a CRS Local Chapter

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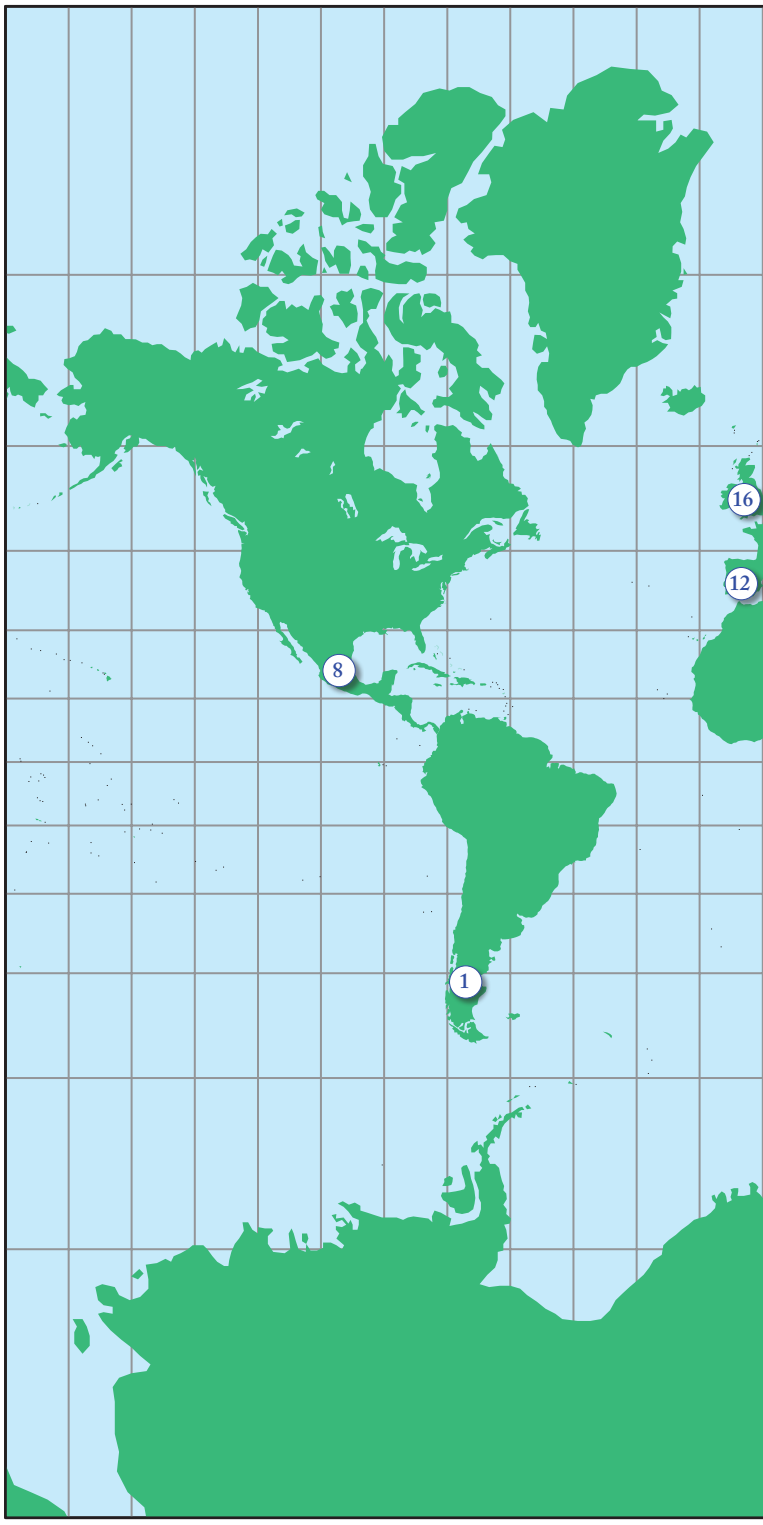

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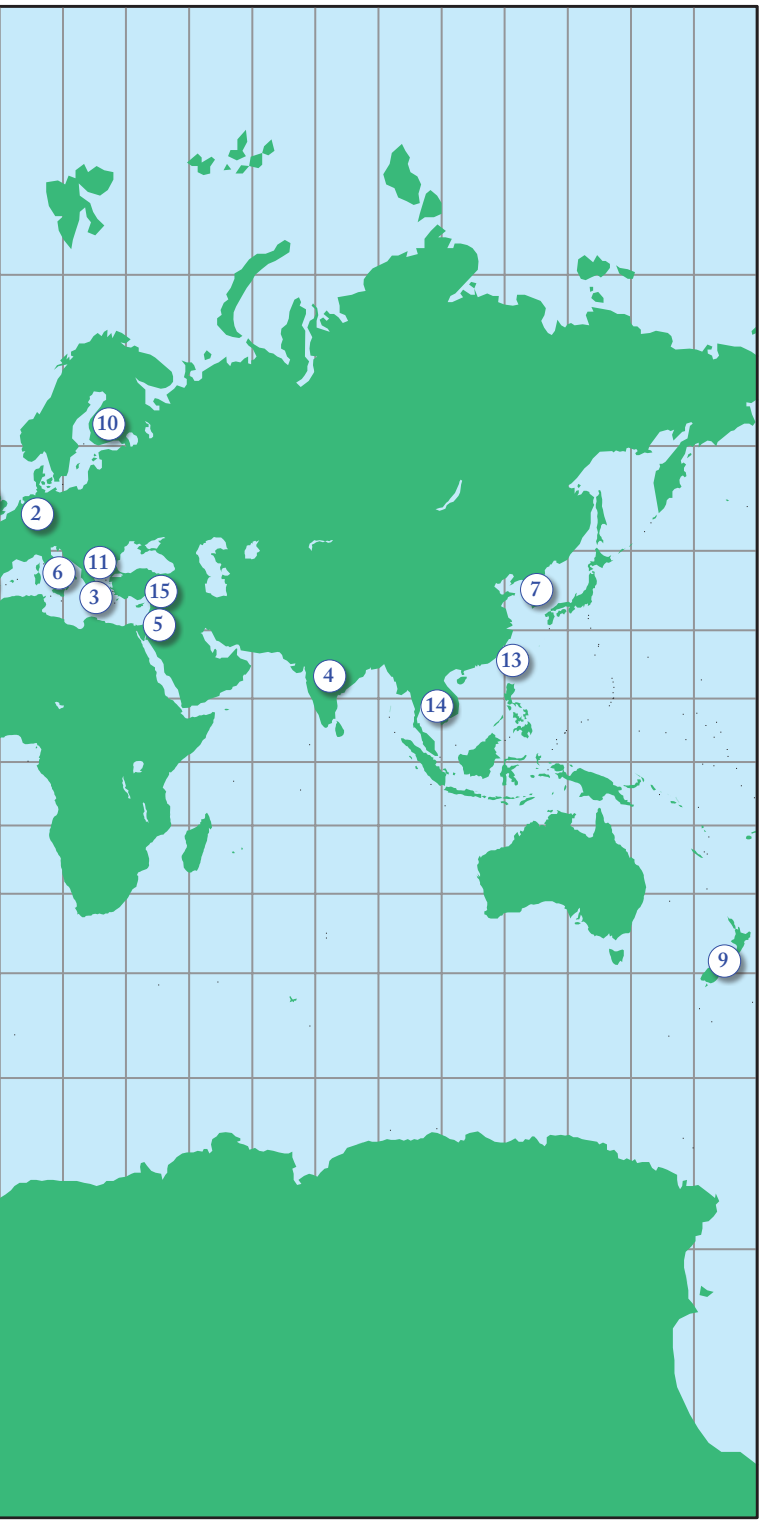

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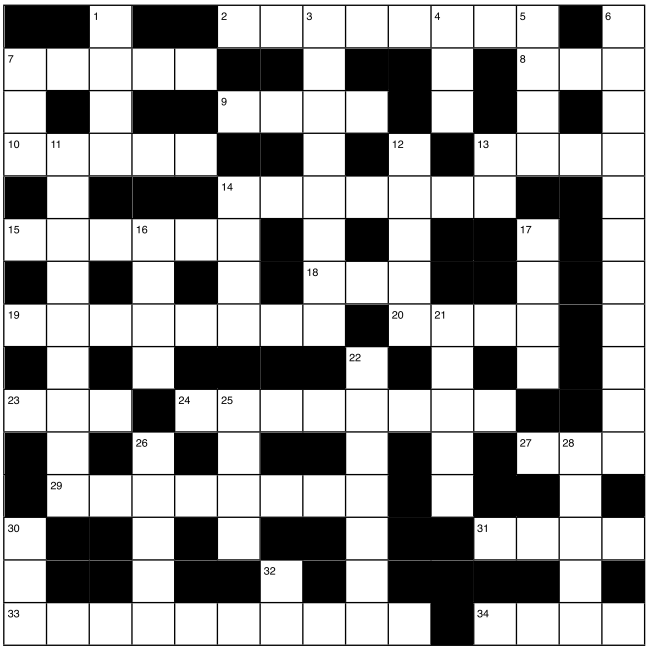
Chapter News

Fancy testing your general knowledge of science? Or, perhaps your logic? In a bid to "share good practice" (the socially acceptable term for plagiarism), here are two puzzles taken from the last UKICRS Newsletter. For the solutions, see http://www.ukicrs.org/Puzzle%20Page.htm. Many thanks to Karl Malcolm of the UKICRS Committee for preparing these puzzles.

UKI CRoSsword

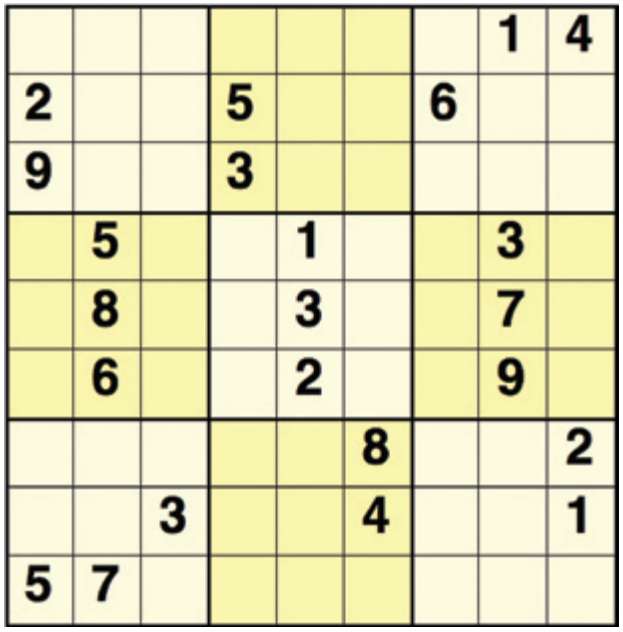


Across

2 Primary constituent in connective tissue and bone
7 Type of diffusion cell
8 Generic term for organic liquids that are not miscible with water
10 Fick's forename
13 A visual presentation showing how something works (abbreviation)
14 A synthetic route to dendrimer molecules
15 Chest pain caused by reduced flow of blood to the heart muscle
18 Diagnostic procedure that provides 3D images of internal body structures
19 Enzyme that digests proteins
20 Irish pharmaceutical company
23 Molecule which is the source of energy for metabolic processes in living organisms
24 Redness of the skin due to capillary dilatation
27 Not a "second-hand" candidate drug molecule? (abbreviation)
29 Type of light microscopy
31 Solid produced by the reaction of an acid with a base
33 Secondary tumour caused by migration of cancer cells to another tissue
34 Small glass bottle for storing samples

Down

1 Prefix meaning one-billionth
3 Closed lipid vesicle surrounding an aqueous interior
4 An HIV protein
5 Point on a stem where a leaf or bud is attached
6 Hormone secreted by the adrenal cortex, affects blood pressure and saline balance
7 U.S. regulatory body for the development, approval, manufacture, sale, and use of drugs
11 Branched, like a tree
12 Forename of the person who discovered radium
13 Abbreviation for the fossilized skeletons of minute, prehistoric aquatic plants
14 Novel CD4-targeted HIV inhibitor, J. Antimicrobial Chemother. 2005 56(2):270-272
16 Type of carrageenan, ninth letter of the Greek alphabet
17 Strain of avian influenza
21 Pale liquid consisting chiefly of plasma and white blood cells
22 A B-complex vitamin that is a constituent of lecithin; essential in the metabolism of fat
25 A violent disturbance of the public peace by three or more people
26 Fluid injected into the rectum for the purpose of clearing out the bowel
28 Hair-like structures that line the airways in the lungs
30 Units of chemical shift in nuclear magnetic resonance spectroscopy
32 God of the sun



Obituary

Joseph R. Robinson (1939–2006)

Noted University of Wisconsin pharmacy researcher and honorary member of CRS Professor Joseph R. Robinson, Ph.D., passed away on September 4, 2006, in Madison, Wisconsin. He was 67 years of age.

Internationally known and beloved for his leadership, scientific integrity, character, and enthusiasm, Robinson is often considered one of the world's most recognized pharmaceutical scientists of his generation. At UW, he served as the Kremers Professor of Pharmacy in the School of Pharmacy and Professor of Ophthalmology in the UW School of Medicine and Public Health.

Professor Robinson's contributions to the pharmacy field spanned more than four decades, and his leadership and vision are credited with helping to change the field of pharmaceutical science, especially in the areas of drug delivery, bioadhesion, and controlled release of drugs. Professor Robinson held more than 30 patents in the United States and Europe, and a new product for break-through pain in cancer patients, using technology from one of Robinson's patents, will be released to the U.S. market by the end of 2006. During his career Robinson successfully founded three companies and was a frequent consultant within the pharmaceutical industry.

Professor Robinson left an indelible impression as a colleague and mentor. As an educator, he helped inspire more than 90 graduate students and post-doctoral fellows, many of whom have become academic and business leaders in the United States and around the world. The author of more than 220 research publications and editor of and contributor to several scientific books, Robinson received his profession's highest national and international awards and was known as an inspiring leader in its most prestigious organizations.

Professor Robinson leaves behind his wife Bonna (Hatfield) Robinson; sons James (Jane) Robinson and Daniel (Marsha) Robinson; daughter Nancy (Gene Washington); and 10 grandchildren: Connie, Sean, Corey, Keenan, and Erin Washington and Ian, Colin, Kelly, Alton, and Mason Robinson.

Memorial contributions may be directed to the Joseph and Bonna Robinson Graduate Student/Faculty Support Fund, c/o University of Wisconsin Foundation, P.O. Box 8860, 1848 University Ave., Madison, WI 53708-8860, U.S.A.

SPOTLIGHT:

Lipo Chemicals Inc.

By Nava Dayan, Ph.D.
Lipo Chemicals, Inc., U.S.A.

As a worldwide supplier of chemical ingredients and delivery systems to the personal care, food, industrial, and pharmaceutical industries since 1962, Lipo Chemicals, Inc. thrives by pursuing innovative solutions within the industry. A worldwide network of affiliated companies and agents represents Lipo in approximately 50 countries. With its unique marketing approach and high quality standards, affirmed by its ISO 9002 certification, the company strives to create an entrepreneurial environment while remaining committed to technical excellence.

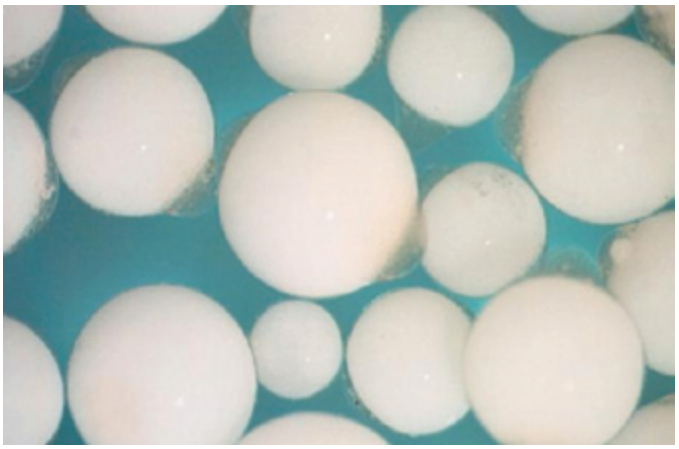
As a highly specialized delivery systems company Lipo Technologies, Inc. provides unique solutions to different industries. The delivery systems provide opportunities to combine incompatible compounds into a single formulated product, convert liquids into solids, and control the release of components. The company designs and manufactures a variety of microcapsules that are made of agar, gelatin, polyoxymethylene urea (PMA), ethyl cellulose, waxes, and a novel patented shell made out of cross-linked polyvinyl alcohol (PVA). The PVA shell is semi-transparent and, therefore, allows the passage of light. It was developed as part of a multi-component personal care ingredient that combines two mechanisms for reducing the appearance of skin imperfections: fluorescent light emission and light diffusion. The florescent compound, embedded in the polymer, absorbs UV light and re-emits it as visible light. In this way, a 5–6 μm particle situated in a wrinkle work as a light bulb to eliminate the shadow the wrinkle creates (1).

This technology is one of many that Lipo offers to the competitive personal care markets. New technologies are continually being developed. In light of the company's goal to become a leader in innovation, scientists at Lipo have established a network of universities and research institutions and are

Spotlight continued on page 26

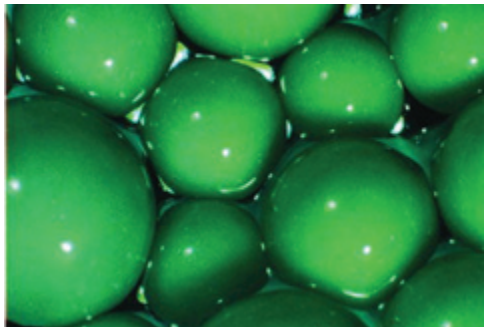
Spotlight continued from page 25

constantly looking to expand it. To compete with larger companies, Lipo believes that top-notch experts should conduct the scientific work required. Therefore, it chooses to work with and support experts in different fields, contributing to the launch of successful, long-lasting products. Among these fields are the study of skin penetration, the study of skin lipids, physical characterization using modern microscopic and thermal techniques, and more. Moreover, when commercializing compounds extracted from natural sources, the company engages universities that specialize in finding a correlation between location of growth and habitats and composition profile. One example of such work is a sea whip extract with anti-inflammatory properties that is harvested in the Bahamas (2). Lipo invests in continuous surveys to assure batch-to-batch consistency but is also careful to ensure the preservation of coral reefs. Finally, as a critical part of the development process, Lipo scientists lead research projects to generate data on skin metabolism, safety *in vitro*, and clinical testing of efficacy in different ethnic populations.



Among the dynamic product lines that Lipo offers are active components to treat the skin and improve its appearance, as well as compounds to improve finished formulation feel and elegance. Lipo offers a 97% isomerically pure, nature identical Ceramide NS (commonly known as ceramide 2). Since Ceramide NS can serve as a precursor for three other ceramides, its unique resemblance to the natural compound is the key to enzymatic recognition. It is believed that this compound can significantly improve skin barrier properties, especially in aged skin where there is a natural decrease in ceramide content. Although the product is available for sale, the company continues to invest in studies with a goal to better understand its mode of action for the benefit of its customers.

A novel skin brightening system that combines hydroxycinnamic acid with a vehicle to improve bioavailability is currently being launched (3). Studies have demonstrated both the safety and efficacy of this product. In recent clinical studies, this system has been shown to perform better than kojic acid in brightening and even toning the skin in both Caucasians and Asians.



A unique polymeric associative thickener that was recently licensed by Lipo is designed to impart an elegant feel to cosmetic formulations. The polymer chains consist of alternating hydrophobic "hard blocks" and hydrophilic "soft blocks." When incorporated into an aqueous environment, the polymer forms a three-dimensional network where the hard blocks associate with each other and the soft blocks associate with water molecules. When applied to the skin, the polymer's unique chemical structure reduces formulation tackiness caused by other ingredients, leaving a pleasant silky feel.

Seeking revolutionary paths to elevate compound efficacy and reduce toxicity, scientists at Lipo created a lamellar delivery system that is designed to target incorporated components in skin sub-tissue. Having proven their hypothesis in *in vitro* skin penetration studies, they currently are proceeding to clinical evaluation (4).

Late last year, the company announced a technical and marketing alliance between Dow Corning, Lipo Technologies, and Lipo Chemicals. Lipo's management believes this alliance will drive the development of creative delivery systems for the personal care and HI&I markets. This combination of entities forms a true delivery system provider for the global market.

Lipo's overall company approach goes beyond delivering a product. There is a long-standing tradition of studying and addressing market needs with the goal of satisfying the customer. Lipo's approach is to partner with the customer to bring unique products to the marketplace and formulators' ideas to life.

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How To Write a Scientific Paper—A General Guide

By Adrian Mulligan with input from David Tempest
Associate Directors, Research & Academic Relations, Elsevier, U.K.

The task of writing a research paper can be daunting. You may have completed groundbreaking research, but unless the paper is written correctly, at best publication will be delayed, at worst it will never published. The purpose of this article is to provide an overview of how to write a well-structured research paper for publication.

The first question to ask is, do I need to write a research paper? Editors and reviewers are looking for original and innovative research that will add to the field of study. If the research you are going to report on relates to a larger study, perhaps it is better to produce one important research paper, rather than a number of average incremental papers.

If you decide to write a paper, you will need to follow a structured format that has been developed over hundreds of years. While this may seem restrictive, the format has the advantage of allowing the paper to be read at several levels—some people will refer to just the title and others may read only the title and abstract, while those who want a deeper understanding will read the majority, if not all, of the paper.

Some authors write a paper with a specific journal in mind, while others write a paper and then adapt it to fit the style of a journal they subsequently choose. Regardless of your preference, there are some fundamentals. The objective is to report your findings and conclusions as clearly and concisely as possible, while avoiding embellishment with unnecessary words or phrases. Use of the active voice will shorten sentence length. It is best to avoid using abbreviations in the text except for units of measure. If English is not your first language, it is recommended that a native English speaker review the paper before you submit it for publication in an English language publication.

Journal Article Format

Most articles will include the following sections:

Section	Purpose
Title	Clearly describes contents
Authors	Ensures recognition of the writer(s)
Abstract	Describes what was done
Keyword list (some journals)	Ensures the article is correctly identified in abstracting and indexing services
Introduction	Explains the problem
Methods	Explains how the data were collected
Results	Describes what was discovered
Discussion	Discusses the implications of the findings
Acknowledgements	Ensures those who helped in the research are recognised
References	Ensures previously published work is recognised
Appendix (some journals)	Provides supplemental data for the expert reader

Title

A title should describe the paper's content clearly and precisely and allow the reader to decide whether it would be appropriate to read the paper further. The title is the advertisement for the article—a poorly titled paper may never reach its target audience, so be specific. Do not use abbreviations and jargon.

Authors

The listing of authors should include only those who have made an intellectual contribution to the research, will publicly defend the data and conclusions, and have approved the final version. The order in which the names of the authors appear can vary from discipline to discipline, in some fields the corresponding author's name appears first.

From the Education Committee continued on page 28

From the Education Committee continued from page 27

Abstract
The abstract should briefly summarise the problem, method, results, and conclusions. It should give sufficient detail so the reader can decide whether to read the whole article. Together, the title and abstract should stand on their own, as they are published in abstracting services. For this reason it is advisable not to include references to figures or tables in the abstract. Many authors write the abstract last so it accurately reflects the content of the paper.

Keyword List
Some journals request a keyword list. This list provides the opportunity to add important words, in addition to those already present in the title. Appropriate choice of keywords will increase the likelihood of your paper being located by other researchers.

Introduction
The introduction should clearly state the problem being investigated, provide background that explains the problem, and state the reasons for conducting the research. Summarize relevant research to provide context, state how your work differs from published work, and explain what questions you are answering. Explain what findings of others, if any, you are challenging or extending. Briefly describe your experiment, hypothesis(es), research question(s), and general experimental design or method.

Methods
The key purpose of this section is to provide the reader with enough details so they can replicate your research. Explain how you studied the problem, identify the procedures you followed, and order these chronologically where possible. If your methods are new, they will need to be explained in detail; otherwise, name the method and cite the previously published work, unless you have modified the method, in which case reference the original work and include the amendments. Include the frequency of observations and what type of data were recorded; be precise in describing measurements and include errors of measurement. Name any statistical tests used so your numerical results can be validated.

Results
In this section you objectively present your findings and explain what was found. This is where you show what your new results are contributing to the body of scientific knowledge. Raw data are rarely included in a scientific paper; instead, the data are analyzed and presented in the form of figures (graphs), tables, and/or descriptions of observations. It is important to clearly identify for the reader any important trends. This section should follow a logical sequence based on the tables and figures that best present the findings that answer the question(s) or hypothesis(es) being investigated. Figures should have a brief description (a legend), providing the reader sufficient information to understand how the data were produced. It is important not to interpret your results—this should be done in the Discussion section.

Discussion
In this section you describe what your results mean, specifically in the context of what was already known about the subject of the investigation. You should link the discussion back to the Introduction by way of the question(s) or hypothesis(es) posed. You should indicate how the results relate to expectations and to the literature previously cited. Most significantly, the Discussion section should explain how the research has moved the body of scientific knowledge forward. It is important not to extend your conclusions beyond what is directly supported by your results. It is advisable to suggest practical applications of your results and outline what would be the next steps in your study.

Acknowledgements
This section should be brief and include individuals who have assisted with your study, including financial supporters, proofreaders, typists, and suppliers who provided materials free of charge, etc.

References
Whenever you draw on previously published work, you must acknowledge the source. Any information not from your experiment and not considered "common knowledge" should be recognised by a citation. How citations are presented varies considerably from discipline to discipline, and you should refer to notes for authors for the specific journal. Quotes that appear in the paper, if long, should have their own indented paragraph; otherwise, if they are incorporated in the natural flow of the article, they should be set within quotation marks. Avoid references that are difficult to find and/or refer to papers not written in the language of the journal to which you are submitting your paper. The References section needs to include all references cited in your paper.

Appendices
Typically raw data are not included in a scientific paper but can be included in an appendix. Appendices can include raw data tables, video footage, photographs, or complex 3D models. If you have more than one set of materials to include, give each a separate number, e.g., Appendix 1, Appendix 2, etc.

Article Submission
Once the paper is completed it needs to be submitted to a journal. The advice here is to follow the guidelines in the journal's author guide and follow them implicitly. Many journals now offer an electronic submission option that allows efficient and timely submission and initiates the peer review process in an online environment.

Peer Review
Once submitted the paper will go through the journal's peer review system. The process varies, but for most journals, the journal editor(s) will make an initial decision on a paper—deciding whether to send it out for review or to reject the paper, at this stage papers are rejected either because they are out of the journal's scope or represent faulty science. Most editors appoint at least two reviewers who will make recommendations. Reviewing speed varies tremendously between journals and subject fields. The editor makes the final decision, and you should receive a decision of Accept, Accept with Revision (Minor or Major), or Reject. If your paper is rejected most editors will write to you explaining their decision. It is very rare that a paper is accepted without some revision, so expect to make some changes. Hopefully, after revision your paper will be accepted for publication in the journal. ■

Vets in Vienna

By Dr. Arlene McDowell
New Zealand's National School of Pharmacy
University of Otago, Dunedin, New Zealand

Veterinary aspects of controlled release were well represented at the CRS Annual Meeting in Vienna, Austria, with a session on Advances in Veterinary Controlled Release held during the first morning of the conference and a Veterinary Mini-symposium held the same afternoon.

The organisers of the Advances in Veterinary Controlled Release Session did an excellent job of bringing together a set of diverse and very interesting talks that featured the use of controlled release products for veterinary and wildlife applications. Dr. David Brayden (University College Dublin, Ireland) kicked off the session by presenting an elegant series of experiments into the potential toxicity of the anti-parasitic agent, ivermectin, in collie dogs. Dr. Brayden explained the work being done by his group investigating the involvement of P-glycoprotein in transporting anti-parasitic agents using epithelial monolayers from collie dogs. There was a Southern Hemisphere flavour to the following talks as the next three speakers were from Australia or New Zealand. Dr. Arlene McDowell (New Zealand's National School of Pharmacy, University of Otago, New Zealand) presented work on delivering biocontrol agents to wildlife and the unique case of the brushtail possum, a pest species in New Zealand. Insulin was proposed as a model compound to assess a nanoparticulate delivery system in this species because there are low levels of endogenous insulin and so there is no need to make the animals diabetic. Dr. Raid Alany (School of Pharmacy, University of Auckland, New Zealand) spoke about the use of *in situ* gelling polymers for intramammary use in cattle as a teat seal (Figs. 1–3). Using data obtained from excised teats, it was proposed that hydroxypropyl methyl cellulose (HPMC) and carboxyl methyl cellulose (CMC) were suitable polymers for intramammary application because drug (amoxicillin trihyhdrate) release from these systems was fastest and their gelling behaviour ensured that the formulation remained in the teat cistern for at least 12 hr. (I must say Raid's images of excised cow teats will stay with me for a while!) Dr. Keith Ellis (CSIRO Armidale, Australia) then turned our attention to the treatment of nematodes in sheep using the Captec system, a device retained in the rumen that can deliver a combination of tablets in a pulsatile manner.

At the Innovations in Veterinary Drug Delivery Mini-symposium, four international experts in the field of veterinary controlled release presented a series of stimulating talks. Dr. Scott Brown (Pfizer Animal Health, U.S.A.) gave an excellent talk on the changes to release profiles obtained for the antibiotic drug ceftiofur by varying the proportion of oxidisable components in the formulation. Dr. Brown presented the talk in such a way as to follow the winding trail in the development process for veterinary formulations and provided useful insights along the way. The issue of drug residues in food animals given slow-release injectables was discussed, and the solution of injecting into an inedible part of the body, such as the ear, was discussed. Prof. Sevda Senel (Faculty of Pharmacy, Hacettepe University, Turkey) gave a comprehensive presentation on the use of chitosan in veterinary medicine and outlined the many

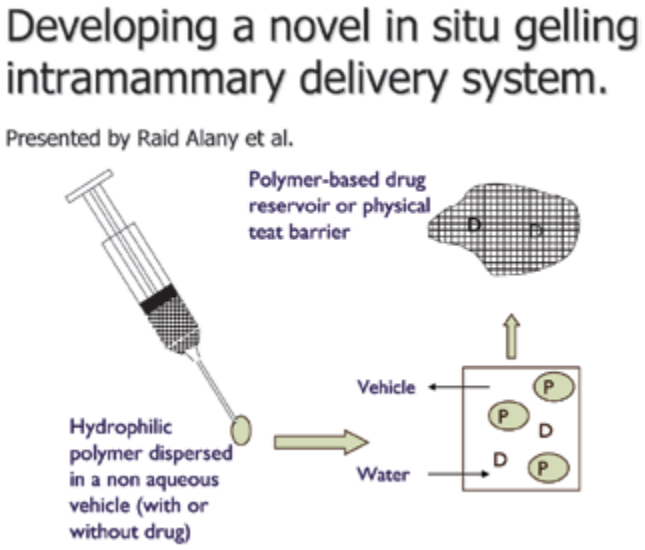

Fig. 1

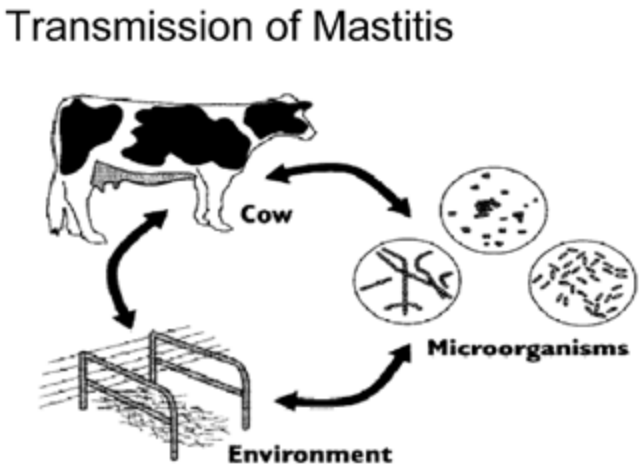

Fig. 2

From the Vet Group continued on page 30

From the Vet Group continued from page 29

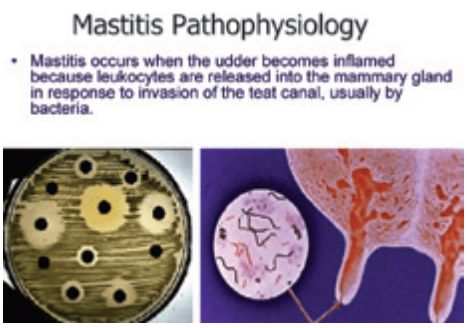

Fig. 3

advantages of this polymer, including biodegradability and adjuvant properties. Prof. Senel also highlighted research in her group on the development of chitosan gels for the administration of vaccines to sheep. Dr. Steven Sutton (Pfizer Global R&D, U. S.A.) discussed the factors that influence the effectiveness of oral dosage forms when administered to companion animals. Gastrointestinal transit time was just one of the factors identified as being important. Dr. Sutton made the important point that we need to be aware of differences in anatomy and physiology between animal and human patients when designing veterinary medicines. Prof. Pierre-Louis Toutain (National Veterinary School, France) presented data from an interesting study in which monozygotic twin calves received a pour-on formulation of ivermectin, and the amount of drug ingested through the process of licking was compared with animals that were restrained from licking themselves. The cattle that were able to lick ingested greater than 60% of the pour-on dose. The study was underpinned by pharmacokinetic/pharamcodynamic concepts, and Prof. Toutain shared some of his vast knowledge in this area. This talk gave useful insights into how the behaviour of animals is an important consideration when designing drug delivery systems for veterinary applications. ■

Journal of Controlled Release Highlights

By Morgan Leaming and Kinam Park

There are many ways to classify a manuscript as a good article. Has the manuscript received high reviews from the peer evaluations? Does the community recognize the novel subject matter through the number of times an article has been downloaded? Or, is the paper classified as good because it receives many citations? Here we focus on the number of downloads and the peer evaluations to share with the Controlled Release Society the exciting research that has been published in the *Journal of Controlled Release* from January to March 2006.

Investigating the uptake and intracellular fate of pH-sensitive liposomes by flow cytometry and spectral bio-imaging. Volume 110, Issue 3. Huth, U.S., Schubert, R., Peschka-Süss, R. This article investigates the uptake and intracellular behavior of pH-sensitive liposomes in two different cell types. Through their research, the authors "show that a combination of flow cytometry and spectral bio-imaging offers the possibility to understand the initial mode of internalization and to follow the intracellular fate of liposomes."

Paclitaxel releasing films consisting of poly(vinyl alcohol)-graft-poly(lactide-co-glycolide) and their potential as biodegradable stent coatings. Volume 111, Issue 1-2. Westedt, U., Wittmar, M., Hellwig, M., Hanefeld, P., Greiner, A., Schaper, A.K., Kissel, T. In this article, the authors investigate the influence of biodegradable paclitaxel-eluting stent coating materials that contain polyesters on release kinetics.

One-step preparation of polyelectrolyte-coated PLGA microparticles and their functionalization with model ligands. Volume 111, Issue 1-2. Fischer, S., Foerg, C., Ellenberger, S., Merkle, H.P., Gander, B. In this article the authors work on developing a novel surfactant-free process for the concomitant formation of poly(lactide-co-glycolide) (PLGA) microparticles (MP) and surface coating with the polyelectrolyte chitosan.

Targeted drug delivery crossing cytoplasmic membranes of intended cells via ligand-grafted sterically stabilized lipo-somes. Volume 110, Issue 3. Lu, J., Jeon, E., Lee, B.S., Onyuksel, H., Wang, Z.J. In this article, the authors examine sterically stabilized liposomes (SSL) with surface ligands specified for the mu opoid receptor (MOR) to determine if they can actively target MOR-expressing cells. Through their experiments, they found that a dermorphin-SSL delivery system is capable of targeting intracellular components of MOR-expressing cells.

Novel oral insulin delivery systems based on complexation polymer hydrogels: Single and multiple administration studies in type 1 and 2 diabetic rats. Volume 110, Issue 3. Morishita, M., Goto, T., Nakamura, K., Lowman, A.M., Takayama, K., Peppas, N.A. This work attempts to find an "optimal formulation and designing carriers for oral insulin delivery using in vivo experiments." The results obtained from the study indicate that the blood glucose levels of diabetic rats can be effectively controlled by oral SS-ILP administration. ■

InTheNews

Compiled by Steven Giannos
Industrial Editor

Aktiv-Dry Awarded Research Grant To Develop Inhalable Vaccine To Help Stop Smoking

BOULDER, Colo., PRNewswire: Aug. 31, 2006 – Aktiv-Dry LLC, a biotechnology company dedicated to developing inhalable aerosol vaccines, has been awarded a $850,000 SBIR grant from the National Institute on Drug Abuse at the National Institutes of Health to develop an inhalable nicotine vaccine to help smokers quit smoking for good. Jim Searles, Ph.D., of Aktiv-Dry, will be the principal investigator; Nabi Biopharmaceuticals and the Minnesota Medical Research Foundation will be collaborators. The SBIR grant is a Fast Track award to fund Phase I and Phase II activities.

NicVAX, Nabi's proprietary investigational vaccine that is being developed to treat nicotine addiction and prevent smoking relapse, is designed to stimulate the immune system to produce antibodies that bind to nicotine and prevent it from entering the brain. It is believed that these nicotine antibodies will act like a "sponge," soaking up nicotine as it circulates in the bloodstream and preventing it from reaching the brain. The positive stimulus in the brain that is normally caused by nicotine is no longer present, thereby eliminating the addictive properties of nicotine and, consequently, helping people to quit smoking.

Because the ability of the body's immune system to produce these antibodies is expected to be long lasting, it is believed NicVAX will also be effective in preventing smoking relapse, a significant challenge with existing smoking cessation therapies. By preventing the pleasurable response, "the rush," that occurs when nicotine reaches the brain, NicVAX takes away what is believed to be the main reason that most people cannot stop smoking.

Oral Spray

Business Wire via NewsEdge Corporation, SOUTH SAN FRANCISCO, Calif.: Aug. 30, 2006 – Hana Biosciences (NASDAQ:HNAB), a biopharmaceutical company focused on advancing cancer care, has announced that the U.S. Food and Drug Administration (FDA) has accepted for review the company's new drug application (NDA) for Zensana™ (ondansetron HCI) oral spray. Hana submitted an NDA for Zensana™ to seek approval for use in the prevention of chemotherapy-, radiation-, and post-operative–associated nausea and vomiting. The acceptance of the filing means the FDA has made a threshold determination that the NDA is sufficiently complete to permit a substantive review.

Hana completed bioequivalence and bioavailability clinical trials of Zensana™ in early 2006 and submitted its NDA under Section 505(b)(2) of the Food, Drug and Cosmetic Act on June 30, 2006. This form of registration relies on data in previously approved NDAs and published literature. The expected Prescription Drug User Fee Act (PDUFA) action date for this NDA is April 30, 2007.

Patheon Breaks into Drug Delivery

In-PharmaTechnologist.com: Aug. 29, 2006 – Canadian contract manufacturer Patheon has teamed up with specialty pharmaceutical firm Depomed to offer its clients a controlled release formulation that can grant their drugs increased bioavailability and less frequent dosing.

By making Depomed's AcuForm drug delivery technology available to its clientele of 200 pharmaceutical and biotechnology companies, Patheon is signaling its determination to join the ranks of companies such as Cardinal Health, Baxter, and 3M that offer proprietary solutions in dosage form development, ranging from controlled release formulation to commercialization.

Although Patheon has a long way to go before it can compete with the outsourcing industry's behemoths in patented drug delivery technology, the deal means that the Toronto-based company's five centers of excellence in Canada, the United States, the United Kingdom, Italy, and Puerto Rico, with more than 550 scientists working on more than 150 projects, will be able to use the AcuForm platform for the purpose of formulating, developing, or improving pharmaceutical products.

Depomed's technology embraces diffusional, erosional, bilayer, and multi-drug systems that can optimize oral drug delivery for both soluble and insoluble drugs. One application of it enables standard-sized tablets to be retained in the stomach for 6–8 hr after administration, thereby extending the time of drug delivery to the small intestine and allowing it to release substantially all of its drug payload to the upper gastrointestinal sites.

Patheon is already familiar with AcuForm because it is used in two of the Depomed products it manufactures; ProQuin XR, a once-daily, extended-release formulation of ciprofloxacin hydrochloride for the treatment of uncomplicated urinary tract infections, and Glumetza, a once-daily, extended-release formulation of metformin hydrochloride (HCl) for the treatment of Type II diabetes, which is expected to be launched in the United States in the coming weeks.

Insulin Absorption After Dry Powder Inhalation Depends on Particle Size and Carrier Lactose

NewsRx.com: Aug. 28, 2006 – Insulin availability for absorption after dry powder inhalation depends on the particle size of the drug as well as the carrier lactose. "Dry powder formulation of insulin for pulmonary administration was prepared to obtain increased drug deposition in the alveolar absorptive region. The deposition was studied by investigating the dispersion and deaggregation of insulin from the carrier lactose using an Andersen cascade impactor and twin stage impinger. The subsequent absorption following the

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deposition was studied by in vivo method," scientists in India report.

T. M. Kumar and A. Misra at the Maharaja Sayajirao University of Baroda explain, "Insulin in solution with absorption promoters was lyophilized. The powder was incorporated with lactose of different grades and their combinations as carriers to deliver using an inhaler device. Solid-state characteristics of the carrier as well as the drug powder were assessed by particle size and distribution measurement. The in vivo performance was studied by deliverance to the respiratory tract of guinea pigs. The intratracheal bioavailability with respect to intravenous route was calculated by measuring the blood glucose reduction."

The researchers conclude, "Insulin formulations containing 1:1 mixture of Respitose ML006 and Respitose ML003 as carrier can impart deeper deposition of drug particles and cause higher bioavailability. This suggests that carrier used in the formulation influenced the amount of insulin deposition in the alveolar region of the lung. Hence, it was concluded that the availability of insulin for systemic absorption depends on the particle size of the drug as well as the carrier lactose."

Kumar and Misra published their study in *Drug Development and Industrial Pharmacy* (Formulation and evaluation of insulin dry powder for inhalation. Drug Dev Ind Pharm, 2006;32(6):677-686).

Free Film Formulations Are Tested for Colonic Drug Delivery

NewsRx.com: Aug. 25, 2006 – Formulations containing sustained release polymethacrylates in combination with inulin have more potential as a coating system for specific colon delivery compared with pH-dependent polymers.

"The aim of this study was to assess some permeability and swelling characteristics of free films prepared by combination of inulin as a bacterially degradable system and time- or pH-dependent polymers as a coating formulation for colonic drug delivery. Different free films were prepared by casting and solvent evaporation method," researchers in Iran report. "Formulations containing inulin with Eudragit RS, Eudragit RL, Eudragit RS-Eudragit RL, Eudragit FS and Eudragit RS-Eudragit S with different ratios of inulin were prepared. After preparation, free films were evaluated by water vapor transmission test, swelling experiment and permeability to indomethacin and theophylline in different media. Formulations containing Eudragit FS had high resistance to water vapor permeation; but were unable to protect premature swelling and drug release in simulated small intestine media," write A. Akhgari and colleagues (Mashhad University of Medical Science).

Akhgari and colleagues published their study in the *European Journal of Pharmaceutical Sciences* (Permeability and swelling studies on free films containing inulin in combination with different polymethacrylates aimed for colonic drug delivery. Eur J Pharm Sci, 2006;28(4):307-314).

TransPharma Medical Completes $18 Million Financing Led by Argonaut, Backed by Teva, Others

NewsRx.com: Aug. 25, 2006 – TransPharma Medical Ltd., a specialty pharmaceutical company focused on the development and commercialization of drug products utilizing a proprietary active transdermal drug delivery technology, has announced that it has secured $18 million in series C financing.

TransPharma will use the funds to progress its lead project, transdermal hPTH (1-34), into advanced clinical trials. Earlier this year, the company announced promising human clinical results demonstrating efficient and effective transdermal delivery of hPTH (1-34) for the treatment of osteoporosis.

The company also plans to use the funds to initiate development of additional drug products in 2007, as well as to develop a new generation of transdermal drug delivery systems and scale-up production of its current ViaDerm delivery system. TransPharma currently has a joint development agreement with Teva for up to five molecules. The company has successfully completed initial clinical trials on the first of these molecules.

Carrington and Brookwood Pharmaceuticals Expand Gelsite Drug Delivery Technology Development

NewsRx.com: Aug. 24, 2006 – Carrington Laboratories, Inc. (CARN) has announced that its subsidiary, DelSite Biotechnologies, Inc., formed a joint development initiative with Brookwood Pharmaceuticals, Inc. The goal of this effort is to carry out an expanded evaluation of GelSite, a DelSite patented drug-delivery technology, as a matrix for injectable applications and for selected classes of drugs.

GelSite is a naturally derived, biocompatible, resorbable biopolymer that can be used to deliver biopharmaceuticals. This technology has the potential to protect and deliver peptides and proteins effectively while reducing the frequency of drug administration. Fewer injections will improve patient compliance, safety, and efficacy. Injectable, controlled-release applications for peptides and proteins are in the multibillion-dollar drug delivery market.

"The team at DelSite has been making great strides with the GelSite technology, particularly in the vaccine area. We are excited to be collaborating with them – combining our teams of polymer and drug delivery experts – to broadly evaluate parenteral applications," said Dr. Arthur J. Tipton, president and CEO. Under this new expanded joint development initiative, the evaluation of GelSite technology will be managed by a team of experts from Brookwood Pharmaceuticals and DelSite.

Antares Inks Development Deal with the Population Council

NewsRx.com: Aug. 24, 2006 – Antares Pharma (AIS) has signed a joint development agreement with the Population Council, an international, nonprofit research organization. Antares and the Population Council will initially develop contraceptive formulation products containing Nestorone, using the council's patented and other proprietary information covering the compound, and Antares' proprietary advanced transdermal delivery (ATD) gel platform.

Antares' ATD system is a clear, cosmetically acceptable drug delivery gel. Within a few minutes of application to the skin, an invisible depot is formed within the epidermis from which the drug is slowly absorbed into systemic circulation. The gel contraceptive products developed under this agreement are expected to be generally safer than most oral contraceptives, convenient to use, and attractive to women who have problems taking oral contraceptives. They will be under the complete control of the user and will be able to deliver multiple active ingredients simultaneously.

Adverse effects should also be minimal compared with standard oral contraceptives, which typically yield more precipitous "peak and trough" levels of drug in the bloodstream. Additionally, compared with the patch or traditional depot systems, adverse effects should be easier to reverse.

Nestorone is a fourth-generation synthetic progestin contraceptive that has a good safety profile. It is not active when administered orally and, therefore, is especially appropriate for topical application, as well as for use when breastfeeding. Certain hormonal contraceptives developed under this agreement could also possibly be effective as male contraceptive products.

Technology To Improve Drug Dosing and Efficacy and Reduce Side Effects in GI Tract

NORCROSS, Ga. (Business Wire): Aug. 22, 2006 – Auriga Laboratories, Inc. (OTCBB:ARGA), a specialty pharmaceutical company dedicated to applying advances in drug delivery to improve and extend the value of medicines for improved patient outcomes and the marketer of the Extendryl® family of products, has announced the execution of a strategic agreement with Degussa to develop a proprietary formulation targeting serious chronic gastrointestinal diseases utilizing Degussa's proprietary EUDRACOL™ technology.

Auriga is developing an oral, controlled-release corticosteroid formulation that targets inflammatory bowel disease lesions at different sites within the GI tract. Degussa, the world's largest specialty chemical company, will provide the proprietary drug delivery technology and formulation concentrating the therapeutic benefits of the selected corticosteroid specifically where it is needed in the GI tract, providing dosing and efficacy and reducing side effects.

Under the terms of the development agreement, Degussa is responsible for development of the prototype formulations. Auriga Laboratories is responsible for formulation scale-up, manufacture, clinical trials, regulatory submission/approval, and product launch and marketing.

Nektar Closes U.K. Site; Focusing on Drug Delivery Technology

NewsRx.com: Aug. 21, 2006 – Nektar Therapeutics (NKTR) has announced the closing of the Nektar U.K. site in Bradford, U.K., as part of its ongoing strategy to realign business operations with a focus on product development using its leading drug delivery technologies. Nektar announced its intent to dispose of its U.K. operation and supercritical fluid technology during the company's first quarter financial results conference call on May 10, 2006.

"As Nektar transitions from being a technology development company to a commercial entity focused on achieving profitability, it is important that we channel our resources into those businesses that will drive future growth. To this end, disposing of our supercritical fluid processing technology represents a significant first step in aligning our spending with those activities that will drive our revenue in the near-term: developing proprietary products based on our drug delivery technology; Exubera (insulin human (rDNA origin)) Inhalation Powder, the product of a developmental collaboration between Pfizer and Nektar, and diabetes life-cycle management products, and high-value partner programs," said Robert B. Chess, chair and acting president and CEO of Nektar.

Frost & Sullivan Lauds EpiCept's Entrepreneurial Skills in the Transdermal Drug Delivery Market

PALO ALTO, Calif., PRNewswire: Aug. 21, 2006 – Frost & Sullivan has selected EpiCept Corporation (Nasdaq: EPCT) as the recipient of the 2006 Transdermal Drug Delivery Entrepreneurial Company of the Year Award for its role as an emerging leader in transdermal therapeutics.

Through a straightforward, low-risk development strategy, EpiCept is poised to rapidly emerge as a leader in the transdermal drug delivery market with its topical patch formulations. The company has gained market eminence by targeting patients with unmet clinical needs and providing them with safe, non-addictive prescription options. EpiCept's strong leadership has enabled its two lead patch products, LIDOPAIN™ SP and LIDOPAIN™ BP, to be potentially launched in the U.S. and European markets by 2010.

The primary focus of the company is delivering topical, non-opioid drugs that target peripheral nerve receptors, utilizing Food and Drug Administration (FDA)-approved active ingredients. This will help the company to cut down the risk of treatment failure since the pharmacology and side-effect profile of the drugs are well understood. The company's business model is to secure corporate partners to assist with the development and marketing of its products, as well as market some products on its own.

Insert Therapeutics Treats First Patient with Nano-Engineered Anticancer Therapeutic

NewsRx.com: Aug. 15, 2006 – Arrowhead Research Corp. (ARWR), has announced that its majority-owned subsidiary, Insert Therapeutics, a company commercializing delivery-enhanced therapeutics using a patented class of polymeric systems, has treated its first patient in a Phase I study of IT-101, Insert's lead anti-cancer compound.

"The initiation of the clinical development phase for IT-101 is an important milestone for Insert Therapeutics. It demonstrates our commitment to bringing innovative therapies to the clinic that address significant, unmet patient needs," said Thomas Schluep, chief scientific officer at Insert Therapeutics.
The study is an open-label, dose-escalation Phase I study in patients with

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inoperable or metastatic solid tumors and has been designed to evaluate the safety, tolerability, and pharmacokinetics of IT-101. Insert expects that between 24 and 48 patients will be enrolled in the study during its course. The study is currently being conducted at The City of Hope Cancer Center (COH) in Duarte, CA, where Yun Yen, M.D., Ph.D., will lead the study.

Animal studies using IT-101 showed excellent anti-cancer activity, including complete remission of certain kinds of lung cancer, among others. IT-101 is a combination of its patented polymer technology, Cyclosert, and the anti-cancer compound camptothecin. Insert's proprietary Cyclosert delivery system is based on small cyclic repeating molecules of glucose called cyclodextrins. Using modified cyclodextrins as building blocks, Insert has developed an entirely new proprietary class of materials called linear cyclodextrin-containing polymers.

To the company's knowledge, Cyclosert is the first nano-particulate drug delivery platform to be designed de novo and synthesized specifically to overcome limitations in existing delivery technologies used for the systemic delivery of therapeutics. The polymers were invented at Caltech in the lab of Mark Davis, a professor in chemical engineering and founder of Insert, and licensed exclusively to Insert.

Iomai Launches Phase II Clinical Study of Vaccine Patch for Travelers' Diarrhea

GAITHERSBURG, Md., PRNewswire-FirstCall: Aug. 15, 2006 – Iomai Corporation (Nasdaq: IOMI) has announced that it has begun enrollment of a Phase II trial designed to test its vaccine patch for travelers' diarrhea in volunteers traveling to sites in Mexico and Guatemala. The field test will provide the investigators with the crucial information needed to launch a Phase III trial of the needle-free vaccine.

The placebo-controlled study is designed to assess the safety of the vaccine and the frequency of enterotoxigenic *E. coli* (ETEC) infection in volunteers traveling to sites where the disease is endemic and offer other details that will be key for the coming Phase III trial. Most cases of travelers' diarrhea are caused by ETEC, and as many as 50% of travelers to areas where the bacteria is endemic are sickened over a 1- to 2-week period. No ETEC vaccine is available in the United States.

Based on Iomai's novel transcutaneous immunization (TCI) technology, the patch works by delivering vaccine to a group of antigen-presenting cells in the skin called Langerhans cells, which transport the vaccine to nearby lymph nodes to produce a sustained immune response.

Exelon Patch, First Transdermal Therapy for Alzheimer Disease, May Provide New Treatment Approach

NewsRx.com: Aug. 14, 2006 – An international study of the first transdermal patch for patients with Alzheimer disease has shown that it may provide a promising new treatment approach. The six-month IDEAL trial of 1,195 patients with moderate Alzheimer disease showed that the Exelon patch provided benefits across a range of symptoms, and the target dose was well tolerated. Results were presented at the 10th International Conference on Alzheimer's Disease and Related Disorders (ICAD) in Madrid, Spain, by the Alzheimer's Association.

Patients receiving the Exelon patch (rivastigmine transdermal patch) had significant improvements in memory and were better able to maintain everyday activities than those receiving a placebo. They could also complete a concentration task faster compared with those taking a placebo, and physicians considered Exelon patch patients to have done better overall.

In addition, over 70% of caregivers in the IDEAL study preferred the patch to capsules as a method of drug delivery for reasons including helping them follow the treatment schedule, citing overall ease of use, and less interference with daily life, according to a questionnaire in the study.

Exelon is a cholinesterase inhibitor already approved in many countries for the treatment of mild to moderate Alzheimer disease and Parkinson disease dementia. The IDEAL results will support the regulatory submission of the Exelon patch to the U.S. Food and Drug Administration, planned by the end of 2006. IDEAL (Investigation of Transdermal Exelon in Alzheimer's disease) was a 24-week, multi-center, randomized, double-blind, placebo- and active-controlled trial to compare the efficacy, safety, and tolerability of the once-daily Exelon patch with conventional twice-daily Exelon capsules in patients with moderate Alzheimer disease.

Transdermal Drug Delivery Achieves Therapeutic Levels of a Peptide Used for Treatment of Infertility in Humans

FAIR LAWN, N.J. (Business Wire): Aug. 10, 2006 – Vyteris Holdings (Nevada), Inc. (OTC BB:VYHN) has reported that data from two Phase I clinical trials demonstrated that Vyteris' Actyve™ transdermal drug delivery technology delivered potentially therapeutic levels of a peptide used for the treatment of infertility in humans. Vyteris and its partner, Ferring Pharmaceuticals Inc., are in the early stages of developing a product that delivers the peptide for the treatment of female infertility. The development goal is that, through this technology, the peptide could be delivered 24 hr a day in short pulses, to induce ovulation.

In these Phase I clinical trials, a pulsatile profile controlled the transdermal delivery of the peptide from patches loaded with different concentrations of the peptide. The amounts of the peptide delivered were compared with subcutaneous (subQ) and intravenous (IV) infusions of the peptide in humans.

The first study, with 45 healthy volunteers, used different formulations within the Vyteris patch that were compared with subQ and IV delivery of the peptide. The plasma concentrations of the peptide demonstrated the feasibility of delivering the peptide in humans using the Actyve™ system. In addition, the pulses obtained were sharper and, therefore, mimicked an IV pulse profile more than a subQ pulse profile. The second study, with 50 healthy volunteers, compared more formulations in the patch and iontophoretic delivery parameters against subQ infusion of the peptide in humans. The plasma profiles of the peptide obtained in the second study achieved potentially therapeutic levels and

provided sharper profiles (closer to IV) than subQ profiles. No unexpected adverse side effects were observed in any of the participants in the trials.

MonoSol Rx Completes U.S. DEA Registration for Two Facilities To Handle Controlled Substances

NewsRx.com: Aug. 04, 2006 – MonoSol Rx has announced that it has completed the registration of both its Portage, IN, manufacturing facility as well as its Kingsport, TN, development facility with the U.S. Drug Enforcement Administration (DEA) to handle controlled substances. The company's development facility has been registered for schedules II–V; the company's manufacturing facility has been registered for schedules III–V controlled substances.

These registrations complement other developments in the company's infrastructure, including bringing packaging in-house and the inauguration of the company's analytical capabilities. These registrations will allow the company to scale up active projects dealing with controlled substances.

MonoSol Rx is a drug delivery company that uses film as a fast-dissolve oral drug delivery platform. MonoSol Rx LLC's manufacturing facility is located in Portage, IN. The company previously acquired substantially all of the assets of Kosmos Pharma, including its extensive oral film intellectual property portfolio. MonoSol Rx's film oral dosage form looks like a postage stamp and dissolves readily on the tongue to deliver drugs to a patient, replacing the use of conventional tablets and capsules. MonoSol Rx currently markets a variety of products together with its marketing partners.

Human Growth Hormone Achieved Using Biodegradable Polymeric Microspheres

NewsRx.com: Jul. 27, 2006 – Recent research from Switzerland has reported on the use of biodegradable polymeric microspheres for the sustained release of human growth hormone (hGH). "A new approach for attaining sustained release of protein is introduced, involving a pore-closing process of preformed porous poly(D,L-lactic-co-glycolic acid) PLGA microspheres," write H. K. Kim and colleagues (Korea Advanced Institute of Science & Technology).

"Highly porous biodegradable PLGA microspheres were fabricated by a single water-in-oil emulsion solvent evaporation technique using Pluronic F127 as an extractable porogen. Recombinant human growth hormone (rhGH) was incorporated into porous microspheres by a simple solution dipping method. For their controlled release, porous microspheres containing hGH were treated with water-miscible solvents in aqueous phase for production of pore-closed microspheres," state the investigators.

"These microspheres showed sustained release patterns over an extended period; however, the drug loading efficiency was extremely low. To overcome the drug loading problem, the pore-closing process was performed in an ethanol vapor phase using a fluidized bed reactor," report the authors. They conclude, "The resultant pore-closed microspheres exhibited high protein loading amount as well as sustained rhGH release profiles. Also, the released rhGH exhibited structural integrity after the treatment."

Kim and colleagues published their study in the *Journal of Controlled Release* (Biodegradable polymeric microspheres with "open/closed" pores for sustained release of human growth hormone. J Control Release, 2006;112(2):167-174).

Biosimilar or Generic?

In-PharmaTechnologist.com: Jul. 19, 2006 – The U.S. Food and Drug Administration (FDA) has turned down Nastech's generic version of the nasal spray Miacalcin for the treatment of osteoporosis because of the possibility of an interaction with a preservative used in the formulation, sparking heated debate in the United States about whether calcitonin should be treated as a generic or a biosimilar drug.

The regulator expressed concerns about the potential for immunogenicity that might result from a possible interaction between calcitonin, derived from salmon, and chlorobutanol, the preservative in Nastech's formulation, which is also used in many nasal sprays already on the market. Such concerns are usually reserved for biosimilar drugs, and Nastech had filed an abbreviated new drug application (ANDA) on the assumption that calcitonin would be treated as a generic. Generic ANDAs are scrutinized less vigorously than biosimilar ANDAs because all a generic maker must do is present laboratory evidence that its copy is chemically the same as the original and human clinical tests showing that the generic behaves like the original in the bloodstream, without any additional clinical data.

The company is now caught in a catch-22 situation because even if it submits additional immunogenicity data, the FDA may not be able to process it under the generic application pathway, and a new drug application as a biosimilar may be required. Meanwhile, Nastech's two manufacturing sites in Washington and New York have passed chemistry, manufacturing, and control (CMC) inspections and are waiting to start production on the spray. They may now have to wait for a while, like everyone in the pharmaceutical industry who expects clarity in the FDA's approach to biosimilar molecules.

Biocompatible Poly(organophosphazenes) for Protein Delivery Have Been Synthesized

NewsRx.com: Jul. 19, 2006 – Scientists have synthesized biocompatible poly(organophosphazenes) for the local delivery of protein drugs. According to a study from South Korea, "Biocompatible and thermosensitive poly(organophosphazenes) with a lower critical solution temperature (LCST) below body temperature have been designed with the aim for the local delivery of peptide and protein drugs. These polymers could be synthesized by introducing short chain tri- or tetraethylene glycol as a hydrophilic group and a dipeptide, GlyGluEt2, as a hydrophobic group into the polyphosphazene backbone. The local tolerance tests using rabbits have shown that our polymers are biocompatible." "Using the amphiphilic properties of these polymers, in vitro studies were performed for loading and releasing of a human growth hormone (hGH) as a model drug,"

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state Ji-Yeon Seong and collaborators at Ewha Women's University and Dong-A Pharmaceutical Company, Ltd. "The entrapment efficiency of hGH by the polymer decreased as its polymer concentration increased, but exhibited high efficiency of more than 95% even at 20% hGH concentration in the polymer. The entrapped hGH has shown to be controlled releasing for three to four days."

Seong and associates published their study in the *International Journal of Pharmaceutics* (Synthesis and characterization of biocompatible poly(organophosphazenes) aiming for local delivery of protein drugs. Int J Pharm, 2006;314(1):90-96).

Sugar and Olive Oil Break Free from the Kitchen

NewsRx.com: Jul. 17, 2006 – U.S. scientists have discovered that sugar and olive oil do not just belong in the kitchen—they could potentially be used to develop naturally-derived nanomaterials for drug delivery systems and biological scaffolds.

Fundamental research from the United States suggests that an enzyme could convert sugars in the presence of olive oil to form organic gels called "nano organogels." These organic gel nanomaterials could be used to encapsulate pharmaceutical products to create new drug delivery systems, as well as being used to build 3D biocompatible scaffolds for tissue engineering and designing membranes, according to Prof. Jonathan Dordick and co-workers from Rensselaer Polytechnic Institute in New York who conducted the research.

The science behind the gels entailed using the enzyme lipase B from *Candida antarctica* (CALB) to form esters of trehalose, a sugar found naturally in mushrooms, honey, lobster, and shrimp. The trehalose diesters then self-assemble into 3D fibers measuring between 10 and 50 nm in diameter. As the fibers entangle, a large amount of solvent gets packed together, trapping some 10,000 molecules. Disintegration of the gels could occur, said the researchers, by re-exposure to lipase, an enzyme that is naturally present in the human intestine.

This research opens up the possibility that active pharmaceutical ingredients (APIs) could be encompassed in the trehalose nano-gels, with release dependent on re-exposure to the enzyme. Dordick believes that the importance of his team's finding is the ability to use the same naturally occurring enzyme both to create chemically functional organogels and to reverse the process and break down these gels into their biologically compatible building blocks. The findings are available online in the journal *Angewandte Chemie*.

Israeli Firm Gearing Up To Make "Supergenerics"

NewsRx.com: Jul. 03, 2006 – Intec Pharma has enlisted two North American dosage form manufacturers to make "supergenerics" using its new method of oral drug delivery that can transform existing drugs into more powerful therapies.

The firm has developed the Accordion Pill, an advanced oral drug delivery system that it claims improves the bioavailability of drugs by increasing the amount of time the active pharmaceutical ingredients (APIs) are held in the gastrointestinal system. By improving bioavailability, the Accordion Pill has the potential to transform drugs that need to be taken as much as five times a day into one-a-day pills that improve patient compliance and reduce unwanted side effects, states the firm.

Intec Pharma plans to launch a series of supergeneric drugs using the Accordion Pill technology and has now signed a deal with film-based drug specialist manufacturer BioEnvelop Agro of Quebec, Canada, and Tapemark of Minnesota, U.S.A., a privately held contract manufacturer, to achieve this.

According to Intec, supergeneric drugs combine the advantages of original pharmaceutical products that have the potential for blockbuster sales, as well as patent protection, with the advantages of generic drugs that can get quick regulatory approval. "We plan to use our platform Accordion Pill technology to transform numerous existing drugs into more powerful therapies," states Cohen-Arazi. "This technology offers a new competitive edge in the area of oral drug development and for product life cycle management."

Magnetic Nanoparticles Show Promise in Targeted Drug Delivery

Decision News Media SAS (NewsRx.com): Jun. 27, 2006 – Researchers have developed a new nanocarrier system for the delivery of drugs that contain iron and so can be directed by a magnetic field to specific areas of the body, a technology which could prove invaluable in the treatment of diseases such as cancer.

The new method, developed by scientists at the University of Buffalo (UB) and recently published in *Molecular Pharmaceutics*, may lead to treatments that exploit the advantages of photodynamic therapy (PDT) and that have the potential to reduce drug accumulation in normal tissues.

Not only does the new system allow the guided and precise delivery of drugs to chosen areas of the body, a tumor for example, avoiding serious side effects, but it also enhances the cellular uptake of the PDT drugs it transfers. For their drug delivery vehicle, researchers used polymer micelles, which are nanosized, water-dispersible clusters of polymeric molecules, and so are excellent nanocarriers for PDT drugs, which are mostly water insoluble. Along with the photodynamic drug, they encapsulated inside the nanocarriers iron oxide nanoparticles, which allowed them to respond to externally applied magnetic fields.

"This is a novel way to enhance drug delivery to cells," says Paras Prasad, executive director of UB's Institute for Lasers, Photonics and Biophotonics. "The externally applied magnetic field acted as a kind of remote control, directing the nanocarriers to the targeted area in the cell culture." Once the magnetic field was applied, the concentration of drug inside the tumor cells in the target area increased. "The magnetically guided drug delivery would allow for the use of lower concentrations of the drug to deliver a therapeutic dose, thus significantly reducing the amount of PDT drug that accumulates in normal tissue," states Prasad.

Preliminary studies in live animals have indicated that an applied magnetic field can effect a localized accumulation in the tumor site, and the team is beginning *in vivo* studies on the new drug delivery method.

SkyePharma Unveils New Controlled Release Technology

NewsRx.com: Jun. 26, 2006 – SkyePharma used its latest business review meeting to announce the imminent arrival of a new rheumatoid arthritis (RA) drug formulated using its novel controlled release drug delivery technology.

The firm has combined its formulation skills with controlled manufacturing processes to develop a new technology, called GeoClock, that allows the preparation of chronotherapy-focused press coated tablets. GeoClock tablets have an active drug loaded inside an outer tablet layer consisting of a mixture of hydrophobic wax and brittle material to obtain a pH-independent lag time prior to core drug delivery at a predetermined release rate. This dry coating approach is designed to allow the timed release of both slow- and immediate-release active cores by releasing the inner table first, after which time the surrounding outer shell gradually disintegrates.

Using this novel technology, the pharma firm has been developing the new RA drug on behalf of another pharma company, Nitec. According to SkyePharma, the drug, called Lodotra, will deliver the undisclosed active pharmaceutical ingredient (API) at the most appropriate time of day to treat the disease.

As well as controlled-release, the GeoClock technology also has applications for the improved release of colonic drug delivery, as well as multiple pulse drug delivery to deliver doses of the drug at specific times throughout the day.

World's First Transdermal Insulin Shows Promise

In-PharmaTechnologist.com (NewsRx.com): Jun. 19, 2006 – Many said it couldn't be done, but Australian pharma firm Phosphagenics has developed what it claims is the world's first transdermal insulin formulation and has received the first signs that the product may have blockbuster potential.
The company, which focuses on drug delivery and drug enhancement, has reported the first positive results from preclinical trials using its novel transdermal insulin (TMP-02/insulin) formulation on pigs. "The study has successfully demonstrated the ability of TMP-02/insulin to deliver insulin across the skin of pigs at levels sufficient to lower glucose in the blood," states the independent principal investigator of the study, Prof. Frank Dunshea, Department of Primary Industries, Victoria, Australia.

Phosphagenics is one of a growing number of new contenders vying to cash in on the non-injectable insulin field, competing with pharma giants such as Pfizer who have recently launched the first inhalable form of insulin; however, the firm believes it has developed a drug delivery technology that is unique, being able to deliver large-size insulin molecules through the skin's surface, without the need for burdensome and expensive drug delivery devices.

Phosphagenics has discovered that a phosphorylated form of vitamin E (tocopheryl phosphate) can be used to penetrate the skin at a nine times greater rate than regular vitamin E. The patented technology uses microencapsulation, which involves capturing the drug molecules with a thin layer of phosphorylated vitamin E to create a nanosphere. This nanosphere acts as a carrier that uses existing natural transport mechanisms to "carry" drugs across the skin without disrupting the skin's surface.

The company has developed two formulations of the carrier—TPM-01 and TPM-02. TPM-01 delivers small molecule drugs (e.g., morphine, fentanyl, oxycodone, atropine, estradiol, testosterone), and TPM-02 delivers both small and large molecule drugs (e.g., insulin, PTH, proteins). Both formulations of the carrier have anti-inflammatory and anti-erythema properties, which minimize skin irritation and can provide sustained transdermal delivery of drugs—a potential gold mine.

Egalet Contracts SP Medical To Make Its Erosion-based Drugs Through Injection Molding

In-PharmaTechnologist.com (NewsRx.com): Jun. 12, 2006 – Drug delivery firm Egalet has asked SP Medical, a manufacturer of molded plastics and coatings, to make sufficient clinical-grade quantities of its therapeutics using injection molding, which allows for greater uniformity and reproducibility in the production of tablets. Injection molding, a method that has been used for decades for medical devices, has been adapted by Egalet to produce pharmaceutical tablets of more accurate weight and content compared with conventional compressed tablets.

Whereas most tablets are made with an accuracy of 4–5%, Egalet's technology can produce tablets with 0.1% accuracy, resulting in little or no variation between one tablet and the next, thereby reducing waste. Moreover, since the manufacturing process follows standard procedures for injection molding of thermoplastic materials, it allows manufacturers to easily vary the rate of production at times of greater demand and produce very high volumes to precise standards of accuracy in a virtually automatic environment.

The Danish company's tablets consist of a biodegradable coat and a matrix, comprising the active drug, which is surface-erodible, hydrophobic, and composed of polyethylene glycol (PEG)-stearate. By changing the properties of the matrix, Egalet has developed a constant-release system and a burst-release system with a predetermined delay. The formulation can be used for virtually any type of medicine and, unlike water-soluble diffusion technology, it is not affected by the pH of the body fluid with which it comes in contact.

All manufacturing will take place in a SP Medical good manufacturing practice (GMP)-certified facility located just south of Copenhagen and is subject to approval by the Danish authorities and the U.S. Food and Drug Administration (FDA).

Generex Biotechnology and Fertin Pharma Announce Metformin Gum Collaboration

TORONTO (Market Wire): May 31, 2006 – Generex Biotechnology Corporation (NasdaqSC:GNBT - News), a leader in the area of buccal drug delivery, and Fertin Pharma A/S (www.fertin.com), a world leader in the development and manufacture of medicinal chewing gum, jointly announced today that they have established a collaboration for the development of a metformin medicinal

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chewing gum for the treatment of Type 2 diabetes mellitus and obesity.

The collaboration will seek to combine Generex's proprietary buccal drug delivery platform technologies with Fertin's know-how related to gum-base formulations, solubilization systems, and taste masking/modification to create a metformin medicinal chewing gum that will deliver metformin into the body via the buccal mucosa (the inner lining of the mouth) rather than in its current tablet form. The companies expect that this new delivery method, in addition to being much more rapid and providing a much more specific and effective dosing regimen, will avoid some of the adverse side effects associated with taking metformin in tablet form, such as nausea, vomiting, abdominal pain, diarrhea, abdominal bloating, and increased gas production. In addition, metformin gum will avoid the bitter taste and large doses associated with the tablet form, thereby improving patient compliance, particularly among younger patients.

SurModics Acquires Biodegradable Polymer Technology

EDEN PRAIRIE, Minn. (Business Wire): May 5, 2006 – SurModics, Inc. (Nasdaq:SRDX), a leading provider of surface modification and drug delivery technologies to the healthcare industry, announced that it has acquired intellectual property covering biodegradable polymer technology from Intralytix, Inc. The intellectual property relates to polyester-amide (PEA) biodegradable polymers, which naturally degrade in the body into amino acid components, the building blocks of proteins.

"SurModics continues to expand its technology offerings in the drug delivery arena," says Bruce Barclay, president and CEO of SurModics. "The acquisition of this technology brings to five the total number of biodegradable polymers suitable for site specific drug delivery available to our customers, and complements our durable polymer drug delivery platforms. As we increase our expertise in the area, we are expanding the potential applications of particular polymer classes with various drugs and other biological compounds. We believe the PEA biodegradable polymers we acquired from Intralytix position us well to provide new site specific drug delivery capabilities to a wide range of customers."

Insulin Delivery Carrier SS-ILP Could Control Blood Glucose Levels in Diabetic Rats

NewsRx.com: Apr. 17, 2006 – The insulin delivery carrier SS-ILP could effectively control blood glucose levels in diabetic rats. "Insulin-loaded polymer microparticles (ILP) composed of cross-linked poly(methacrylic acid) and poly(ethylene glycol) are multifunctional carriers showing high insulin incorporation efficiency, a rapid insulin release in the intestine based on their pH-dependent complexation properties, enzyme-inhibiting effects and mucoadhesive characteristics. Thus, they are potential carriers for insulin delivery via an oral route," scientists writing in the *Journal of Controlled Release* report.

M. Morishita and colleagues at Hoshi University explain, "Recent studies suggest that the polymer composition and particle size of ILP strongly influenced insulin bioavailability. Therefore, the present study aimed at finding an optimal formulation and designing carriers for oral insulin delivery using *in vivo* experiments."

Morishita and colleagues published their study in the *Journal of Controlled Release* (Novel oral insulin delivery systems based on complexation polymer hydrogels: Single and multiple administration studies in type 1 and 2 diabetic rats. J Control Release, 2006;110(3):587-594).

Transcutol P May Improve the Ocular Drug Delivery of Hydrophilic Compounds

NewsRx.com: Apr. 14, 2006 – According to a study from the People's Republic of China, "Our purpose was to explore the use of Transcutol P (Trans) in an ocular drug delivery system. The effect of Trans on the corneal permeability of drugs was investigated in-vitro, using isolated rabbit corneas," according to Z. D. Liu and colleagues from Shenyang Pharmaceutical University.

They continue, "The ocular irritation of Trans was also tested in rabbits in-vivo. In the presence of Trans, at a concentration of 0.005–0.03%, the maximum increase in the apparent permeability coefficient (P-app) was 1.5, 1.5, 3.0 and 3.3 fold for ribavirin, gatifloxacin, levofloxacin hydrochloride and enoxacin, respectively. However, the P-app value of oxaprozin was reduced in the presence of Trans. The maximum reduction was found to be 2.8 fold at a concentration of 0.03% Trans. The results of the ocular irritation studies showed that Trans was non-irritant at the concentrations studied (0.005–0.03%), while it produced slight irritation at a concentration of 0.05%. It was also found that Trans did not cause any visible ocular damage or abnormal clinical signs involving the cornea, iris or conjunctivae at all concentrations." The researchers conclude, "We concluded that Trans may have potential clinical benefits in improving the ocular drug delivery of hydrophilic compounds."

Liu and colleagues published the results of their research in the *Journal of Pharmacy and Pharmacology* (Effects of Transcutol P on the corneal permeability of drugs and evaluation of its ocular irritation of rabbit eyes. J Pharm Pharmacol, 2006;58(1):45-50).

Conor Medsystems Licenses Pimecrolimus from Novartis for Use in Reservoir-based Drug-Eluting Stents

NewsRx.com: Apr. 12, 2006 – Conor Medsystems, Inc. (CONR) has announced that the company exercised its option to obtain a worldwide, non-exclusive license from Novartis Pharma AG (NVS) to the pharmaceutical compound pimecrolimus for use with Conor's next-generation controlled vascular drug delivery technologies.

Conor expects to begin a clinical trial this year evaluating the therapeutic potential of two novel stents incorporating pimecrolimus for the treatment of coronary artery disease. Both stents will utilize the company's reservoir-based cobalt chromium drug-eluting stent platform. One stent will be loaded with pimecrolimus, and the other stent will be a dual-drug stent loaded with both pimecrolimus and paclitaxel.

Cationic Liposomes Are Promising in Drug and Gene Delivery

NewsRx.com: Apr. 12, 2006 – According to recently published research from Japan, cationic liposomes are promising in drug and gene delivery. "After intravenous administration of plasmid DNA (pDNA)/cationic liposome complexes, the gene expression is predominantly observed in the lung due to the physicochemical properties of the liposome complexes and the physiology of the lung," write W. Yeeprae and colleagues from Kyoto University.

"To determine the physicochemical properties and distribution behavior of cationic liposomes for lung-selective drug and/or gene delivery systems, N-[1-(2,3-dioleyloxy)propyl]-n,n,n-trimethylammonium chloride (DOTMA)/cholesterol and 1,2-dioleoyl-3-trimethylammoniopropane (DOTAP)/cholesterol liposomes were studied," they explain. "The particle sizes of DOTMA/cholesterol and DOTAP/cholesterol liposomes were very similar: 126 and 128 nm, respectively. Furthermore, the zeta potentials of these two liposomes were 51 and 66 mV, respectively. After intravenous injection into mice, both cationic liposomes were rapidly eliminated from the blood circulation and preferentially recovered in the lung. Interestingly, the highest lung accumulation was observed at 1 min, and then, decreased gradually," the researchers report.

Yeeprae and colleagues published their study in *Pharmazie* (Physicochemical and pharmacokinetic characteristics of cationic liposomes. Pharmazie, 2006;61(2):102-105).

Targeted Drug Delivery Now Possible with "pHLIP" Peptide

M2 PressWIRE via NewsEdge Corp., NEW HAVEN, Conn.: Apr. 12, 2006 – Scientists at Yale and the University of Rhode Island have reported the development of a peptide that can specifically and directly deliver molecules to the inside of cells like a nano-syringe, creating a new tool for drug delivery, gene control, and imaging of diseased tissues.

Their "cargo carrier" peptide called pHLIP, for pH (low) insertion peptide, accumulates in the membranes of cells in acidic environments and spontaneously transfers attached molecules across the membrane. The cargo is then released by cleavage of a sulfur-sulfur bond that is only unstable if it is inside the cell. The study, published early online in the *Proceedings of the National Academy of Sciences*, was led by Donald M. Engelman, professor of molecular biophysics and biochemistry at Yale.

Itraconazole Has Been Formulated with Improved Dissolution and Oral Absorption

NewsRx.com: Apr. 7, 2006 – Scientists in South Korea have conducted a study "to enhance the dissolution and oral absorption of poorly water-soluble itraconazole. A self-emulsifying drug delivery system (SEDDS) composed of oil, surfactant and cosurfactant for oral administration of itraconazole was formulated, and its physicochemical properties and pharmacokinetic parameters of itraconazole were evaluated. Among the surfactants and oils studied, Transcutol, Pluronic L64 and tocopherol acetate…showed the maximal solubility to itraconazole."

Hong and colleagues published their study in the *Journal of Controlled Release* (A new self-emulsifying formulation of itraconazole with improved dissolution and oral absorption. J Control Release, 2006;110(2):332-338).

A Mucoadhesive Hydrogel May Serve as a Drug Delivery Device to the Mucosal Epithelium

NewsRx.com: Apr. 7, 2006 – A mucoadhesive hydrogel may serve as a drug delivery device to the mucosal epithelium. A self-folding miniature device has been developed to provide enhanced mucoadhesion, drug protection, and targeted unidirectional delivery. The main part of the device is a finger-like bilayered structure composed of two bonded layers

H. Y. He and colleagues from Ohio State University write, "One is a pH-sensitive hydrogel based on crosslinked poly(methylacrylic acid) (PMAA) that swells significantly when in contact with body fluids, while the other is a non-swelling layer based on poly(hydroxyethyl methacrylate) (PHEMA). A mucoadhesive drug layer is attached on the bilayer. Thus, the self-folding device first attaches to the mucus and then curls into the mucus due to the different swelling of the bilayered structure, leading to enhanced mucoadhesion. The non-swelling PHEMA layer can also serve as a diffusion barrier, minimizing any drug leakage in the intestine. The resulting unidirectional release provides improved drug transport through the mucosal epithelium." The researchers conclude, "The functionality of this device is successfully demonstrated in vitro using a porcine small intestine."

He and colleagues published their study in the *Journal of Controlled Release* (An oral delivery device based on self-folding hydrogels. J Control Release, 2006;110(2):339-346).

Shire's DAYTRANA™ Transdermal Patch Approved

PHILADELPHIA, Penn. and BASINGSTOKE, England, PRNewswire: Apr. 7, 2006 – Shire plc (LSE: SHP, NASDAQ: SHPGY, TSX: SHQ) has announced that the U.S. Food and Drug Administration (FDA) approved DAYTRANA™ (methylphenidate transdermal system), the first and only non-oral medication for the treatment of attention deficit hyperactivity disorder (ADHD). DAYTRANA™, a once daily transdermal patch formulation of methylphenidate, will be available in 10, 15, 20, and 30 mg dosage strengths.

Shire and Noven Pharmaceuticals, Inc. submitted an amended New Drug Application (NDA) for DAYTRANA™ to the FDA in June of last year. DAYTRANA™ is licensed globally to Shire by Noven and will be available in pharmacies in the United States in 2006.

As part of the agreement between Shire and Noven for DAYTRANA™, Shire completed an up front payment to Noven of $25 million in 2003 and may make separate milestone payments up to $125 million: $50 million will be paid based on FDA approval, and $75 million will be paid based on the achievement of certain sales targets.

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SCHWARZ PHARMA Presents Clinical Data on Rotigotine Transdermal Patch

Apr. 6, 2006 – SCHWARZ PHARMA presented results at the 58th Annual Meeting of American Academy of Neurology (AAN) from an open-label extension of a Phase III trial of rotigotine transdermal patch, a non-ergolinic dopamine agonist, currently under investigation in the United States for Parkinson's disease. As reported earlier the multi-center, double-blind, placebo-controlled trial preceding the open-label long-term extension demonstrated that Parkinson's disease patients treated with rotigotine showed statistically significant improvement in the Unified Parkinson Disease Rating Scale (UPDRS). In this interim analysis of the open-label extension, rotigotine was well tolerated and improved the symptoms of early-stage Parkinson's disease.

The results revealed that early initiation of rotigotine may indicate a long-term advantage. Overall, patients experienced better long-term outcomes when treated with rotigotine compared with placebo. The most common side effects were somnolence, application site reactions (ASRs), nausea, and dizziness.

Novel Oral Disc Technology Breaks Through Cancer Pain

MORRISVILLE, N.C., PRNewswire: Apr. 6, 2006 – Cancer patients fraught with painful flare-ups, or breakthrough pain, may soon receive some assistance in the form of a new easy-to-use oral adhesive disc developed by BioDelivery Sciences. Chronic cancer patients frequently experience two types of pain: persistent and breakthrough. Persistent cancer pain is characterized as continuous pain present for long periods of time. Breakthrough pain is a brief and often severe shooting pain that can even afflict patients regularly taking pain medication for persistent pain. It is called breakthrough pain because it "breaks through" a regular pain medicine schedule. According to the American Cancer Society, it is common for people with persistent pain to also experience episodes of breakthrough pain.

Breakthrough pain is unpredictable and manifests itself differently in each person. It typically comes on quickly and lasts as long as an hour, and it can be as severe as persistent pain.

The next generation of fentanyl is a patient friendly, small oral adhesive disc called BEMA™ Fentanyl, which is currently being testing in Phase III trials by BioDelivery Sciences. The BEMA™ technology is a layered disc that is applied to a mucosal surface in the same way a transdermal disc is applied to the skin. The small disc is composed of an adhesive layer and a non-adhesive backing layer, with both layers capable of holding the medicine. The disc adheres to the inside cheeks and delivers the dose of medication. Instead of requiring removal upon completion of the drug delivery, the BEMA™ disc disintegrates in the mouth and leaves no drug residue.

In a cross-over study comparing BEMA™ Fentanyl and Actiq®, the lozenge formulation of fentanyl that is the current market leader in fast-dissolving fentanyl products for breakthrough cancer pain, results showed that the BEMA™ Fentanyl formulation provided faster absorption and greater concentration of the drug. ■

Welcome New Members

Magdy Abdel-Malik
Niuris Acosta
Roger Adami
Manuela Aigle
Achim Aigner
Saghir Akhtar
Bernd Albrecht
Monzur Ali
Yusuf Ali
Aniruddha C. Amrite
EunJung An
Kavya Anjani
David Armbruster
Sonja C. Arnold
Rathapon A-sasutjarit
Kazuhide Ashizawa
Nataliya Asmolova
Reyhaneh Astaneh
Anthony Attama
Patrick Augustijns
Jin Woo Bae
JoonHo Bae
Sibu Balan
Mario Bandulik
Anna Angela Barba
Brice Bardel
Jerome Barra
Stan Bastiras
Hassan Benameur
Massimo Bergamin
Erick Bernard Berglund
Gerald Bernstein
Vivekanand Bhardwaj
Babette Biruss
Steven Bitler
Caroline Blackshields
James Blanchette
Paolo Blasi
Henning H. Blume
Ross Blundell
Peter A. Boderke
Georg Boeck
Christof Boehler
Marija Bogataj
Antonio P. Boix-Montanes
Sanjay P. Boldhane
Susanna Bosi
Mary Bossard
Ben Boyd
Nolwenn Brandhonneur
Olivier Brass
John R. Bric
Tatiana Bronich
Heike Bunjes
Patrick J. Burns
Christopher Busch
Youngro Byun
Carmen Calinescu
Maria Grazia Calvagno
Pilar Calvo
Martin L. Caney
Carla M. Caramella
Bob Carr
Simon Cawthorne
Nevin Celebi
Christian Celia
Ana Maria Mendes Cerdeira
Erdal Cevher
Julie Champion
Judy Chan
Dong-Hoon Chang
Li-Chien Chang
Doungdaw Chantasart
Hassan Chaouk
Marie-Elise Chateau
Caroline Chemin
Lingyun Chen
Paonien Chen
Yung-Ming Chen
Ruth R. Cheng
Tsai Chia-Hui
Chia-Ming Chiang
Jason Chittenden
Hea-Young Cho
Seon-Haeng Cho
Kyung E. Choi
Young Kweon Choi
Shruti Chopra
Estelle Chouin
Keat Theng Chow
Tze-Wen Chung
Petr Chytil
Felisa Cilurzo
Yasemin Cirpanli
Andreas Clausen
Sasson Cohen
Stefania Conti
Donato Cosco
Paulo J. C. Costa
Abina Mary Crean
Andrew Crockett
Patrick J. Crowley
Sean Culbertson
Hana Danan
Ivana D'Angelo
Ann Daugherty
Nigel M. Davies
Patrick B. Deasy
Ismail Tuncer Degim
Zelihagul Degim
Bastiaan J. DeLeeuw
Cosme A. de Los Santos
Kurt de Meyer
Daniel D. Ditullio, Jr.
K. C. Donovan
Robert H. Douglas
Chidi C. Dozie
Sebastian Dreis
Lea Dseigaux
Susan S. D'Souza
Lisa C. Du Toit
Thomas Dean Dziubla
Gillian M. Eccleston
Markus Elfinger
Lidia Elfstrand
Mazen El-Hammadi
Homero Endara
Giora Enden
Sven Engstrom
Francisco Escorcia Rodriguez
Frank Everaerts
Julia Fahrmeir
Yi Ping Fang
Rain Fasching
Dimitris Fatouros
Keith Michael Faucher
Abdel A. Fawzy
Mikhail Feldstein
Kristina Ferderber
Eduardo Fernandez-Megia
Barrie C. Finnin
John G. Fletcher
Massimo Fresta
Doron I. Friedman
Michael Friedman
Jane C. Frimodig
Martin Funk
Acaturk Fusun
Songqi Gao
Grzegorz Zdzislaw Garbacz
Elisa Garbayo
Maria Garcia-Amo
Leire García Navarro
Marie Garinot
Jerome Gaucheron
Andrea Gazzaniga
Manish Ghimire
Bilal Ghosn
Dong-Hyun Go
Mike Goekbora
Tomer Gold
Riki Goldbart
Seth Goldblum
Nieves Gonzalez
Takeshi Goto
Michael Guenther
Jaime Guevera-Aguirre
Mark Gumbleton
Pardeep Gupta
Ibon Gutierro Aduriz
Walid Hachicha
Azita Haddadi
Eleonore Haltner-Ukomadu
Kyu Won Han
Muri Han
Pavan Handa
Sara J. Hanson
Helene Hardre
Katharina Harkamp
Kevin Harper
Debra Leigh Harris
Mark G. Hartell
John P. Harvey
Sophia Hatziantoniou
Oliver Hauser
Clare L. Heaysman
Toru Hibi
Herve Hillaireau
Keiji Hirota
Yamasaki Hiroyuki
Ken-ichiro Hiwatari
Gunther Hochhaus
Manfred Hof
Andrew Hoffman
Sonja Holler
Melisande Holzer
Harry Holzmueller
Soheila Honari
Jae-Sun Hong
Seokcheon Hong
Margit Hornof
Herbert Hoyer
Feixiong Hu
Ihor Huk
Man-Wook Hur
Pepi Hurtado-Lopez
Kang Hyun Suk
Svetlana Ibric
Rie Igarashi
Hendrikje Immig
Yuuki Ishida
Keiji Itaka
Fuminori Ito
Rajesh Jain
Anna-Maria Janner
Eugeen Jans
Je Kyo Jeong
Ok-Ja Jeong
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calendar of events

who…what…where…when

13th International Symposium on Recent Advances in Drug Delivery Systems
February 26-28, 2007
Little America Hotel
Salt Lake City, Utah, USA
www.drugdeliverysymposium.utah.edu

FDA Pharmaceutical Quality Initiatives – A Modern Risk-Based Approach
February 28-March 2, 2007
Bethesda North Marriott Hotel and Conference Center
Bethesda, Maryland, USA
www.aapspharmaceutica.com/FDAQualityInitiatives

SOT 46th Annual Meeting and ToxExpo
March 25-29, 2007
Charlotte Convention Center
Charlotte, North Carolina, USA
www.toxicology.org/ai/meet/am2007/index.asp

Pharmaceutical Sciences World Congress
April 22-25, 2007
Amsterdam, The Netherlands
www.fip.org/PSWC/index1.htm

34th Annual Meeting of the Controlled Release Society
July 7-11, 2007
Long Beach Convention Center
Long Beach, California, USA
www.controlledreleasesociety.org
ph: 651-454-7250

36th Annual Meeting of the American College of Clinical Pharmacology
September 9-11, 2007
The Palace Hotel
San Francisco, California, USA
www.ACCP1.org

35th Annual Meeting of the Controlled Release Society
July 12-16, 2008
Hilton New York
New York City, New York, USA
www.controlledreleasesociety.org
ph: 651-454-7250