

NEWSLETTER

Memoirs of an Iowa Farm Girl on Travel to Korea

GEOMATRIX® Oral Drug Delivery Systems

Spotlight: Eurand

Members Release: The Challenges of Today



Sunset at the Hangang River, Korea

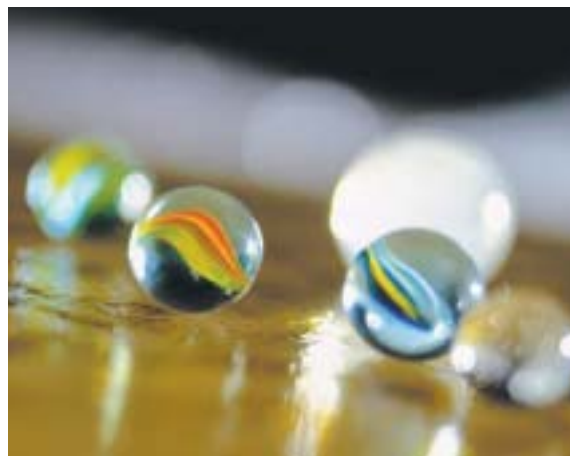


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Editors

David Friend & Bozena Michniak

Managing Editor

Rosealee M. Lee

Thanks to members of the Publications Newsletter Subcommittee for helping with this issue: Agis Kydonieus, Harlan Hall, and Mike Rathbone.

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

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Controlled Release Society
13355 Tenth Avenue North, Suite 108
Minneapolis, MN 55441-5554
+1(763)512-0909 telephone
+1(763)765-2329 facsimile
pstone@controlledrelease.org
rlee@controlledrelease.org

Contact member@controlledrelease.org regarding new or existing membership service or publication purchase issues.

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The new mission statement for the Controlled Release Society

Journal of Controlled Release Highlights

By David Friend

These highlights were taken from Volume 77, issues 1-2, of the Journal of Controlled Release. P-Glycoprotein is currently a fashionable topic in the pharmaceutical sciences. An article by Sawada and coworkers describes efforts to use monoclonal antibodies to P-glycoprotein (MRK-16) to reverse multidrug resistance. Their data suggest that the interaction between liposomes containing vincristine and multidrug resistant cells is increased by modification with MRK-16. From the gene delivery section of the journal, Guo and Lee report the use of folic acid to enhance the efficiency of gene delivery using polyethylenimine. An article by Krishnaiah et al. presents data on the potential of a guar gum-based colonic delivery system in the treatment of enteric nematodes (a common problem in some parts of the world). They investigated the drug mebendazole, useful in treating helminthiasis. •



England Leads the Focus on Diabetes

Jacqui Smith, England's Health Minister has published new national standards to improve care for the approximately 1.3 million people with diabetes across the country. The Standards form the first part of the new Diabetes National Service Framework (NSF). The final part of the Diabetes NSF - the Delivery Strategy - will be published next summer to be implemented in 2003. The delivery strategy will include the early milestones, service models, performance indicators, and details of local implementation and national support for local action.

Diabetes, the center of many CRS member initiatives, is the topic of a CRS 2002 Workshop entitled *Advances in Diabetes Management*, chaired by Dr. Lisbeth Illum. Diabetes is a serious, complex condition that can increase the risk of developing other illnesses, as well as resulting in potentially debilitating complications. Diabetes is an important health issue in terms of morbidity and resource use (affecting around 1.3 million people in England and consuming up to 10% of hospital resources). If not properly managed, diabetes can result in a range of long term complications such as heart disease, stroke, kidney disease, blindness, and foot problems that may lead to amputation.

The new NSF standards for diabetes services contains 12 standards in nine areas: prevention of type 2 diabetes, identification of people with diabetes, empowering children, young people and adults with diabetes, clinical care of adults with diabetes, clinical care of children and young people with diabetes, including the transition from specialist pediatric diabetes services to specialist adult diabetes services, management of diabetic emergencies, care of people with diabetes during admission to hospital, diabetes and pregnancy, and detection and management of long-term complications of diabetes and the provision of integrated health and social care.

Jacqui Smith said, "This blueprint of care heralds a new beginning for the many thousands of people with diabetes in England. There are currently considerable variations around the country in the organization and quality of diabetes services. Our new NSF standards will make sure that people receive high-quality care at the right time and in the right place. The Diabetes NSF is the first to focus on a chronic disease and clearly sets out the partnerships that must be at the centre of modern diabetes services; partnerships between people with diabetes and professionals; between primary care and specialist services; and between doctors, nurses and allied health professionals. These partnerships are the key to delivering the NSF to improve the care received by the many thousands of people with diabetes."

A new Implementation Group is being set up to develop the delivery strategy along with the NHS and other interested parties. The Group will be chaired jointly by Dr Sheila Adam, Director of Policy at the Department of Health and Professor Mike Pringle.

CRS members working in the area of diabetes will take note of a recent statement by Paul Streets, Chief Executive of Diabetes UK, who said, "The Standards published today offer a vision of diabetes care to which we can aspire. The really tough job however is still to be done. That is finding a way to turn the vision into reality. We look forward to working with the Department of Health to make these Standards truly work for people with diabetes."

As other countries adopt such targeted initiatives, the work of CRS members will become even more in focus. For information about the *Advances in Diabetes Management Workshop* that will be held in Seoul, Korea on July 20 and 21, 2002, please visit www.controlledrelease.org. •

scientifically speaking

GEOMATRIX® Oral Drug Delivery Systems

By Guy Vergnault

Controlled release technology has experienced increased interest during the last decade. Sustained release of drugs increases the time a drug resides in the therapeutic zone leading to optimum efficacy without reaching toxicity levels. Furthermore, as dosing is generally reduced to once-a-day, improved patient compliance is achieved.

Originally developed in the late 1980's, GEOMATRIX® tablets are orally-administered, multi-layer tablets, based on a swelling drug-containing hydrophilic matrix. The drug release rate is controlled by the modulation of the surface area available for drug diffusion and by hydrophilic polymers used in the matrix and support platform formulas.

Principle of GEOMATRIX® Systems Hydrophilic matrix vs. GEOMATRIX®

When a traditional matrix tablet formulation is immersed in the dissolution medium or in biological fluids, solvent penetrates into the dosage form. Before the polymer(s) begin to swell and control the release rate of the drug, a significant portion of the drug, located close to the surface, can dissolve leading to what is known as the burst effect. Then, the polymer swells and gels, limiting more and more strongly the drug release rate, providing an overall release profile which is proportional to the square root of the time.

In the GEOMATRIX® concept, the surface available for drug release is limited by

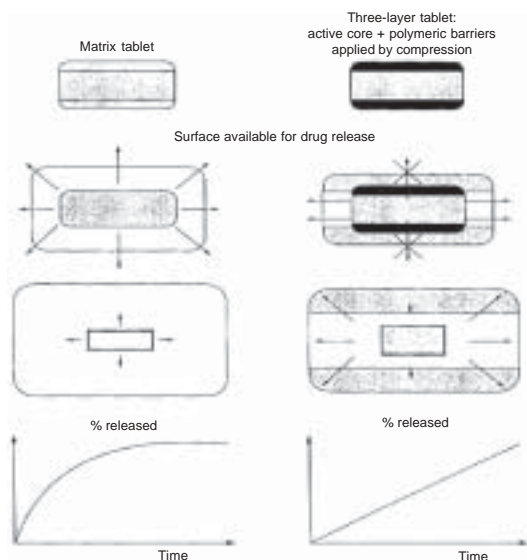


Figure 1. Comparison of monolithic and multilayer tablets for drug controlled release.

placebo support platforms (non-drug containing excipients) which are almost impermeable at t_0 and therefore, sudden and rapid release of the drug cannot occur (no burst effect). Later on, the decrease of release rate from the active layer is compensated by diffusion through the support platform. The final profile obtained is close to a zero order one (see Figure 1).

GEOMATRIX® system formulation

The GEOMATRIX® technology is based on the use of different types (chemical substitution) and different grades (MW, viscosity) of hydroxypropyl methylcellulose (HPMC) polymers incorporated at various concentrations in the matrix and in the support platform(s). Polymer/filler ratio is one of the main parameters controlling the drug release rate.

Although a wide range of hydrophilic polymers can be used, HPMC USP type 2208 and HPMC USP type 2910 are the polymers of choice for this technology. The swelling and dissolution behaviors are directly linked to the chemical structure and molecular weight (viscosity) of these compounds.

Among the marketed grades of HPMC, the 2208 type is characterized by a low level of methoxy substitutions and a high level of hydroxypropoxyl substitution confers upon them high swelling properties and low solubilization rate. This type is particularly adapted for formulation of highly soluble drugs.

On the other hand, the 2910 type, which contains more methoxy substitutions and slightly less hydroxypropoxyl substitutions on the cellulose skeleton, is characterised by a less swellable behaviour and dissolves more rapidly than the 2208 type giving therefore a quick erosion of the layer. This type of HPMC is well suited for the formulation of sparingly soluble drugs. All ingredients used in GEOMATRIX®

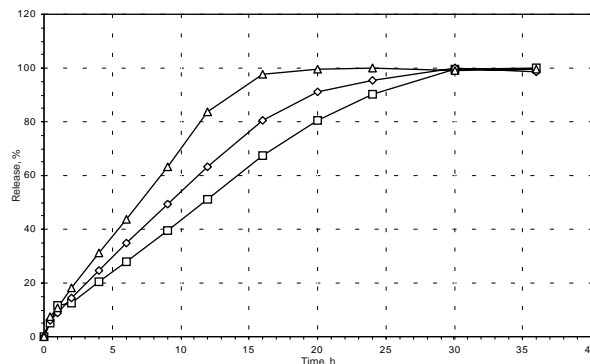


Figure 2. GEOMATRIX® tri-layer tablets. Various support platform compositions.

formulations are with Gras status and BSE free.

Applications of GEOMATRIX® systems

From a general point of view, GEOMATRIX® technology can improve efficacy and enhance compliance by permitting less frequent dosing, by reducing side effects, and by releasing drug at specific locations in the body.

Dual control release

By comparison with a regular monolithic hydrophilic matrix, the GEOMATRIX® technology is more versatile. GEOMATRIX® offers the possibility of tuning the drug release profile through formula changes of the active layer and the support platform(s) as well as through various layer arrangements. Different types and grades (MW) of HPMC can be used for the formulation of this drug delivery system (see Figure 2 and section 1.2).

Various layer arrangements available (bi, tri-layer, one, two, three, four faces coated tablets) allow many different release kinetics (see section 0). Furthermore, drugs can be combined with other active substances to improve effectiveness and be released at different rates.

Thanks to the use of various types of HPMC, highly soluble drugs as well as poorly soluble drugs can be released in a controlled manner. The multilayer-tablets allow very slow sustained release even with high doses of highly water soluble drugs. A broad range of dosage strengths can be formulated as well.

(continued on page 4)

The release kinetics obtained with the GEOMATRIX® technology can be shifted toward zero order rate. As opposed to monolithic hydrophilic matrix, the surface available for active release can be increased during release to counterbalance the increase of the diffusion path-length of the active due to the swelling of the core.

Robust formulation and manufacturing process

Robust formulation

GEOMATRIX® tablets formulation was proven to yield In Vitro Profiles independent of pH variations and paddle speed (see Figure 4).

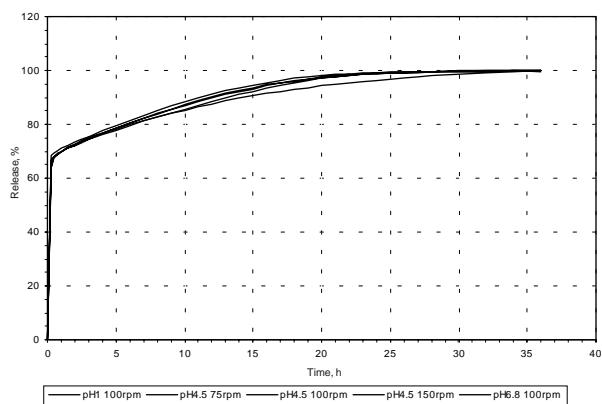


Figure 4. Quick / Slow IVPs of tri-layer active tablets under various pH and paddle speed dissolution conditions.

Proven ease of manufacturing

Manufacturing processes and equipment used are based on well-known tablet technology expertise and scale up from prototype batches to full scale production gives reliable and repeatable In Vitro Release Profiles as illustrated in Figure 5.

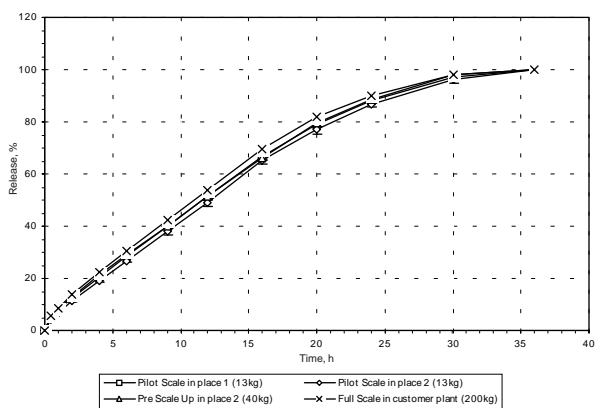


Figure 5. IVPs of prototype, pilot scale, pre scale up, and full scale batches.

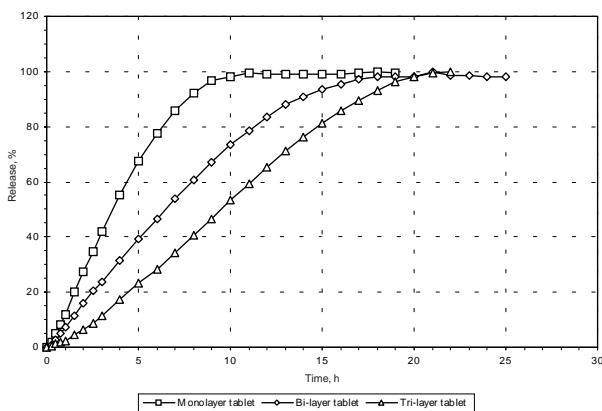


Figure 3. Comparison of mono, bi and tri-layer tablets.

In vivo performance

In vivo reproducibility

Pharmacokinetic studies showed a good reproducibility even when two active grades were compared (see Figure 6). Furthermore, dose proportionality between a 0.75 mg and a 3 mg dosage strength was measured as shown in Figure 7.

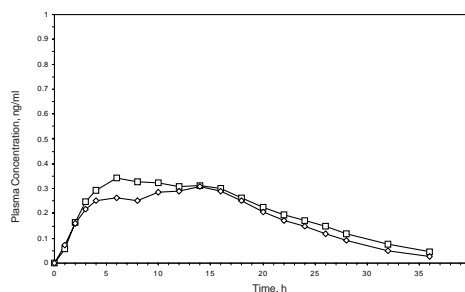
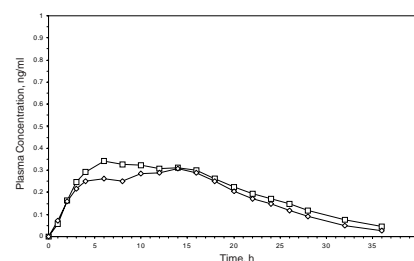


Figure 6. Comparison of Plasma concentration - Time curves for two different grades of the same active formulated with Geomatrix technology. (m) Fine active, (l) Coarse active.

Figure 7. Comparison of Plasma concentration - Time curves for two dosage strengths of the same active formulated with Geomatrix technology. Data are dose-normalised. (m) 0.75mg dosage strength, (l) 3mg dosage strength readjusted to a 0.75mg dose.



GEOMATRIX® and food effect

Limited exposure of the drug to biological fluids reduces impact of meal on drug bioavailability. The results of the pharmacokinetic study represented in Figure 8 gave Fed / Fasted ratios for C_{max} = 0.95 and AUC^* = 0.98. Tablets disintegrate completely in the patient's digestive system, leave no residue and yield 100% of the active drug released.

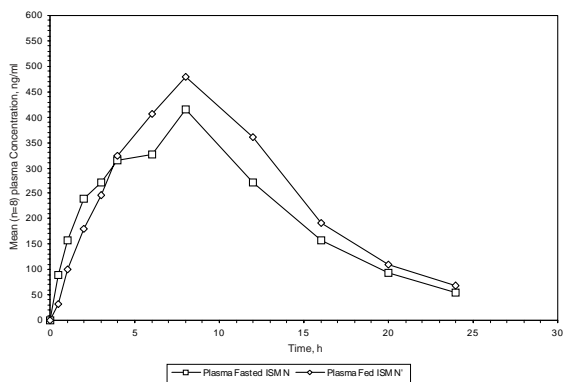


Figure 8. Mean plasma ISMN concentration-time curves

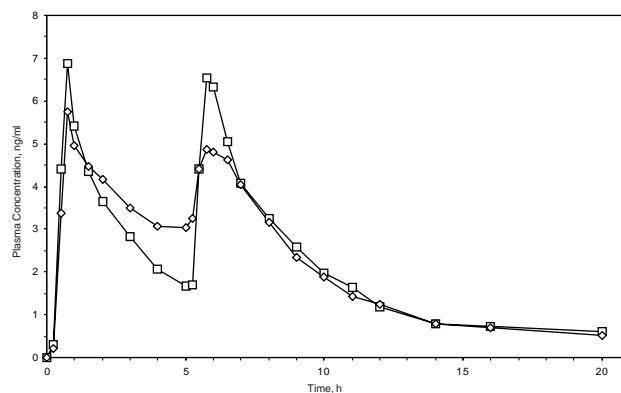
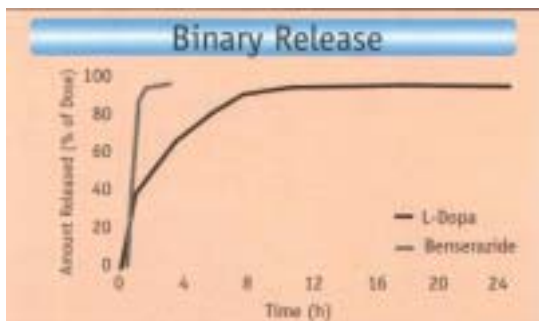


Figure 9. Comparison of one dose of multipulse technology tablet(\diamond) and two successive commercial tablets intakes (\square).

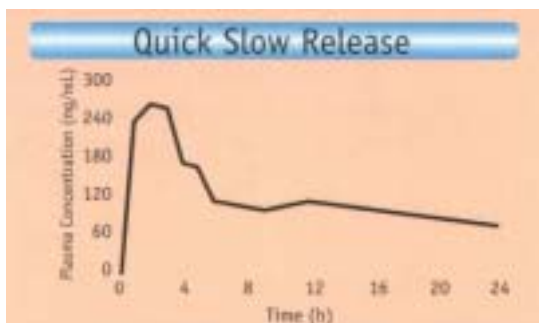
Geometry and release pattern

The classical geometry used comprising a core of HPMC containing the active drug(s) enclosed in one or two barrier layers gives a zero order release rate of the drug.

The Binary Release system is used to provide the controlled release of two different drugs in a single formulation. The drugs may be released at different rates and times. This system is designed for drugs that work best in combination. SkyePharma has one Binary Release formulation that was approved and launched in Switzerland in 1997, Madopar DR (Roche) which contains L-Dopa and benserazide.



The Quick Slow release provides a quick burst of drug release followed by a constant rate of release over a defined period of time. SkyePharma has one approved Quick Slow Release formulation currently on the market, Diclofenac-ratiopharm uno in Germany.



The Positioned Release system is designed to deliver the tablet to a predetermined position in the digestive system before it begins to release the active drug compounds. Xatral XL, which uses this technology, is currently marketed in Europe and has been filed in 2000 for approval in USA.

The Delayed Release system provides a predetermined time lag before it begins releasing drug molecules.

The Multi Pulse system provides an initial quick burst of drug release followed by a second burst of drug release after a period of no release. SkyePharma has a Multi Pulse Release formulation currently in Phase II, using Methylphenidate HCl as active ingredient.

SkyePharma client product pipeline using the GEOMATRIX® technology

SkyePharma Client Product Pipeline - Oral								
Client	Drug	Clinical Feasibility	Ph.I	Ph.II	Ph.III	Filed	Approved	Launched
Ratiopharm	Diclofenac	→	→	→	→	→	→	→
Watson	Diclofenac	→	→	→	→	→	→	→
Roche	Madopar DR	→	→	→	→	→	→	→
Rundpharma	Nifedipine	→	→	→	→	→	→	→
Sandoz/Synthelabo	Xatral XL	→	→	→	→	→	→	→
Sandoz	Parl EX	→	→	→	→	→	→	→
SkyePharma	Risperidone	→	→	→	→	→	→	→
SkyePharma	Perindopril	→	→	→	→	→	→	→
SkyePharma	ISMN	→	→	→	→	→	→	→
Abbott	Zincron	→	→	→	→	→	→	→
Unfiled	Unfiled	→	→	→	→	→	→	→
SkyePharma	Methylphenidate	→	→	→	→	→	→	→
Merck KGaA	Unfiled	→	→	→	→	→	→	→
Pfizer	Unfiled	→	→	→	→	→	→	→
Synthelabo	Propyl	→	→	→	→	→	→	→

Patents portfolio

The GEOMATRIX® technology is covered by a comprehensive and growing family of U.S. and worldwide patents portfolio. •

University of California, Santa Barbara Biomaterials, Biomolecular Materials, Bioengineering

The University of California, Santa Barbara seeks to hire highly creative, innovative and productive individuals for multiple new faculty openings at the junior and senior levels in fields related to Biomaterials, Biomolecular Materials and Bioengineering. UCSB is broadening the interfaces among biology, physical science and engineering and is developing a vigorous interdisciplinary and intercollegiate Program in BioMolecular Science and Engineering (BMSE). This Program builds on and is an integral part of UCSB's unique environment for multidisciplinary collaboration, and its recognized strengths in Materials, Chemistry and Biochemistry, Chemical, Mechanical, Electrical and Computer Engineering, Computer Science, Physics, Molecular and Cellular Biology and Device and Nanosystems Science and Technology. UCSB's core strengths are supported and enhanced by a collection of interdisciplinary research and education centers, including the California NanoSystems Institute, the NSF-sponsored Materials Research Laboratory and Institute for Theoretical Physics, the Neuroscience Research Institute, the Marine Science Institute and the Marine Biotechnology Center. The facilities available to carry out research in these fields at UCSB are superb. The positions advertised here are in addition to positions in related areas being advertised by the UCSB Department of Chemistry, though there is coordination between the searches. Suitably qualified candidates are welcome to apply to both calls.

Research and new instructional initiatives in biomaterials, biomolecular materials and bioengineering are being formulated to build on and enhance current associated strengths. The new faculty appointments may be in BMSE, or in the departments mentioned above, or in some combination of these administrative units, in order to optimize the effectiveness of each hire. Applications from individuals from all disciplinary backgrounds with interests in the areas of Biomaterials, Biomolecular Materials and Bioengineering are encouraged. Specific areas of interest include, but are not limited to: biomolecular materials, motors, machines and electronics, bio-sensors and other bio-devices, biosynthesis and genetic engineering of materials, bio-nanotechnology, metabolic engineering and bioinformatics. Individuals appointed will come in with the opportunity for and expectation of active participation in shaping future hiring and other developments, commensurate with the individual's background and experience.

Applications for these positions are open until they are filled. Consideration of candidates will begin immediately; those received by January 1, 2002 will be considered thoroughly for the first round of interviews. Please address all applications, which should contain a letter briefly outlining career plans, a statement of research and teaching interests, curriculum vitae and names and contact information on 3 – 5 references, or have letters of reference sent directly, to:

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An EO/AA employer.

spotlight: Eurand

By Lisa Fern

With nearly 350 drug delivery companies in the world today, the drug delivery industry has become an intensely competitive marketplace. How does a company distinguish itself from the pack?

In this issue, we spotlight Eurand, a multinational company specializing in oral drug delivery.

A mere two years after becoming independent from American Home Products, Eurand has become one of the world's leading drug delivery companies. Since 1999, the company has almost doubled its revenues, signed more than 20 development agreements with major pharmaceutical companies, successfully completed two acquisitions, received an FDA approval for an ADHD treatment, and launched and validated a groundbreaking solubility enhancement technology.

With a global infrastructure, diverse technology platform, and a strategic eye toward the future, Eurand believes that it has positioned itself to maintain its leadership position for years to come.

Leading the company is a management team with over 100 years of pharmaceutical experience in multinational corporations. In the past two years the company has gone from a 300-person organization to a 500-person organization and management is confident that the company has in place the team of people it needs to ensure continued success.

Eurand was founded in the 1960s. The company changed hands a number of times in the 70s and became part of American Home Products in 1989, where it stayed for the next ten years. In April of 1999, with the help of Warburg Pincus, Eurand's management, led by CEO Gearoid Faherty, bought the company from American Home products. With offices, research, and manufacturing facilities in Milan, Paris, Ohio, and New York, Eurand is strategically located to offer its customers fully integrated drug development programs.

Eurand's diverse technology platform has

helped to distinguish it from other drug delivery companies. With 11 proprietary technologies, Eurand has one of the broadest technology platforms in the industry. All of Eurand's technologies are patent protected and the company continues to file for new patents on its established technologies and on technology developments. With so much competition, patent protection is fundamental to maintaining a strong position in the industry. Protecting their technologies is essential to their success.

Of these technologies, Eurand's biggest drivers are its controlled release, solubility enhancement, and taste masking technology platforms. The company has six different customized release technologies. In addition to traditional customized release offerings, Eurand's technologies provide a range of benefits including higher drug loading, more reproducible release rate control, biphasic release, gastro protection, and improved drug stability.

One of the most exciting opportunities for the company comes from its solubility enhancement technology platform. Given the fact that more than 40% of all new chemical entities are poorly soluble in water and therefore, poorly absorbed by the body, the company believes that solubility enhancement is a major growth driver for the drug delivery industry. Although pharmaceutical companies have been faced with this problem for years, overcoming this challenge has traditionally proved difficult and many companies have been forced to abandon development of drugs that exhibited this problem. With the recent launch of the company's newest technology, Biorise, Eurand is one of the few companies that has been able to offer a solution to this problem. Biorise is a validated solubility enhancement technology that improves the onset of action and reduces plasma level variability of drug substances. Over the past two years, Eurand has generated significant business based on this technology and already has a product on the market that utilizes this technology. In fact, the response to Biorise has been so positive that the company has recently completed construction of new laboratory spaces in

Europe and in the United States to meet the demand for this technology. Additionally, the company has already begun developing the second generation of Biorise and is developing another solubility enhancement technology that enables the oral delivery of macromolecules.

Eurand's taste masking technologies have become a mainstay for the company and continue to generate significant business. They offer three taste masking technologies, all of which have been used in a wide range of drugs currently on the market. These technologies have made the company a world leader in microencapsulation and offer customers significant marketing benefits such as more convenient dosage forms for pediatric and geriatric populations, cost effective manufacturing, and improved patient compliance.

While Eurand believes that their technology platform speaks for itself and will continue to drive the success of the company, Gearoid Faherty has a multi-faceted approach to driving the growth of the business. At the core of this strategy is a move to continuously develop new drug delivery technologies and products that address the needs of the pharmaceutical industry and patient population. Eurand believes in technical innovation and the company has one of the strongest R&D teams in the industry.

In addition, Eurand views itself as an industry consolidator. The company continues to monitor the industry for companies and university institutions working on new drug delivery technologies that can enhance the companies product offerings. Since 1999, the company has acquired and successfully integrated Vectorpharma and Pharmatech. In looking for acquisition targets, the company searches for opportunities with long term potential such as technologies that anticipate and address drug delivery problems its customers will face five years from now. Given Eurand's established and growing revenue base, the company also keeps its eye open for companies that are

(continued on page 17)

patentwatch: Flavour Encapsulation Technology

By Jack J. Burger

In the first 3 quarters of 2001, 246 patents were found via the Derwent World Patent Index in the area of flavour encapsulation technologies and the application of encapsulated flavours in food products. The technologies range from traditional spray drying to sophisticated methods like multiple coating with different wall materials.

SPRAY DRYING

Among the different encapsulation technologies, spray drying is the most frequently used method to convert liquid flavours into free flowing powders with certain properties. This is reflected by the large number of patents which were published in this period. **Quest** (WO 200135764) issued a patent on the preparation of a moisture and oxygen stable spray dried composition with the amorphous carbohydrate matrix consisting of a high molecular weight film forming agent (e.g gum acacia), maltodextrin, and sucrose. Oxidation of sensitive flavours is prevented by forming a glassy state. Using a multi-stage spray drying unit, **Givaudan-Roure** (EP 1064856) claims the preparation of free-flowing microparticles of 100 to 400 microns in diameter containing active ingredients, with the carrier matrix also in the glassy state. In two patents (US 6251193 and US 6251463), **Int. Flavors & Fragrances** describe the benefits of spray-dried sugarcane leaf essence for the taste masking of the bitter aftertaste of products with disagreeable chalky taste such as calcium fortified supplements. **Takasago** claims the

use of paratinose and/or raffinose in the carrier matrix to produce flavouring powders with excellent stably suspended aroma components for a long period of time (JP 2001186858). In a second patent from **Takasago** (JP 2001152179), spray-dried flavours are claimed which have been made with e.g. lecithin and high pressure homogenisation to make flavour oil droplets of less than 1 micron. The powders thus produced would have sustainable flavour for a long period of time. Excellent time-dependent flavour stability after spray drying is also claimed by **Ogawa Koryo** (JP 2001064667). This company is using a mixture of saccharides and a desalting emulsifier such as gum arabic as the carrier matrix. In US 6159522, **Kraft Foods** describes the application of a spacing agent and a suspending agent to reduce undesirable build-up of material on the sides of the mixing tank thereby improving the throughput and yield of the spray drying process to produce a clouding agent having increased opacity due to the presence of titanium oxide particles. Spray drying has further been claimed for making powders containing viable microorganisms (**INRA**, WO 200144440) and for the recovery of aroma components from fresh coffee grounds (**Nestle**, EP 1078575). Improvement of spray dry equipment is an ongoing process. **NIRO** (WO 200133971) claims a drying process for food, especially baby food, in which the food is atomized high and centrally in the drying chamber with blunt conical base. Drying gas at 160–400 °C is passed downwardly. In the bottom and/or a lower extension, a fluidized bed is maintained at 45–80 °C, with an upward drying gas flow, which also classifies and agglomerates particles.

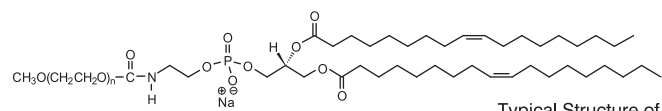
EXTRUSION

Extrusion has often been claimed as an alternate process to spray drying for making particles with a long shelf life, especially for flavours prone to oxidation such as citrus flavourings. **Haarmann & Reimer** (EP 1099385) claim a continuous or discontinuous process to manufacture carbohydrate-encapsulated aroma particles which have been obtained by emulsifying an aroma in a carbohydrate melt and which are treated with an inert gas. The benefits of the H&R process are that the various steps are integrated, that the product has no surface oil, and that the product has a high glass transition temperature. **Firmenich** (WO 200117372) filed a patent on the shaping of a flavour or fragrance delivery system in a granular form involving making a mixture of a continuous phase carrier containing volatile compounds having a low water content, heating the mixture to form a molten mass and extruding followed by immediately chopping the molten mass to obtain a product having a glass transition temperature same as that of the continuous phase carrier. The benefit of the Firmenich process is the production of particles with a narrow size distribution and uniform size in only one step. Under low shear and low temperature conditions, **General Mills** (WO 200125414) encapsulates an active compound in a matrix via mixing plasticizable and non-plasticizable matrix

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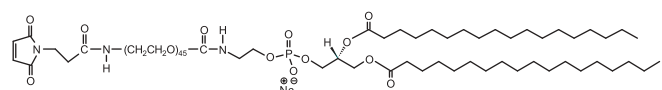
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materials, active compound, and a component for controlling the rate of the release of the encapsulated active.

COATING AND SPRAY CHILLING

Next to spray drying and extrusion, coating and spray chilling are frequently used to manufacture flavour delivery systems with controllable release characteristics. For example, **Kraft Foods** (EP 1121859) claims a cereal-based product comprising a dough containing an aroma enhancing component and a crust enhancing component. The aroma-enhancing component is obtained by micro-encapsulation of aroma components into a hard fat with a melting point of 38-82 °C. In WO 200115545, **Wrigley** coats cores of comestible materials, such as sugarless chewing gum having a hard coating, with hydrogenated isomaltulose in a reduced amount of time, yet having a high quality appearance. The coating is obtained by a number of repetitive steps.

OTHER TECHNOLOGIES

There are a number of other, lesser used technologies to encapsulate flavours or to produce liquid flavour delivery systems. For example, the use of **cyclodextrin** to form inclusion complexes was patented by Cerestar (WO 200148024) and Nestle (NZ 506241). In the Nestle patent, a simple, wet process to form the complexes is claimed while the Cerestar patent claims a wet process in which an emulsifying agent is used during the complex formation. **Chitosan** microcapsules for food and other applications are described by Lab Oligocaps (WO 200134289) and in three patents from Primacare (EP 1064913, EP1077060 and EP 1101527). In the patent of Lab Oligocaps, a complex-forming catalyst is incorporated which is forming a complex with the chitosan membrane. In the Primacare patents, microcapsules are formed by dropping (a) a matrix comprising a gel-former, an anionic polymer, and an active component into (b) an aqueous chitosan solution. The gel-forming agents are heat-gelling natural heteropolysaccharides, proteins, or anionic polymers. Together with chitosan, microparticles are formed which are significantly more stable in the presence of surfactants. Although applicable in food, the primary application area is cosmetics.

Nippon describes in two patents the formation of microcapsules with entrapped flavour containing polar substances for seasonings and food stuffs via the classic **coacervation** process with gelatin (JP 2001046010 and JP 2001113158). The novelty of the two Nippon patents is the use of lecithin to form a W/O emulsion which is added to the aqueous gelatin solution and, secondly, coating of the dried microcapsules with a material containing bivalent or trivalent aliphatic alcohol or sugar alcohol.

Other lesser used technologies for the encapsulation of flavours for food products are the use of **gelatin** for the encapsulation of honey (Immuno Lab Ltd., NZ 332872), **silica** and saccharide for plating of fragrances or flavours via fluid bed, extrusion, and grinding (Int. Flavors & Fragrances, US 6235274), **W/O/W double emulsions** for the encapsulation of polar actives in the internal aqueous phase (CNRS, WO 200121297) and **liposomes** made with hydrogenated lecithin for essential oil encapsulation as aroma additive (Sonnenberg, DE 19922193).●

Now that many of the genomes of organisms associated with the leading causes of infectious diseases have been sequenced, the next major challenge is to determine the biological function of genes and the proteins they produce. This is a challenge for both biology and technology. But, functional genomics resources for the production and utilization of DNA arrays and genotyping activities remain prohibitively expensive for many researchers to set up or access.

To meet this challenge, the National Institute of Allergy and Infectious Diseases (NIAID) has awarded a \$25 million/five year contract to The Institute for Genomic Research (TIGR) to establish a center for functional genomics that will be an invaluable resource to the scientific community.

“TIGR is extremely pleased to receive this contract from NIAID. It will allow us to continue our work at the forefront of genomics while also providing a unique service to the scientific community,” says TIGR president Claire M. Fraser, Ph.D. “Because of the collaborative nature of the partnership the new Center will have with its clients, we believe that novel ideas will be generated to help us reach our goal of finding new research tools as well as practical solutions to microbial diseases.”

The Pathogen Functional Genomics Resource Center (PFGRC) at TIGR will centralize production, access, and training in the use of a variety of resources for exploring the roles of genes and gene products (including proteins) in a significant number of microbes known to cause disease. It will be a multidisciplinary laboratory, resource, and teaching facility. The PFGRC at TIGR will provide scientists with centralized resources necessary to conduct functional genomics studies on a variety of pathogens and vectors for which genomic sequence information is currently, or will soon be, available. The near-term goals of the PFGRC are to provide researchers with microarray and genotyping technology, along with access to clone sets, genomic DNA, and type strains.

TIGR’s strong bioinformatics capacity will provide the resources for data analysis and storage. The new PFGRC will develop a Center-Client web-based interface that will make it easy for scientists to access and acquire resources.

These new technologies in functional genomics hold great promise for identifying the roles played by the thousands of novel but as yet uncharacterized genes that have been revealed by genome sequencing, and for unraveling the complex relationships among genes. While such research will dramatically increase our understanding of the basic biology of pathogenic organisms, it should also accelerate the identification of new diagnostic markers of infectious disease, new therapeutic targets, and new vaccine candidates. The importance of such anticipated advances cannot be overemphasized. Infectious and parasitic diseases are the second leading cause of death worldwide and increasing levels of antibiotic resistance are posing ever-increasing threats to public health. ●

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From the President: A world and its people on the mend

By Kinam Park

Fire Fighters and GI Joes

On behalf of all scientists and staff of the Controlled Release Society, I would like to send our thanks to the fire fighters in New York who showed the world the true meaning of courage and sacrifice. I would also like to express our appreciation to the American soldiers who are serving in cold mountains and valleys for keeping the peace for us all. I served in the army as a lieutenant, once upon a time, and I still vividly remember the difficulty and coldness while I was crossing the mountain with my platoon on a windy winter night. That was without any danger of facing enemies with weapons. Our GI Joes in Afghanistan are doing their job at the risk of their lives. We go on with our daily routine at the cost of their sacrifice.

Speaking of our own Joe, I am very happy to inform you that Joe Robinson is recovering very well after his kidney transplantation surgery in October. As Bill Moyer described in his book *Healing and the Mind*, the mind-body connection is important in recovery in a way that has no precedent. Joe's recovery has been extraordinary, and is in part, due to control of his body by his mind. Joe has been very determined to get back to his normal activities, including traveling all over the world. His first overseas trip will be to attend the CRS annual meeting in Seoul in July. Joe is very upbeat about the fact that he will see all of you again soon.

Alternative Medicine

The control of the body by the mind has been one of the central themes in Oriental medicine. Acupuncture, herbs, meditation, pray, and energy healing, collectively known as alternative medicine in the Western World, have become not so alternative anymore. For example, acupuncture has been accepted and endorsed by the National Institutes of Health as an alternative and complementary

treatment for a miscellaneous host of ailments. Acupuncture relieved the pain on my knees that resulted from training during my military days, when even repeated X-ray tests could not find any problems. The CRS meeting in Seoul will offer an opportunity to learn and feel the alternative medicine. You may even try acupuncture yourself to stimulate or redirect the flow of your life force, known as qi in Chinese medicine, to a certain part of the body of your choice. This summer I plan to redirect the flow of qi to my arms so that my golf swing becomes as powerful as Tiger Wood's. I would probably not try to redirect qi to my brain since there is no channel going to my brain in the first place.

Joe and Allan

Of the friends that I know, Joe Robinson and Allan Hoffman may be the two Americans who have visited Korea more often than anybody else, including me. Allan has a Korean nickname, "Alby Baek." This is because every time he leaves Korea for heading back to his Seattle nest, he always says "I'll be back." Indeed, he has been back several times a year for the last 20 years or more. Joe has been saying the same words even before his surgery, and I am very much looking forward to seeing him again in Korea. Korea offers unique experiences for all visitors. There will be no problem for any visitors with transportation, food, hotel, and communication. Everybody speaks English, and all signs are written in English also. The country that hosted the Olympics in 1988 and that will host World Cup Soccer Games in 2002 will surely be ready for our CRS visitors. If you enjoy foods, try Korean barbecue with a glass of Korean traditional wine. If you enjoy shopping, go to Itaewon to buy anything that you have wanted to buy but didn't because it was not on 90% sale. If you enjoy history, visit several palaces hidden in the middle of the city.

(continued on page 20)

Pharmaceutical Co-Promotions: Managed Partnerships Prove Profitable

As the world's leading pharmaceutical companies increasingly pair off to co-market new products, partnership management tactics become vital to joint venture success. According to a study from benchmarking leader Best Practices, LLC, the most lucrative relationships involve formal initiatives designed to cultivate teamwork and cooperation between allied organizations.

The study, "Best Practices in Pharmaceutical Alliances and Co-Promotions," reveals that co-promotions supported by effective teamwork increase sales across entire product portfolios. Examples of the report's best practices include the following:

- In one partnership, two leading companies set up a unique team that was

solely responsible for co-promotion activities. With this single entity developing strategy, issuing directives and delivering incentives, employees on both sides of the alliance quickly overcame the competitive mind-set that pervades the pharmaceutical industry.

- One district sales manager required his reps to share calendars and call schedules with their partners. After this move, his district had the highest market share in the country for the co-promoted product. "Reps should always have the written schedules of their co-promotion partners to ensure field coordination," he observed.

The report explores the winning strategies and practices of 26 successful strategic alliances, including partnerships struck by the pharmaceutical industry's leading

companies. Through extensive interviews with top-level pharmaceutical executives, project analysts identified the key drivers of successful co-promotions.

"As companies look for new, innovative ways to drive profitability, the development of win-win relationships becomes increasingly important," observes Best Practices, LLC CEO Chris Bogan. "Companies that understand how to build strong alliances will gain a great deal — and by this I mean billions of dollars — through well-managed co-promotions."

A report summary of "Best Practices in Pharmaceutical Alliances and Co-Promotions" is available at <http://www.Benchmarking Reports.com/pr/sm117.htm>.

members release: The Challenges of Today

By Rosealee Lee



In a recent poll members were asked to comment on the challenges they face in the performance of their position and in professional development efforts.

Results of this poll show a clear call to our society and its members to “pump up the name value of our technology”. One member summed up the status very well by responding, “We need to better highlight, even advertise practical and marketable successes of controlled release technologies.” Members aptly pointed out that creating a more visible focus will enhance funding opportunities. The CRS Board of Directors recognizes this as an opportunity for the future, and member comments like these have helped to ramp up strategic plans for CRS to address these issues.

Keeping up with technology is another challenge shared by controlled release and delivery researchers. One respondent summarized our community well by stating, “The single biggest challenge I face is finding out about which technologies might have broader application and finding collaborators interested in adapting the technologies to other industrial applications.”

Also on the list were challenges such as meeting development schedules, finding qualified employees, negotiating agreements, a lack of support from management in what was termed “the eternal struggle between management and technology”, and increasing demands to improve teaching and research performance.

Professional development challenges focused on keeping up with technological and biological advances and sharing information with other members of the community. Time and expense budgets have had a diminishing effect on the number of conferences that CRS members can attend and members desire alternative educational opportunities that address the diverse applications of controlled release and delivery. Networking was noted as an ongoing challenge. (Thanks to those of you who commented that the new Peer to Peer Network has met the network challenge.) •



Additional Cancer Targets Delivered by Exelixis to Protein Design Labs

Exelixis, Inc. delivered five additional cancer antibody targets to Protein Design Labs, Inc. (PDL) in the companies' ongoing oncology collaboration. The collaboration, signed in May 2001, joins Exelixis' expertise in target identification and validation and PDL's proficiency in antibody clinical development and manufacturing to create humanized antibodies for the diagnosis, prevention and treatment of cancer. The targets delivered to and accepted by PDL have met a number of stringent criteria that Exelixis applies to all of its targets prior to initiating drug discovery. Each of the targets has been shown to modulate a cancer-related cell growth pathway in a model organism, has been analyzed for expression in a variety of normal and tumor tissues, and has met defined intellectual property criteria. Exelixis has the right to co-fund and co-develop antibodies resulting from the collaboration. For antibody products developed by PDL that Exelixis elects not to co-develop, Exelixis will be entitled to specified milestone payments and royalty payments on any product sales.

AnorMED Announces AstraZeneca's Intention to Return All ZD0473 Development Rights

AnorMED Inc. states that AstraZeneca has given notice of its intention to discontinue its development of ZD0473 and return all rights for the product candidate to AnorMED. Results from clinical studies, specifically in ovarian and lung cancer patients who have previously failed a platinum based therapy, indicate that ZD0473 does not meet the differentiated profile required by AstraZeneca, particularly in overcoming platinum resistance. Emerging data from ongoing Phase I and Phase II clinical studies in a variety of tumors continue to support the conclusion that ZD0473 is an active drug with a manageable toxicity profile.

AnorMED's plans for ZD0473 will proceed once the transfer of clinical data is completed and following consultation with a clinical advisory board. In conjunction with relevant market analyses, AnorMED will be evaluating the development options for ZD0473 as an intravenous and oral formulation in order to maximize partnering opportunities.

"While AstraZeneca's decision not to pursue ZD0473 is disappointing for AnorMED, it is important to note that it is only one of a number of product candidates in AnorMED's pipeline, that also includes AMD-3100 for stem cell transplantation and Foznol, which is licensed to Shire Pharmaceuticals Group plc, among others. Since the announcement in August regarding AstraZeneca's decision to re-assess the ZD0473 development program we have been operating under an updated business strategy to account for its possible return and future development

while remaining focused on the work we have been conducting for the past three years. Under this strategy, the bulk of our human and financial resources will continue to be invested into the AMD-3100 clinical program and the development of new oral chemokine inhibitors for inflammation, cancer as well as HIV. Over the next twelve months these product candidates will have greater visibility as we move them into further clinical development and publish new data. We believe these products have the most potential going forward", said Dr. Michael Abrams, AnorMED's President and CEO.

AnorMED recently announced the first data from the AMD-3100 clinical program in stem cell mobilization, supporting its potential in stem cell transplantation for cancer patients. The company plans to be in a Phase II trial for this indication by the second half of 2002 and could potentially continue the clinical development of AMD-3100 independently to capture a significant part of the market, estimated to be between US\$70-120 million in 2005. In addition, Foznol, which AnorMED exclusively licensed to Shire Pharmaceuticals Group plc for the treatment of hyperphosphatemia in end stage kidney failure patients, is on track for a US filing and a EU market approval by mid-year 2002.

Avanir Pharmaceuticals Identifies Small Molecule Found To Be Effective In Regulating The Causes Of Allergy And Asthma

Immunoglobulin Epsilon, also known as IgE, considered to be the underlying cause of allergy and asthma symptoms may have met its match. AVANIR Pharmaceuticals, states that its scientists have identified a small molecule found to be effective in suppressing the synthesis of immunoglobulin epsilon (IgE) and other critical mediators of the allergic response.

As a result of the IgE findings, AVANIR is seeking to develop an oral formulation that is intended to significantly prevent or reduce the signs and symptoms of allergy and asthma. "The identification of an effective, safe, small molecule inhibitor of IgE has been the main focus of our pre-clinical research in allergy and asthma.", said Gerald J. Yakatan, Ph.D., President and CEO of AVANIR Pharmaceuticals. "AVP-893 is one of the most potent of the lead compounds we have tested, and it has proven efficacious in several laboratory and animal models. We continue to advance our research on the series of compounds represented by AVP-893, and hope to file an investigational new drug application (IND) next year."

AVP-893 is one of a series of active compounds that was discovered to be the optimal candidate through an irradiation-enhanced IgE response model in animals. Development of AVANIR's IgE technology is in an advanced pre-clinical stage and no human trials have yet begun.

Biosante Pharmaceuticals Received Positive Insulin Pre-Clinical Trial Results

BioSante Pharmaceuticals, Inc. received positive results in pre-clinical testing of its Bio-Air™ calcium phosphate nanoparticulate (CAP) delivery system for improved effectiveness of insulin administered by injection or inhalation. The pre-clinical trial examined the use of BioSante's Bio-Air™ system to administer proteins like insulin subcutaneously and into the lungs. In the study, proprietary Bio-Air™/insulin was formulated by scientists at BioSante's research center in Smyrna, Georgia and therapeutic efficacy was evaluated in diabetic mice.

When administered subcutaneously, Bio-Air™ extended the hypoglycemic effect of insulin from 4 to five hours to 10 to 15 hours compared with insulin alone. When administered into the lungs, Bio-Air™ with human insulin reduced blood glucose levels by 60 percent, versus only 30 percent in mice administered the same amount of insulin without Bio-Air™. The Bio-Air™ effect was maintained for 15 hours, compared with only 3 to 5 hours without Bio-Air™. These data indicate that Bio-Air™ preserves the biological activity of insulin and significantly extends its therapeutic effect when administered subcutaneously or directly into the lungs.

"Clearly, the efficacy results far surpassed our expectations for this trial." Said Stephen M. Simes, President and Chief Executive Officer of BioSante. "Moreover, they will advance our ongoing efforts in establishing partnerships with other companies to maximize the value of the Bio-Air™ drug delivery system as well as Bio-Vant™, our calcium phosphate-based vaccine adjuvant."

Boehringer Ingelheim and ImmunoGen Sign Exclusive License Agreement

Boehringer Ingelheim International GmbH and ImmunoGen, Inc. are collaborating to develop a new product combining ImmunoGen's maytansinoid Tumor-Activated Prodrug (TAP) technology with a Boehringer Ingelheim antibody. Under the terms of the agreement, Boehringer Ingelheim will receive exclusive worldwide rights to commercialize maytansinoid TAPs using antibodies targeting CD44. Boehringer Ingelheim will be responsible for the manufacturing, product development, and marketing of products resulting from the license; ImmunoGen will manufacture preclinical and initial clinical materials for manufacturing payments. ImmunoGen will receive an up-front payment and milestone payments, in addition to royalties on net sales.

ImmunoGen developed its tumor-activated prodrug, or TAP, technology to address the therapeutic need for improved cancer therapies

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Cell Genesys and JT Modify Agreement for GVAX® Cancer Vaccines

Cell Genesys, Inc. and its collaborator, the pharmaceutical division of Japan Tobacco (JT), have agreed to modify their ongoing collaboration for GVAX® cancer vaccines. The two companies, which previously had a 50/50 worldwide profit sharing arrangement for GVAX® prostate and lung cancer vaccines, will now have a royalty arrangement on sales of GVAX® lung cancer vaccine as well as a royalty arrangement on sales in other cancer indications that may be derived from a certain form of that vaccine, and Cell Genesys will now have full commercial rights for GVAX® prostate cancer vaccine. Under the new agreement, JT will pay Cell Genesys an undisclosed royalty on GVAX® lung cancer vaccine sales in Japan, Taiwan and Korea, and Cell Genesys will pay JT the same royalty on such sales in North America and the rest of the world. The companies will continue to equally share in the development costs of GVAX® lung cancer vaccine products, and JT will continue to pay Cell Genesys milestone payments.

Chiron Grants Non-Exclusive HCV License to Bristol-Myers Squibb Company

Chiron Corporation granted to Bristol-Myers Squibb Company, a non-exclusive license for the research, development, and commercialization of small molecule therapeutics against a broad spectrum of hepatitis C virus (HCV) drug "targets" contained in the HCV genome. The license expands the agreement entered between the parties in 1997 and allows Bristol-Myers Squibb to operate under certain Chiron patents to screen for drug candidates that inhibit HCV. The financial terms of the license were not disclosed.

In 1987, Chiron scientists Michael Houghton, Ph.D.; Qui-Lim Choo, Ph.D.; and George Kuo, Ph.D. cloned and first identified HCV as the cause of transfusion-related non-A, non-B hepatitis. This discovery marked the first time a virus was cloned before it had been grown in tissue culture or otherwise isolated. The Chiron scientists recently received the prestigious Lasker Award in recognition of this discovery. Since the initial discovery, Chiron has been granted more than 100 HCV-related patents in over 20 countries, including patents directed to hepatitis C polypeptides encoded throughout the genomes of HCV. Such polypeptides can be used in a variety of medical applications, including blood screening, clinical diagnosis, vaccines, and as

therapeutic targets for drug screening. A number of therapeutic companies have been granted non-exclusive licenses to Chiron's HCV technology for drug screening purposes, including, Glaxo Wellcome plc., the R. W. Johnson Pharmaceutical Research Institute, Japan Tobacco, Inc. and Pharmacia.

CyDex, Inc. Licensed CAPTISOL® Drug Delivery System To OSI Pharmaceuticals, Inc.

CyDex, Inc., entered into an agreement with OSI Pharmaceuticals, Inc., licensing CAPTISOL®, the formulation system from CyDex, as a drug delivery vehicle. The agreement calls for development of supplemental formulations for development stage drug candidates. In addition to OSI Pharmaceuticals, CyDex has licensed CAPTISOL to several companies for use in drugs under development for a variety of disease states. CyDex partners include Pfizer, Inc.; Allergan, Inc.; Bristol-Myers Squibb; Daiichi Pharmaceutical Co., Ltd., of Japan; PTC Pharma AG, of Switzerland; and Suntory Ltd., of Japan.

Decode and Roche Map Gene Linked to Rheumatoid Arthritis

deCODE genetics and Roche announced that deCODE scientists have mapped the first gene with genome-wide significant linkage to rheumatoid arthritis (RA) outside the MHC region. The companies will use the discovery as the basis for further research and development in both diagnostics and therapeutics. deCODE receives milestone payments for this discovery under the companies' 1998 gene and drug development alliance.

deCODE's study was conducted in two stages. First, with the collaboration of physicians from the National University Hospital in Reykjavik, more than 2500 volunteer patients and their relatives from more than 100 families across Iceland were screened for certain common variations in the MHC that are known to be associated with an increased risk of developing RA. Data from a genome-wide scan of the members of this group were then analyzed and led to the identification of a well-defined genetic locus that is independent of the MHC and is associated with additional risk of RA.

deCODE's findings, combined with existing knowledge on the links between variations in the MHC and RA, provide genetic markers that predict an increased risk of RA. This marks a large step towards the development of molecular diagnostic tools that will improve the diagnosis of RA, as well as help recognize predisposition to the disease and enable the development of novel prevention regimes.

Discovery Partners International Establishes European Headquarters in Basel, Switzerland

Discovery Partners International, Inc. has established its European headquarters in Basel, Switzerland. This operation will be part of Discovery Partners International AG, the Swiss legal entity that also encompasses Discovery

Partners' high throughput screening and biology operations formerly known as Discovery Technology Ltd.

Ethypharm's Microgranule Sustained-Released Morphine Sulfate Formulation to Be Marketed in Japan

Ethypharm will soon launch its novel oral microgranule formulation of morphine sulfate in the Japanese market under the name of MS-TWICELON®. MS-TWICELON® is the first proprietary sustained-release morphine sulfate formulation based on microgranules (tiny coated pellets) that has been approved in Japan for the management of cancer related pain on a "twice a day" basis. MS-TWICELON® was developed in Japan jointly by Nippon Kayaku and Teikoku Seiyaku. The product gained marketing authorization on March 15th, 2001 from Japan's Ministry of Health, Labour and Welfare and was granted reimbursement tariffs on July 6th, 2001. MS-TWICELON® will be manufactured by Teikoku Seiyaku under an exclusive technology license from Ethypharm in a facility that it has constructed specially for the production of narcotic analgesics, while Nippon Kayaku will be responsible for its marketing and distribution.

Annual sales of BID morphine sulfate products have been around Yen 15.5 billion (US\$ 132m) in Japan for the last several years, with the overall sales of all morphine sulfate being around Yen 17 billion (US\$ 145m) in 2000.

"We are pleased to launch our novel microgranule formulation of morphine sulfate in Japan, our first product in this important market. I am confident that the combination of the product's patient friendly benefits and Nippon Kayaku's marketing strength will allow MS-TWICELON® to capture a significant share of one of the world's largest markets for morphine analgesics," commented Patrice Debregeas, Ethypharm's Chairman and CEO. "Ethypharm's morphine sulfate formulations have been approved in over 50 countries and marketed by more than 20 partners, with Ethypharm being the leader in Europe with 26% market share. In order to strengthen and ensure our leading position in oral pain management, we are currently developing a 'once a day' formulation of morphine sulfate, currently in phase III, as well as Flasztab® formulations designed to increase patient comfort for Oxycodone and Tramadol," he added.

Matrix Submitted IntraDose® Application to EMEA

Matrix Pharmaceutical, Inc. submitted an application for the approval of IntraDose® (cisplatin/epinephrine) Injectable Gel for the treatment of recurrent or refractory head and neck cancer to the European Medicines Evaluation Agency (EMA). The application is based on results from two randomized, placebo-controlled Phase III studies. One of the studies was conducted predominantly in Europe. Matrix presented results of two, Phase III studies

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Travel to Korea

By Rosealee Lee

Memoirs of an Iowa farm girl may be an odd title to the new reader. If you missed the first column in CRS News, Volume 18, Issue 3, I encourage you to back up an issue and begin there. (Visit www.controlledrelease.org for the archived copy.) The title phrase stems from a comment which Kinam Park, President of CRS, made recently. The implication, was that if someone from Iowa (stubborn and pigheaded as we Iowans are sometimes) can like Korea, anyone can like it. In the last issue we addressed "Why Korea?", that Korea was quite a distance for many people and the imagined language barrier. The answers, as you may recall, were "Why not?", "Yes, but with some planning, the plane trip can be the first part of your good time.", and that the language barrier quite simply isn't there.

This is the Seoul, Korea of today. It is a world-class city, known for its gracious culture and friendly people. The hotels selected for the CRS 2002 Annual Meeting attendees are equally world-class, friendly and gracious. All of the selected hotels have been designed for the international traveler, with sophisticated amenities we have all come to expect. Each of the hotels have fitness centers, multiple restaurants and bars on-premises, business centers, voice mail, and data ports.

The COEX Inter-Continental Seoul is connected to the World Trade Centre and COEX Convention and Exhibition Center, just off the famous Han River. Grand Inter-Continental Seoul is conveniently located adjacent to the COEX Convention and Exhibition Centre, World Trade Centre, and has the largest guestrooms in the city. Renaissance Seoul Hotel located south of the Han River, in the heart of the Kangnam commercial district, is one of the flagship hotels of the Renaissance Hotel & Resorts. The Ritz Carlton Hotel received the 2001 "Best Hotel in Korea" by Korea Times. The Ritz is located in the heart of Seoul's Kangnam business district.



Seoul is a fascinating place whose 5,000-year history blends vibrantly with the modern city.

Getting to and from your hotel, as well as exploring Seoul, is easy and inexpensive. This is one of the few world-class cities that doesn't take a big bite out of your travel cash to get around. The airport is approximately 65-70 km from the Annual Meeting hotels. Options for airport transfer range are transfer buses which run every 30 minutes (current fare KRW10,000), deluxe taxi KRW75,000, and regular taxi KRW45,000. \$1U.S. is equal to more than KRW 1,200. The subway is an

excellent choice for airport transfer of attendees staying at one of the COEX Inter-Continental Hotels or the Renaissance Hotel. Inter-Continental guests will take the green line to Samsong Station, located on the corner next to the Grand Inter-Continental. Renaissance Hotel guests will take the green line to Yeoksam Station and then walk or taxi to the hotel (about a 15-minute walk or \$5U.S. cab ride). First section subway fare is KRW600 and second section is KRW700. Bus service is also available from the airport to the Annual Meeting hotels. Current fare set for limousine buses is KWR11,000 and KRW5,500 for city buses. Take the Gangnam bus route for Ritz Carlton, Inter-Continentials and Renaissance Hotels.

Transportation to and from the Annual Meeting hotels to the COEX Center is equally easy and inexpensive. Guests staying at one of the Inter-Continental hotels are already at the COEX Center. Renaissance and Ritz Carlton guests can take the subway or taxi (taxi fare estimated at \$5-\$7U.S.). Ritz Carlton guests have the option of a bus line that will bring them close to the COEX Center.

Because it is not possible to provide all the options here, attendees are encouraged to visit www.controlledrelease.org and click on the 2002 Annual Meeting. Links to hotel and transportation websites are available there for further research.

Dining in Seoul can be as adventurous or as "back home" as you like and it can be as inexpensive as you desire. Most eating establishments offer a balance of fare for visitors that prefer "Westernized" food and options for those that wish to dine on more traditional Korean food. There is something here for all tastes and pocketbooks. Expect most restaurants to have menus translated to English. You will find sandwiches, entrees, salads, and more, all expertly prepared and modestly priced. There is no need to carry tuna and crackers in your suitcase for "insurance" as I did on my first trip to Seoul. The COEX World Trade Center



Sunset at the Hangang River

(continued on next page)

(Memoirs, continued from previous page)

(home to CRS' 2002 Annual Meeting) and adjacent hotels offer many restaurants. Many of them (including Burger King) are located in the shopping center beneath the COEX Center.

A recent lunch in Seoul cost \$3.00 U.S., and dinners were readily available for \$5.00 U.S. These prices do not translate in every restaurant, since, like every international city, visitors have many choices. If you prefer fine dining, you will not be disappointed. Seoul restaurants are accustomed to serving guests from all over the world and do so graciously. Like many other large cities, ethnic offerings abound. I chuckle at the realization that one of my favorite Italian meals was purchased at an Italian restaurant in Seoul.

Traditional Korean fare is, quite simply, great. And, while I have spent time responding to those readers worried about going hungry because they will miss their regular dining options, the obvious begs to be stated . . . try Korean food while you're there. Try it early in your visit, so that you have more opportunities to enjoy it! A safe menu choice is *chongshik*, a table d'hote menu of several dishes which will come together with a bowl of *bap* (rice) and a dish of the national relish, *kimchi*, pickled and fermented vegetable usually based on cabbage or radish. This will give you an overview of what Korean cooking has to offer and you can learn what appeals to you most.



Traditional Dancers At Jongno Hall

Other dishes you will see on menus are *namul* (vegetables) that can be cooked or raw but are always fresh, seasoned in some way and served on a small plate. A *guk* or *tang* (boiled soup or water) may also be served to each diner in his or her own wide bowl. Meat, poultry and fish can be cooked in a number of ways. Dishes described as *kui* will be grilled or broiled, the best known of these being *pulgoggi*. They can also be cooked *pokkum* (sautéed or stir-fried) or *tchim* (steamed) or *puchim* (panfried).

Unlike a Western meal, most of the dishes in a Korean meal will arrive at the table together. There is also less of a tradition of eating dessert or having coffee at the end of a meal. Except occasionally in very high-class establishments, tipping is not required.

Seoul's history goes back as far as 18 B.C. when the newly established kingdom of Paekje built its present capital on the outskirts of the present city. History enthusiasts will be delighted in this city that has incorporated rich legacies with the 21st century modernism. True Korean flavor earned Seoul international recognition as host to the 1988 Olympics. Join us in Seoul to celebrate the fabric of the past and promise of the future that is Korea. •

(Eurand continued from page 7)

developing ground breaking technologies but are not capable of taking them to the market due to financial constraints or limited experience in commercializing product offerings.

While drug delivery will continue to be the core of Eurand, the company is working towards a specialty pharmaceutical structure where it develops and markets or co-markets its own proprietary pharmaceutical products. Given the company's broad technology platform, Eurand has been particularly successful at securing traditional partnerships based on its drug delivery technologies. One of the ways Eurand is distinguishing itself from the other companies in this field and moving towards a specialty pharmaceutical model, is through non-traditional partnerships that are mutually beneficial to both Eurand and its customers. For example, Eurand is currently in discussions with a number of pharmaceutical companies surrounding joint ventures. In these JV's Eurand will co-develop and gain co-marketing or co-licensing rights for new drug compounds that could benefit from Eurand's drug delivery technologies.

A final corporate driver is Eurand's internal drug pipeline. Throughout its history, the company has developed a significant number of pharmaceutical products using its drug delivery technologies that have been successfully licensed to pharmaceutical companies for marketing. In fact, the company has internally developed more than 50 products that are currently being marketed in 75 countries. Historically, these have been improved versions of existing products that have come off patent. However, in the past year, the company has expanded this pipeline to include the development of proprietary pharmaceutical compounds that utilize Eurand's drug delivery technologies. These will either be licensed to pharmaceutical companies for marketing or, where possible, marketed by Eurand directly.

As the drug delivery market continues to grow, Eurand intends to lead the industry through technology and product innovation.

Editors note: Contact Rosealee Lee, rlee@controlledrelease.org, to discuss spotlighting your corporation or institution in a future issue of the CRS Newsletter. •



Call for Applications

EURAND
Award 2002

For Outstanding Research in Oral Drug Delivery

Submission Deadline

April 12th, 2002

Winning Submissions To Be Honored And Presented At:

The Controlled Release Society's 29th International Symposium on Controlled Release of Bioactive Materials. July 20-25, 2002 COEX World Trade Center, Seoul, Korea

Selection Criteria for Grand Prize, Second Prize and Honorable Mention

All submissions should be original, non-published work detailing innovative research and must be in the field of oral drug delivery. Research cannot be previously published or presented but may contain references to previously published or presented work. Submissions will be judged on the following:

- *Innovation*
- *Potential commercial application*
- *Quality of research and technical content*
- *Potential impact on the drug delivery industry*
- *Potential to solve an industry-wide drug delivery challenge(s)*

Selection Criteria for Career Achievements in Oral Drug Delivery

An award will also be presented to an industry thought leader that has demonstrated innovation in the field of oral drug delivery throughout their career. Nominations are encouraged and will be broadly accepted. The Eurand Award Evaluation Board will judge nominees on the following:

- *Quality and quantity of research over the duration of their career*
- *Research resulting in innovative and applicable drug delivery technologies*
- *Applicable patents*
- *Entrepreneurial activities related to drug delivery*
- *Broadly recognized by their peers*
- *Editorial contributions to industry publications*
- *Participation on applicable boards and in industry associations*

Selection Process

The Eurand Award Committee will review all submissions and select all of the award winners. The decision of the board will be final. The selection committee will also be responsible for selecting the recipient of the career achievement award. All award recipi-

ents must be available to attend the 29th International Symposium on Controlled Release of Bioactive Materials in Seoul, Korea to present their winning submissions during the Eurand Award Special Session. If the selected winners are unable to attend, prizes may be forfeited and another winning submission may be selected.

Awards and Presentations

Winning researchers will receive the following:

- *Lifetime Achievement Award: \$5,000*
- *Grand Prize: \$5,000*
- *Second Place Prize: \$3,000*
- *Honorable Mention: \$1,700*

All winners will also receive:

- *Waived registration to the 2002 CRS conference*
- *Roundtrip transportation to the conference (coach class)*
- *Two nights lodging in Seoul*
- *A ticket to attend the CRS banquet*
- *Winners names will be published in 1-2 industry publications*
- *Winners will have an opportunity to present research opportunities to Eurand and potentially gain additional research grants*

For more information, please contact Lisa Fern at lfern@eurand.com or call +1 212-389-5772 (United States) or visit the Eurand Award Web Site at www.eurandaward.com

of IntraDose for recurrent or refractory head and neck cancer at the recent European Congress on Clinical Oncology (ECCO) meeting in Lisbon, Portugal, October 2001. The overall tumor response rate was 29% (35 out of 119 patients) with 19% achieving a complete response. Patient benefit was also measured in these studies through the use of a treatment goal questionnaire. Of patients treated with IntraDose, 27% achieved a patient benefit, defined as the achievement of a single, pre-selected primary treatment goal. Overall, 34% of patients treated with IntraDose met a primary or secondary treatment goal and 21% of patients noted additional benefits (which were not pre-selected) such as improved swallowing, speech or psychological state and others benefits.

On November 2, 2001, Matrix received a non-approvable letter from the U.S. Food and Drug Administration (FDA) for its IntraDose New Drug Application (NDA) as a treatment for recurrent or refractory head and neck cancer. Matrix is currently evaluating the next steps for IntraDose in the U.S. with the FDA.

Mendel Biotechnology Announces a New Five-Year, \$20 Million Research And Commercialization Partnership With Monsanto

Mendel Biotechnology, Inc. (Mendel) today announced a new, five-year, \$20 million research and commercialization partnership with Monsanto Company (Monsanto). This new partnership expands the relationship initiated in 1997 in which Mendel successfully identified many genes that regulate high-value plant traits such as enhanced yield, drought resistance, and disease resistance. If commercialized, Mendel will receive royalties from Monsanto on products containing these genes.

"Mendel is extremely pleased that Monsanto has agreed to this expansion of our strategic partnership to discover and advance high value plant genes," said Dave Summa, Mendel's president and Chief Executive Officer. "Our first collaboration was about discovering gene function. This new collaboration will continue that successful work and move into lead advancement." Rick Stonard, Ph.D., Vice President of genomics at Monsanto added, "Mendel has delivered on time and on budget. This extension provides Monsanto with continuing access to Mendel's gene function discovery and lead advancement capabilities. We expect that Mendel will continue to play an important role in our integrated genomics network."

Myriad Genetics and Biosearch Italia Collaborate

Myriad Genetics, Inc., and Biosearch Italia formed a collaboration to discover novel therapeutic compounds. Biosearch Italia will provide Myriad with access to its natural product compound library. Myriad will select promising drug targets, develop high-throughput screening assays, and screen the assays against Biosearch Italia's natural product libraries. "This

collaboration is an exciting opportunity to discover novel drugs through analysis of naturally occurring bioactive compounds," said Adrian Hobden, President of Myriad Pharmaceuticals, Inc. "The combination of Myriad's novel validated drug targets and Biosearch's proprietary natural products libraries may lead to the development of new therapeutics to treat a variety of important diseases."

Nano-C LLC Extends Commercial Production to Lower Price of Fullerene Carbon Molecules

Fullerenes, unique carbon molecules that hold the promise for breakthroughs in pharmaceuticals, electronics, semiconductors, super-conducting and many other industrial applications, are closer to affordability for researchers and companies because of a new mass production process from Nano-C LLC. The company is currently scaling up a patented combustion synthesis process that will reduce the cost of fullerenes by a factor of 10 to 100. "The new combustion process will drop the price of fullerenes from today's \$15 to \$20 a gram to as little as 20 cents a gram," says Jack Howard, a professor of Chemical Engineering at MIT, Nano-C's Chairman and Founder.

Nastech Initiates Intranasal Interferon Beta Phase I Clinical Trial

Nastech Pharmaceutical Company Inc. commenced a Phase I clinical trial in the United States to evaluate the nasal administration of interferon beta. The clinical program will explore the tolerance, safety and absorption of interferon beta in 12 healthy male subjects and ultimately aims to validate this technology in the treatment of Multiple Sclerosis (MS).

"We believe that a nasal formulation of interferon beta with an improved safety and efficacy profile may address a significant unmet medical need in patients with this CNS disease," stated Steven C. Quay, M.D., Ph.D., Chairman, President, and Chief Executive Officer of Nastech. "Initiation of clinical trials with interferon beta is a further execution of our strategy to identify and assess macromolecules that are FDA approved, administered by injection, have two or more innovators, and address billion-dollar market opportunities."

Interferon beta is indicated for the treatment of relapsing forms of Multiple Sclerosis (MS). It is a protein of relatively high molecular weight (approximately 19-24kD) and is currently administered by injection only. Interferon beta is marketed worldwide by Biogen, Inc. and Berlex Laboratories, Inc., and in 72 countries outside the U.S. by Ares-Serono. Total sales exceed \$1.1 billion annually.

Nutra Pharma Corp. Closed Acquisition of Nutra Pharma, Inc.

Nutra Pharma Corp. closed its acquisition of 100% of the capital stock of Nutra Pharma, Inc., signaling the company's expansion from an Internet-based health food supplement company to a diversified biotech company seeking to

market organic medicinal compounds for veterinary, agricultural, and human use. The acquisition of Nutra Pharma, Inc. is the first step in the company's worldwide marketing of a revolutionary organic wound healing compound. The company has appointed Dr. Rafael Gonzales-Vizoso as a director of the company, and as Medical Director and Chief Medical Officer of Nutra Pharma, Inc. Dr. Gonzales-Vizoso is the current Associate Director of Clinical Research for Health Research Associates, Inc. in Seattle, Washington.

OncoGenex Technologies and Isis Pharmaceuticals To Develop Antisense Drug for Prostate Cancer

OncoGenex Technologies Inc. and Isis Pharmaceuticals, Inc. have established a drug development collaboration to co-develop and commercialize OGX-011, an anti-cancer antisense drug candidate. OGX-011 combines OncoGenex's proprietary antisense position in inhibitors to the target, clusterin, with Isis' proprietary second-generation antisense chemistry. OGX-011 is designed to inhibit the secretory protein clusterin, which acts as a cell-survival protein that is over-expressed in response to tumor killing strategies, such as chemotherapy, hormone ablation and radiation therapy. Based on analysis of human tumor tissue, clusterin is over-expressed in several cancers, including prostate, renal, bladder, lung, ovarian, and urothelial. Inhibiting clusterin is intended to enhance the effects of drug therapies in the treatment of the disease. In preclinical animal studies, scientists from both OncoGenex and Isis demonstrated OGX-011 improved the potency of traditional chemotherapies more than 10-fold in prostate cancer without compromising safety. OGX-011 has also been shown to reduce levels of clusterin, as well as significantly delay disease progression in prostate and renal tumor models in animals. These findings support the continued development of OGX-011 in combination with chemotherapeutic and other agents.

Pharmacia to Spin Off Ownership Stake in Monsanto Company

Pharmacia Corporation will spin off its Monsanto agricultural subsidiary and distribute its entire ownership of Monsanto stock to Pharmacia shareholders by means of a tax-free dividend during the second half of 2002. Pharmacia currently owns approximately 85 percent of Monsanto. Pharmacia Chairman and Chief Executive Officer Fred Hassan stated that the spin-off will allow the company to fully unlock the value of its pharmaceutical and agricultural business. He stated, "These are two distinct businesses serving different markets and customers. Separating these businesses positions both to realize their full potential and serves the best interests of our shareholders."

(From the President, continued from page 11)

CRS: a Rosetta Stone in Pharmaceutical Science

Through the years, the CRS has become, in effect, a Rosetta stone in modern pharmaceuticals. The drug delivery science can be found written in the languages of both physicochemical scientists and biological scientists. The CRS may be the only place where all scientists from seemingly totally different scientific disciplines get together and communicate eye to eye. The drug delivery science by the CRS members holds the key to the future applications of all new drugs that may come out of the genomics and proteomics. The drug delivery research area has a tremendous opportunity to play a major role in the advances of the pharmaceutical industry as a whole.

The CRS meeting in Seoul will feature one of the best scientific programs in controlled release. The highest scientific quality of the meeting is presented by the three plenary speakers: Larry McIntire from Rice University, Gerald Pollack from University of Washington, and Sung Wan Kim from University of Utah. Their talks include microarray analysis of gene expression for tissue engineering, unorthodox explanation of cellular functions by polymer gel phase transitions, and state of the art gene delivery.

Seoul, Seoul, a Wonderful Town

As the CRS prepares for the activities in 2002 and beyond, the Board of Director has a firm resolution to continue the remarkable growth in scientific progress and global member participation. Please plan to join the 2002 CRS Annual Meeting in a city where modern medicine and alternative medicine coexist, where thousand-year old palaces shy away from skyscrapers, where ancient traditions thrive in a modern culture, where serious science is followed by fun activities, and most of all, where your mind meets your body. If Frank Sinatra visited Seoul again, he would sing a song "Seoul, Seoul, what a wonderful town!" •

(in the news, continued from page 19)

Roche to Dismiss Delaware Patent Suit Against IGEN; IGEN Continues Jury Trial Against Roche in Maryland

IGEN International, Inc. and F. Hoffmann-La Roche have settled a patent infringement action brought by Roche against IGEN in the U.S. District Court for the District of Delaware ("the Delaware Litigation"). The settlement follows Roche's offer last month to resolve the Delaware Litigation. Trial in the Delaware Litigation was completed in February 2001 and the parties have been awaiting a ruling from the Delaware District Court. Under the terms of the settlement announced today, Roche is dismissing all claims against IGEN and is reimbursing IGEN for the legal fees that IGEN incurred in defending that suit, which total approximately \$5.7 million.

On a separate matter, at press time, IGEN had concluded its presentation to the jury in its multi-count lawsuit against Roche Diagnostics, a division of F. Hoffmann-La Roche, which commenced on October 23, 2001 in the U.S. District Court for the District of Maryland ("Maryland Litigation"). The Delaware Litigation settlement does not affect the continuation of the Maryland Litigation, in which IGEN charges Roche with multiple breaches of a license agreement, violating its duty of good faith and fair dealing, and engaging in unfair competition. The Maryland Court had previously advised the jury that Roche's offer to settle the Delaware Litigation would not prevent IGEN from pursuing its unfair competition claim against Roche in the Maryland Litigation or from seeking damages from Roche relating to its behavior.

Sheffield Pharmaceuticals Initiates Clinical Trial To Study Budesonide Inhalation Suspension

Sheffield Pharmaceuticals, Inc. will initiate a clinical trial to study a proprietary formulation of unit-dose budesonide inhalation suspension for delivery by a standard commercial nebulizer. This trial will compare the safety and pharmacokinetics of this novel budesonide formulation to Astra Zeneca's Pulmicort® Respules® (budesonide inhalation suspension). The technology utilized to formulate this budesonide product was licensed to Sheffield's subsidiary, Respiratory Steroid Delivery, Ltd., from Elan Corporation and employs Elan's novel NanoCrystal™ dispersion technology. This randomized, crossover, placebo-controlled study is being conducted at Thomas Jefferson University in Philadelphia, Pennsylvania U.S.A.

Wyeth-Ayerst Licenses Ludwig Institute Antibody

Wyeth-Ayerst Laboratories, the pharmaceutical division of American Home Products Corporation, entered into an exclusive option and license agreement with the Ludwig Institute for Cancer Research (LICR) for an anti-cancer therapy based on an LICR antibody. Under the terms of the agreement, Wyeth-Ayerst has the exclusive option to research, develop, manufacture, and commercialize antibody-based drug conjugates for the treatment of cancer in humans, and will assume full responsibility for the related costs. In addition, Wyeth-Ayerst will pay LICR undisclosed option fees, development and approval milestone fees, and royalties on sales of any potential products. •

eventcafe

SMI Conference

Bioinformatics in the 21st Century

January 16-18, 2002

The Hatton Conference Centre
London, UK

ghudson@smi-online.co.uk

www.smi-online.co.uk/bioinformatics/asp

ph: +44-(0)20-7827-6704

UWEB (University of Washington Engineered Biomaterials)

Sixth UWEB Industry Symposium

January 16-18, 2002

Best Western University Tower
Seattle, WA, USA

info@uweb.engr.washington.edu

www.uweb.engr.washington.edu

ph: +1-206-616-9716

Gordon Research Conference

Bacterial Cell Surfaces

January 23-28, 2002

Colby-Sawyer College
New London, NH, USA

www.grc.uri.edu

Institute for International Research Speed-to-Site for Biological Clinical Materials

January 28-30, 2002

Omni Parker House, Boston, MA, USA

skohen@iirusa.com

www.iirusa.com/

biologicalclinicalmaterials

ph: +1-888-670-8200

6th Annual Drug Delivery Partnerships

January 28-30, 2002

The Century Plaza Hotel and Spa

Los Angeles, CA, USA

skohen@iirusa.com

www.drugdeliverypartnerships.com

ph: +1-888-670-8200

Institute for International Research How to Measure and Maximize R & D and Clinical Trial Performance with Metrics

January 28-30, 2002

Hyatt Regency Princeton

Princeton, NJ, USA

skohen@iirusa.com

www.iirusa.com/performancemetrics

ph: +1-888-670-8200

**Institute for International Research
3rd Annual Clinical Trials for
Anti-Cancer Drugs**

January 30 - February 1, 2002
Crowne Plaza San Francisco Union
Square San Francisco, CA, USA
skohen@iirusa.com
www.iirusa.com/anticancer
ph: +1-888-670-8200

**Gordon Research Conference
Drug Carriers in Medicine and Biology**

February 24 - March 1, 2002
Holiday Inn, Ventura, CA, USA
www.grc.uri.edu/programs/2002/
drugcar.htm

**Drug Carriers in Medicine and Biology
Gordon Research Conference**

February 24 - March 1, 2002
Holiday Inn, Ventura, CA, USA
www.grc.uri.edu

**3rd Annual HDL CHOLESTEROL
Metabolic Pathways & Drug
Development**

February 25-26, 2002
Royal Sonesta Hotel
Cambridge, MA, USA
www.knowledgefoundation.com

2nd Annual eCRM for Pharmaceuticals

February 25-27, 2002
Park Hyatt at the Bellevue
Philadelphia, PA, USA
skohen@iirusa.com
www.iirusa.com/eCRM
ph: +1-888-670-8200

**AAPS (American Association of
Pharmaceutical Scientists)**

**AAPS Workshop on Critical Issues in the
Design and Applications of Polymeric
Biomaterials in Drug Delivery**

February 28 - March 1, 2002
Crystal Gateway Marriott
Arlington, Virginia, USA
meetings@aaps.org
www.aapspharmaceutica.com
ph: +1-703-243-2800

**University of Delaware, Engineering
Outreach**

Biomaterials, The Next Frontiers
March 12-13, 2002
Trabant Center, University of Delaware
Newark, DE, USA
enggoutreach@udel.edu
www.udel.edu/engg/outreach
ph: +1-302-831-4863/2401

**Association for the Advancement of
Medical Instrumentation
International Conference on Medical
Device Standards and Regulation**

March 27-28, 2002
McLean, VA, USA
www.aami.org
ph: +1-703-525-4890

**Society For Biomaterials
28th Annual Meeting**

April 24-27, 2002
Tampa Convention Center
Tampa, Florida, USA
registration@biomaterials.org
www.biomaterials.org
ph: +1-763-543-0908

**Liposome Research Days & Max
Delbrück Center for Molecular Medicin
8th Liposome Research Days-Beyond
the Impossible**

May 21-24, 2002
Max Delbrück Center for Molecular
Medicine (MDC) Berlin-Buch
mhensel@mdc-berlin.de
www.lrdi.org
ph: 011-49-30/9406-3720

**Wound Healing Society
12th Annual Educational Symposium**

May 28 - June 1, 2002
Baltimore, MD, USA
member@convenemachine.com
www.woundheal.org/whs2002
ph: +1-763-765-2300

**Association for the Advancement of
Medical Instrumentation**

AAMI 2002 Annual Conference & Expo
June 1-4, 2002
Minneapolis, MN, USA
www.aami.org
ph: +1-703-525-4890

**Environmental Bioinorganic Chemis-
try**

June 15-21, 2002
Proctor Academy
Andover, NH, USA
www.grc.uri.edu

**National Institutes of Health,
Bioengineering Consortium (BECON)
Sensors in Biological Research and
Medicine**

June 24-25, 2002
Natcher Conference Center
Bethesda, MD, USA
www.becon.nih.gov/
symposium2002.htm

**Gordon Research Conferences
Drug Metabolism**

July 14-19, 2002
Holderness School
Plymouth, NH, USA
www.grc.uri.edu

**Controlled Release Society
29th International Symposium on
Controlled Release of Bioactive
Materials**

July 20-25, 2002
Seoul, Korea
register@controlledrelease.org
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ph: +1-763-512-0909

**Surfaces in Biomaterials Foundation
presents *BiolInterface* 2002**

September 4-7, 2002
Fairmont Scottsdale Princess
Scottsdale, AZ, USA
kkazmierczak@ardel.com
www.surfaces.org
ph: +1-763-512-9103

**European Society for Biomaterials
17th European Conference on
Biomaterials**

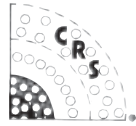
September 11-14, 2002
Barcelona, SPAIN
esb2002@esb2002.com
www.esb2002.com

**Academy of Surgical Research 18th
Annual Meeting**

October 2-5, 2002
Hyatt Regency, Greenville, SC, USA
registration@surgicalresearch.org
www.surgicalresearch.org
ph: +1-763-765-2300

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events, log on to
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