

About The Graduates



Class of 2008

Master of Science in Biotechnology

School of Medicine and Public Health

University of Wisconsin - Madison

Class of 2008

Sarah J. Barrett (B.S., Botany) is a Supervisor of Study Coordination in Pharmaceutical Analysis at Covance Laboratories, Inc. She was drawn to the M.S. in Biotechnology due to its integration of science, business and legal/ethical studies. Having this education has already contributed to Sarah's success in her professional endeavors. Sarah's aspirations are to be a strong leader in the pharmaceutical and biotechnology industry, and seek additional responsibilities and advancement within her company going into the future.

Phages vs. Superdrugs – The Battle Against Antibiotic Resistance

Antibiotic resistant bacteria have now become a global threat and have a profound effect on the current health care system in the United States. It is estimated that more than 70% of hospital-acquired infections are from bacteria that are resistant to the drugs routinely used to combat these types of infections. "Superbugs" – those that are resistant to almost all known forms of treatment - are now the most pressing concern. At least one strain of "Superbugs" are present in 46 of every 1000 hospital patients. (Centrose) Available and effective treatments for bacterial infections are few and far between, and have been in steady decline since the 1960's. (Wright) Two new approaches to help mitigate this crisis have presented themselves: neoglycorandomization and phage therapy.

The first option is the use of neoglycorandomization through the addition of sugar compounds to antibiotics that have been discontinued due to resistance. This new technique allows researchers to generate vast libraries of compounds in both a cost-efficient and safe manner. The second option is bacteriophage therapy, first discovered near the beginning of the century, which uses the bacteria's natural enemy to destroy it.

Neoglycorandomization and bacteriophage therapy both currently give researchers a unique advantage in generating new therapies against antibiotic resistant bacteria. However, both are not without their disadvantages, especially in how they will be approved for human use. Drugs generated from neoglycorandomization still face many of the same regulatory hurdles faced by the pharmaceutical industry, and may not be available for faster approval usually given for drugs of this nature. Phage therapy has never been addressed by the FDA or other regulatory agencies for use in humans. Although the idea of using phages for treatment of bacterial infections has been contemplated and used for almost 100 years, efficacy in clinical trials must still be demonstrated. These two new developments in the fight against antibiotic resistance need to be developed safely and quickly before "Superbugs" are in control.

Brian Bennwitz (B.S., Paper Science) with minors in business and chemistry has worked for eight years as a Senior Process Engineer developing aqueous coatings for the paper industry. His primary objectives for the program included gaining a deeper appreciation for rapid advancements emerging in the biotechnology industry, and strengthening his background in intellectual property. He recently assumed an R&D position with Kimberly-Clark in Neenah Wisconsin.

Ethanol Production from Synthesis Gas

Bio-fuels have recently attracted significant attention and investment as concern grows over global climate change. Recent spikes in energy costs in combination with improving alternate fuel technologies have begun to make biofuels an economic alternative to traditional fossil fuels. Determining which technology or combination of technologies will ultimately have an impact on the transportation sector is difficult as this early stage since competing technologies are advancing in both the automobile and biofuel industries. The technologies that will ultimately be adapted will not only need to economically meet transportation demands, but in addition minimize

environmental impacts, will coexist with current infrastructure, and benefit all levels of society. Currently there is not one perfect solution, but ethanol production through anaerobic fermentation of synthesis gas will be one of the leading sustainable alternatives to fossil fuels.

Jennifer L. Bernstein (B.S., Medical Microbiology and Immunology) is the Research Compliance Educator at Marshfield Clinic Research Foundation (MCRF), responsible for developing and implementing continuous compliance training for all members of the clinical trials team and overseeing quality assurance. She also provides project management for the Institute of Clinical and Translational Research, a joint venture between the University of Wisconsin-Madison and MCRF. Prior to moving to Marshfield, Jennifer was a Clinical Research Coordinator for the University of Wisconsin School of Medicine and Public Health, where she managed clinical research trial activity for subjects. Her goals for enrolling in the M.S. in Biotechnology were to secure a leadership position using a unique combined knowledge of science, study design and business perspective.

Microbicides: Placing the Power of HIV Protection in the Hands of Women

For the first time since the discovery of human immunodeficiency virus (HIV) as the etiologic agent of acquired immune deficiency syndrome (AIDS) in the early 1980s, there is an evident feminization of this public health crisis that was once regarded as a disease of gay men. Nearly all new cases of HIV infection are a result of heterosexual transmission, and roughly half of the 42 million people currently living with HIV are women. Existing prevention strategies such as abstinence, monogamy, and condoms have proven to be insufficient, particularly in regions of the world where gender inequality is prominent. A relatively small fraction of the global female population has the ability to negotiate the use of condoms, and sex is often forced upon them. Thus, in the absence of a safe and effective vaccine, women have few options for protecting themselves.

There is an urgent need for alternative prevention strategies, specifically ones which can be initiated and controlled by women. The availability of an intravaginal microbicide is a promising option which could prevent further dissemination of HIV. This paper will review the microbicide candidates currently in research and development and build a case for advancing live microbicides. One product candidate which could potentially address the unmet needs of women employs genetically engineered lactobacillus as a delivery vehicle for cyanovirin-N, a potent viral entry inhibitor. This second generation microbicide possesses many positive attributes. Most notably, this self-renewable therapeutic targets the initial stage of infectivity and can colonize the cervicovaginal tract, thereby providing long-lasting protection and eliminating coitally dependent application. In addition to providing persistent protection, the use of Lactobacillus eliminates costly protein purification steps during manufacturing, enhances innate defense through the production of lactic acid and hydrogen peroxide, and supports the prospect of a temperature stable formulation with a long shelf life. While it is too early to ascertain safety and efficacy, results of preclinical studies appear promising. Based on these distinct characteristics, a live microbicide such as the proposed holds the potential of becoming a commercializable therapeutic for curtailing the HIV pandemic.

Nicolas Cindric (B.S., English, M.S., Management) holds nearly two decades of management experience with expertise in marketing and sales strategy, strategic planning, e-commerce, brand management and new product introduction. His goal in entering the program is to leverage his education and work experiences to secure a leadership position with a biotechnology start-up or growth company.

Impact of the Federal Funding Ban on Stem Cell Research

Basic stem cell research represents the promise of some of the most advanced therapeutic breakthroughs in the history of medicine. The miracle of this technology was unlocked in 1998 by Dr. Jamie Thompson at the University of Wisconsin-Madison. The resulting therapies will redefine our future expectations for medicine, and should dramatically extend the lifespan of most human beings.

As with most disruptive technologies, a number of conflicting opinions have arisen as to how best orchestrate the changes that are about to occur. With embryonic stem cell research, these opinions are further fueled by ethical concerns regarding the possible destruction of a human embryo, and accordingly, a possible termination of life. These moral and ethical considerations have created a regulatory and funding environment that is, at times, at odds with our chosen capitalistic ways of governing.

The intent of this paper is not to focus on the ethical and moral considerations of this technology, but rather make an assessment on the impact of the federal government's ban on funding embryonic stem cell research on cell lines created after 2001. At the heart of this ban lies President Bush's now famous 2001 policy statement that has shaped the direction of the National Institute of Health's research spending guidelines for the past seven years. Specifically, this paper will attempt to draw conclusions on how this policy has impacted our country's leadership position in this emerging field.

Included in this discussion is an assessment of the amount, type, and source of research spending that is occurring for stem cell research. Equally, the worldwide regulatory environment is reviewed to discern whether regulation alone can provide competitive advantage. Finally, the paper concludes with a projection of the future as driven by possible outcomes of the upcoming presidential election. Although some of the arguments are subject to debate, no one is disputing the potential of human embryonic stem cell technology.

A. Catherine Cirillo (B.S., Chemistry) has been involved in the pharmaceutical industry for more than a decade. Presently, she is an Associate Analyst in the Quality Control department of SAFC, a division of Sigma-Aldrich Corporation in Madison, Wisconsin. She is responsible for validation, release analysis, and in-process analysis of potent API manufacturing. She participated in the M.S. in Biotechnology Program to gain a greater understanding of the business, ethical and legal issues encountered in this industry.

Is Cellulosic Ethanol The Best Transportation Fuel Alternative?

Experts estimate that the global supply of petroleum produced from fossil fuels will be exhausted by the year 2040 at the current level of consumption of 80 million barrels of oil a day (Steinbach 2008). In order to avoid any interruption in fuel production, ethanol production from biomass seems to be the method of choice, to hopefully reach the goal of uninterrupted fuel production when the petroleum products run dry. The question remains, however, of whether cellulosic ethanol is truly the best fuel alternative, especially in the realm of transportation fuels. The current expectations are that by 2030, the United States will be using close to 190 billion gallons of liquid fuels, most of which will be used exclusively for transportation. In order to effectively replace only 20% of that amount of gas with alternative fuels (such as ethanol, butanol and biodiesel), about 60 billion gallons would need to be produced annually. Currently corn is being used as the sole source of these fuels, but this is not a feasible option, since only about 30 billion gallons would be produced from the entire amount of corn produced annually in the United States today (Dhugga 2007). This falls short of the necessary levels of production. Extracting energy from plant and animal matter, known as biomass, and introducing new agricultural techniques and technologies will help regenerate non-arable land worldwide, as well as address the

rising need for renewable fuel sources at the same time. We must, however, find a way to do this without sacrificing the current food crops or land used for food to grow fuel crops.

Shirley Eckes (B.S., Accounting and Finance) has nearly two decades of experience in state government, global business, information technology, and real estate. Her recent endeavor includes co-founding a multi-million dollar real estate company in August 2006. Prior to that, she was Director of a global business and IT company and served as Deputy Secretary of the Wisconsin Department of Revenue as well as the Wisconsin Department of Electronic Government. Committed to life-long learning and with a family history of cancer, she entered the program in order to assist the policy-setting community to create a balance that allows biotechnology companies focused on advancing cancer therapies to flourish within a controlled environment to allow for a positive impact on human lives. Since then, she has been afflicted with the disease. Now, she has added a goal of advocating for personalized medicine on behalf of herself and other cancer patients who are genetically pre-disposed with cancer.

Prescribing Off-Label Drugs: Roadblocks for Cancer Patients and Opportunities for Regulated Personalized Medicine

Maya Fuerstenau-Sharp (B.S., Genetics) works as an R&D Scientist at Invitrogen Corporation where she develops cell-based assays for drug discovery. The M.S. in Biotechnology program provided Maya with the opportunity to gain the business and legal foundation needed to move into a position of greater responsibility. Upon completion of the M.S. in Biotechnology, it is Maya's goal to transition from the scientific bench to a position in product management.

Can Hesc-Derived Cardiomyocytes Serve As A Better *In Vitro* System For Pharmacological Safety Studies Ultimately Leading To The Development Of Safer Drugs?

At present, only 10% of new chemical entities will ultimately make it through the drug development process priced at an average of US \$900 million per new drug (Kola and Landis, 2004). In addition, 10% of already marketed drugs are withdrawn due to cardiac safety issues indicating that the *in vitro* and *in vivo* models currently in place are poor predictors of cardiac toxicity. Cisapride, astemizole and grepafloxacin have all been withdrawn from the market due to their cardiac risks. Notably, these three drugs represent different classes of non-cardiac drugs such as prokinetic agents, antihistamines, and antibiotics; yet their commonality is that they cause QT interval (QTc) prolongation, cardiac arrhythmias such as TdP or even sudden death. Therefore, identifying and screening out new chemical entities that pose safety risks will reduce the costs and may eliminate safety concerns that have routinely been part of the development of new drugs in the past (Sanguinetti & Mitcheson, 2005). HESC-derived cardiomyocytes may be an *in vitro* model that could be used to reliably weed out new drug candidates based on their cardiac toxicity. While research has shown that hESC-derived cardiomyocytes resemble adult cardiomyocytes phenotypically and functionally, hESC-derived cardiomyocytes are far from being adapted as a standard system for cardiotoxicity screens. This is due to technical obstacles in regards to purity and scale-up that have to be overcome first.

Nonetheless, if these technical issues can be resolved, it is possible that hESC-derived cardiomyocytes will become the preferred *in vitro* screening system not only for cardiac safety studies, but also for target identification and validation studies. Successful implementation of hESC-derived cardiomyocytes in drug discovery and development, however, will also depend on public acceptance, as there are many ethical concerns and regulatory constraints associated with the use of hESCs in research.

Brent Geiger (B.S., Biomedical Engineering) is a Quality Compliance Specialist at Genzyme Corporation in Middleton, Wisconsin. His work with Genzyme Corporation (formerly BoneCare International) has focused on the support of quality assurance activities; however he has experience with metrology and quality control laboratory functions. His work experience and transition between Genzyme and BoneCare International has

offered him a unique insight into both the micro and macro-scale aspects of the biotechnology industry. His goal in entering the program is to develop the skill base necessary to take on roles of increased responsibility and to make contributions to further the growth of local biotechnology industry.

Follow-on Biologics: Issues, Challenges, and Future Considerations

A significant contemporary issue facing the biotechnology industry is the debate over the appropriate regulatory process and extent of supporting information required for approval, manufacture, and marketing of so-called “biogenerics,” or more accurately, “follow-on” or “biosimilar” versions of complex biologic drugs. Although generic versions of traditional pharmaceuticals are historically well established and widely accepted, the conventional regulatory model for low-molecular-weight generic drugs cannot be applied to biologics due to the markedly increased complexity of their physical, chemical, and manufacturing process characteristics. However, the impending patent expiry of high-value biological drugs and increasing trend in global sales of biologics has led to pressure from generic drug makers, healthcare providers, and public representatives for the allowance of generic alternatives to expensive biologic drugs for pharmacoeconomic benefit. Alternatively, biotechnology companies and other innovative drug manufacturers generally resist follow-on biologics citing safety concerns and worries that copied versions of their drugs will undervalue their technological innovations and intellectual property thereby stifling future research and development. The purpose of this evaluation is to examine the critical technical challenges, safety concerns, regulatory policy issues, global perspectives, and future considerations associated with the follow-on biologics debate in order to ultimately provide a recommendation as to a course of action toward future resolution of the issue.

The main focus of this analysis is on the technical challenges that arise from the physical, chemical, and manufacturing complexity of biopharmaceuticals and the resulting safety concerns associated with follow-on biologics. A comparison of biologics and traditional pharmaceuticals is presented to illustrate the distinctly increased physical and chemical complexity of biological drugs. Such complexities present difficulties for the analytical and quality methods used to assess complex therapeutic products, which can lead to inadequate analytical characterization of follow-on biologics. Biomanufacturing processes are examined in the context of their overall complexity to demonstrate that biological products are defined by the process used to produce them and minor changes or inconsistencies in the production process could result in drastic differences in the final product. Critical safety concerns such as immunogenicity, bioequivalence, and explicit demonstration of clinical safety and efficacy are examined. The most important safety concern is immunogenicity because it is difficult to characterize without controlled clinical trials and could lead to severe adverse effects if not properly understood prior to use of follow-on biologics. Aside from technical and safety issues, regulatory policy issues such as the period of brand-name exclusivity, evaluation of therapeutic equivalence, and post-marketing surveillance are presented. Finally, global perspectives focusing on the status of the biosimilars issue in both the European Union and Canada are discussed, and future considerations such as diminished innovation, uncertain pharmacoeconomic benefit, and barriers to market entry are presented.

It is clear from the information presented throughout that the follow-on biologics issue is of contemporary significance because of distinct differences between biologics and traditional pharmaceuticals, and that change to the current biologics regulatory status-quo is inevitable. Therefore, it is recommended to adopt a proactive approach where follow-on biologics are allowed on a case-by-case basis only after review and careful consideration of the risks and benefits of each. Innovators should be given at least 12 years brand-name exclusivity in order to recoup development costs and encourage continued innovation. At least one clinical trial to evaluate safety and immunogenicity should be required to identify any adverse differences in safety profile compared to the branded product. The supporting information required for approval should also be determined on a case-by-case basis, but at a minimum should include data addressing clinical and non-clinical safety, quantitative comparability, comprehensive quality characterization, manufacturing process controls, and post-marketing surveillance plans in order to establish a minimum level of assurance that a follow-on product is as safe and effective when compared to the reference product. Finally, follow-on biologics should not be

considered completely interchangeable with the innovator product, but rather a separate product with unique labeling and prescribing information. Creation of such a follow-on biologics pathway will increase competition and reduce prices, while at the same time ensuring patient safety and not undervaluing the technological innovations that drive the development of novel medicines.

Elizabeth Jacobs (B.S., Animal Biology) is a Toxicologist at Covance Laboratories in Madison. As such, she is responsible for designing and managing toxicology research studies, and for drafting reports to be filed with regulatory agencies for drug applications. After a year of rest and relaxation, Elizabeth's goal is to attend law school to pursue a career in intellectual property law.

Global Feasibility of Hydrogen Production by Genetically Modified *Chlamydomonas ReinhardtII*

The 2008 Presidential Elections in the United States are riddled with discussions on 'greenhouse gases', 'biofuels', and 'alternative energy sources'. What does all of this mean? Why do we need alternative energy sources, and what are those alternative energy sources? I will give you a moment to imagine a car, fueled solely on the waste products of natural photosynthesis – the stuff of plants all around us – and the only waste product from your car, is water. Do you think this is too far from a reality? Think again. Researchers around the world have devoted their entire professional careers to studying photosynthesis, its products, and its potential as an energy source. The following paper outlines the potential in our green friends and the future of hydrogen powered cars.

Kristopher R. Moore (B.S., Microbiology and Molecular Biology and Biochemistry) is a Senior Supervisor and Toxicologist with Covance Laboratories in Madison, WI. His background includes over a decade of experience in animal efficacy assessment and preclinical safety assessment. During his time at the University of Idaho and following graduation he worked with pathogenic *E. coli* and *S. aureus* to develop a vaccine for cattle and identify mechanisms of pathogenesis, respectively.

Mr. Moore joined SNBL USA in 2000 where he started his career in the drug development industry in a variety of roles of increasing responsibility, including Research Manager and ultimately Study Director for Toxicology Safety studies. In 2005, Mr. Moore joined Covance Laboratories, working closely with several large biotechnology and pharmaceutical companies while managing a client team of Study Toxicologists.

Preservation and Sustainment of Global Fisheries Using Stem Cells in Surrogate Species

The World's fisheries are on the path to extinction, models suggest as early as 2048, due to both over-fishing and environmental change. Additionally, there is the need for additional nutritional protein-sources; therefore, we must intervene scientifically. Scientifically, we can assist in both the preservation of species as well as assist in sustaining current fishery resources. The preservation and sustainment of global fisheries, using stem-cells in surrogate species does, represent a possible solution to an increasing problem.

This advancement is achieved by the isolation of a target species germ-line, stem-cells from mature fish. Upon the successful implantation, via IP injection, of stem-cell into a recently hatched triploid surrogate species, whose immune system has not matured to cause stem-cell rejection, the cells are allowed to migrate into the genital ridge of the surrogate. The stem-cells then give rise to the target specimens gametes in what normally would have been a sterile surrogate. Once the surrogate matures, sexually, the gametes (oocytes or sperm) can be collected, fertilized, giving rise to target embryos and ultimately the target fry, upon the eggs' hatch.

This model allows for the preservation of genetic material for endangered species, which can be used actively or in the future to supplement the fishery. Additionally, this model does allow for the sustainment of fisheries through aquaculture, by using surrogates as broodstock for fisheries such as Bluefin tuna, reducing the

broodstock that would need to be acquired from the wild. Environmentally, hydro-electric plants can continue to be used without the further risk of species extinction, due to effects associated with fish passage, allowing for inexpensive power, free of production of greenhouse gases from the consumption of fossil fuels. Lastly, by investing in this technology, we can avoid the predicted global fishery resource collapse and the exponentially related decrease in recovery potential, population stability and water quality. Assuming that commercial scale, saltwater hatcheries are successful, the preservation and sustainment of Global Fisheries Using Stem Cells in Surrogate Species would be completely self-sustainable, commercially, allowing for natural recovery of self-sustaining fisheries.

Nicholas L. Neds (B.S., Chemistry-Biology) is a Research Assistant I in the Dose Analysis Department of Covance. He will soon be transitioning to a new role to pursue business oriented opportunities in the department. As he pursues a career in biotechnology he would like to complete the transition from the laboratory as a scientist into a business management role and focus more on the business issues that challenge the industry. Additionally, he is seeking to learn more about business practices and legal issues within the biotechnology industry that effect drug development.

Smallpox Has Been Eradicated: Why Not Pneumococcal Diseases?

In the history of mankind there has been only one disease that has ever been intentionally eradicated by a collective effort of people around the world. Looking closer at the factors surrounding smallpox and another deadly group of diseases, pneumococcal, there are specific factors that enabled the smallpox program to be successful and why that success has never been repeated.

Smallpox is a virus with no reservoirs in animals or nature and 100% of people infected with smallpox become sick and show the symptoms of the disease. The smallpox vaccine is highly effective and rugged, as it does not require a cold-chain. These factors combined with the weight of the World Health Organization all helped to make the eradication effort successful.

Pneumococcal diseases are deadly like smallpox, especially in the young and old, but the causative agent is a bacterium rather than a virus. The bacterium possesses the ability to mutate, which is why there are 90 different serotypes of pneumococcal bacteria. There are two vaccines that exist: a 7 valent conjugate form for kids and a 23 valent polysaccharide for adults. The vaccine requires a cold-chain for storage and while it is effective and provides significant coverage, the serotypes that are responsible for infections can vary by area decreasing the coverage of the vaccine. In addition, the pneumococcal vaccines carry an approximate cost of \$53 a dose versus \$0.10 per smallpox dose. Also, a large portion of people exposed to the bacteria can carry it, but will never become symptomatic; making it difficult to control the spread of these diseases. These factors combined with the WHO decree that there are seven other diseases that better meet eradication criteria means there is not enough scientific, economic, or political ability for eradication to become a reality.

The best strategy for pneumococcal disease management is one of controlling the disease and limiting the number of people who become infected and die, rather than trying to eradicate the bacteria. The means of accomplishing this is to increase the number of serotypes covered by vaccines and to get the vaccines to the developing countries where the majority of deaths occur. The most promising strategy is through the use of Advance Market Commitments to give manufacturers incentives to develop the vaccines and at the same time guaranteeing the poor and developing countries a price they can afford.

Eileen Ng (B.S., Food and Bioprocess Engineering) is currently an Application Technologist specialized in Dairy cultures and ingredients in Danisco USA, Inc. She also has 3 years experience in a Quality Control Lab,

with responsibilities to test and qualify bacterial cultures and dairy ingredients from on-site manufacturing. Her goal in entering the M.S. in Biotechnology was to learn more about the advanced techniques and theories in both technology and business, develop enhanced professional business skills and leadership capabilities, and foster a deeper understanding of practical biotechnology theories.

Scientific and Regulatory Challenges in the Development of Probiotics as Food and Dietary Supplements

There is a growing interest in self-care and demand for health-wellness products in population, where the recognition of the link between diet and health has never been stronger. The interest in the use of functional foods and dietary supplement to promote health beyond providing basic nutrition gain increases, and has become a major area of interest within the food industry. The market demand for these foods by the public to improve their general health and prevention of diseases is flourishing. Of these many functional foods, the probiotics – live microbial food supplements that beneficially affect the host through its effects in the intestinal tract and contributes to health and disease – is rapidly expanding in the global market.

The definition of “probiotic” set forth by the United Nations Food and Agricultural Organization and the World Health Organization in a joint report on the topics identifies probiotics as “live microorganisms, which, administered in adequate amounts, offer a health benefits on the host” (FAO/WHO, 2001), and this definition is adopted in this paper. Such probiotic microorganisms from a substantial number of studies have supported the idea that they are promising candidates to use to prevent infectious diseases and immune dysfunction.

The consumer’s overwhelming interest in and demand for functional foods, including probiotics, not only drive the emerging of new products in the market, but also making an impact in scientific researches. Today, hundreds of probiotic foods and dietary supplements that offer a variety of health benefits are available to the consumers. In the increasing scientific and commercial interest in the use of beneficial probiotics, there is the need in ensuring the safety of the organisms for wide variety of individuals, the efficacy of present and potential probiotic therapies that claimed, and such commercial probiotic product has meet the scientific criteria. Also, as the science among probiotics is being expanding to explore the possibilities behind the beneficial microorganisms, it is necessary to review and clarify the state of regulatory issues surrounding he probiotics, to avoid unclear, untruthful and misinterpretation on when and how probiotics are to be used for the treatment and prevention of various diseases and conditions.

Lynn M. Olstadt (B.S., Biology) started the M.S. in Biotechnology program working in the Covance Information Technology Department on a team to develop a new Laboratory Information Management System (LIMS) for the nutritional chemistry business. Since, she has accepted a supervisory position in the Client Services department of Nutritional Chemistry and has been in that position for 2 years. She is eager to use her degree to develop her career in management.

Global Nutraceuticals: A Regulatory Analysis

The lack of regulations surrounding the nutraceutical industry is a potential health hazard to the world’s population. Safety and efficacy are not always required to be tested prior to introducing a product to the market. In some cases, this lack of regulation has led to death of the consumer.

What is a nutraceutical? Any nutritional supplement in the form of a tablet, capsule, softgel, gel cap, powder or liquid that adds nutritional value to a person’s diet. This term can also include functional foods, which are food-type products that have been altered to have increased nutritional values, such as bars, shakes and genetically modified plants. There are many other synonyms for these types of products. Nutraceuticals are hard to categorize, they fall somewhere between food and drug. There are no well defined lines between

Nutraceuticals and food or Nutraceuticals and drugs. Interpretation is up to individuals and various regulatory agencies.

Since these compounds or products have not been formally classified as a food or a drug, they may have been well or consistently regulated.

There is a large market surrounding Nutraceuticals, up to 500 billion dollars is estimated to be spent annually worldwide. This is an attractive business to small and medium sized businesses because the cost to start up is relatively small compared to the pharmaceutical company. The lower start up cost can be attributed to the lack of regulations. Strictly regulated industries tend to be more costly to enter.

Some of the deaths caused by nutraceuticals could also be attributed to the lack of regulations in this industry. Some nutraceuticals that have been recognized as dangerous include: Ephedra, Aristolochic Acid, Kava, Yohimbe, Bitter orange, Chaparral, Comfrey, Germander, Scullcap and Androstenedione. (Consumer's Reports 2004) If rigorous safety and efficacy testing requirements were in place, the proper dosages or chemical interactions may have been known and the deaths could have been avoided.

Many people are under the misnomer that if something is "natural", it must be safe. In reality little is known about some nutraceuticals because they have not been subjected to thorough testing. It is not known if some dietary supplements have harmful dosage levels or if they will interact dangerously in the body with certain foods, supplements or medications.

Around the world, different countries are handling Nutraceuticals in their own way. Briefly, the US segments these products more similarly to food, whereas, China, Japan and Australia have stricter, more drug-like regulations around nutraceutical products.

This market is relatively new to government regulation and many countries are trying to figure out the best way to incorporate safety into this industry. Countries are looking at what other countries to see what they are doing and figure out what will work best for them. Harmonization is also a goal amongst dietary supplement regulations. Exportation is a major part of this industry; the more similar regulations each country holds the easier it will be to import/export these products.

Khelan Patel (B.S., Genetics) is presently a Safety Pharmacologist within Toxicology Services at Covance Laboratories in Madison, WI. His primary responsibilities involve assisting study direction in designing, conducting and analyzing GLP (Good Laboratory Practice) non clinical studies. His work revolves around the core battery of ICH (International Conference on Harmonization) S7A and S7B guidelines for the safety assessment of drugs for human use. Prior to this, Khelan worked in Covance Laboratories Anatomic Pathology group, where his focus was studying drug induced histopathology. Khelan's goal in entering the program was to gain a deeper insight into how different aspects of the industry interrelate with each other, as well as with regulatory agencies worldwide. Another area of Khelan's interest is intellectual property and its importance in sustaining technology innovation in the biopharmaceutical arena.

Bioremediation of Toxic Metals: An Innovative Way of Dealing with Nuclear Waste

Curbing environmental pollution has become one of the main focuses of governments around the world in response to the alarming consequences of global warming. While the world races to find new technologies to lower carbon emissions; another important environmental concern often gets pushed aside: Heavy metal and radionuclide contamination of soils and aquifers by leaked nuclear waste. The current radioactive waste contamination in the United States includes 120 sites in 36 states, including 475 billion gallons of contaminated

groundwater; 75 million cubic meters of contaminated sediment, and 3 million cubic meters of leaking waste buried in landfills. The cost to clean up these sites using current technology is estimated at 400 billion dollars a year. This waste poses a significant threat to human health and is a known cause of cancer and birth defects in humans. Unfortunately, the current technology of decontamination of nuclear waste spills is not environmentally friendly or cost effective; and involves burying contaminated soil in an ex situ (off site) location. The purpose of this research is to show that the use of genetically engineered, specialized metal sequestering bacteria can help prevent the spread of contaminated soils, a process known as bioremediation used successfully in the past on organic pollutants such as oil spills. Bioremediation of contaminated soils using an in situ (on site) approach followed by an ex situ approach is the most environmentally friendly way of dealing with radioactively contaminated soils. However due to the nature of the technology various scientific, ethical and regulatory challenges arise. Increased dialogue between the various stakeholders involved, as well as an increased understanding of microbial ecology, backed by a sustained political commitment will ultimately provide us with a powerful clean up tool to help restore our delicate planet.

Jeremy Roberts (B.S., Biology) is presently considering Law School options while traveling the country to contend for a Division II USA Rugby National Championship. Grateful to have been part of such a talented class, he looks forward to applying what he has learned in his future endeavors, and thanks all of his instructors and classmates for the exceptional last two years.

Microbial Carbon Dioxide Sequestration: Biotechnological alternatives to greenhouse gas mitigation

Since the Industrial Revolution, anthropogenic carbon dioxide emissions have been released at an ever increasing rate. In the past two decades this trend has been correlated with increased global temperature variance and climate change. Earth's history has detailed cyclical climate change, but none due to human influence. Current political and social attitudes have not demanded a change to stabilize the current trends. Looking into Earth's carbon cycle, one can see that microorganisms play a very influential role. Photosynthetic prokaryotes have removed atmospheric carbon dioxide and metabolized it to organic carbon which is then stored in terrestrial and oceanic sinks since the origins of life on this planet. Biotechnology can be used to help mitigate carbon dioxide by manipulating photoautotrophs and using them to sequester carbon dioxide for long term storage in the soil or ocean carbon sinks. Difficulties of scope, scale, governmental regulation, and public perception limit the prospective uses of prokaryotes. Ultimately, the implementation of point source closed systems at power generation and manufacturing facilities of algae bioreactors could successfully and significantly curb carbon dioxide emissions in efforts to stabilize green house gas effects on climate change until alternative energy sources are put into use.

Abdalla A. Saad (B.S., Zoology) is a Research Specialist in the Department of Anesthesiology in the School of Medicine and Public Health at the University of Wisconsin-Madison. He is currently working on the development of high throughput drug screening technologies. Abdalla supervises undergraduate students and trains students and researchers in electrophysiology techniques. His long-term goal is to establish a biotechnology company, utilizing skills in management and entrepreneurship.

Drought Tolerant Crops For Solving Food Shortages In Sudan

As the world population expected to increase at an alarming rate, the food supply needs are expected to triple in the next few decades. Food shortages remain a significant problem for hundreds of millions of people around the world and food access has been the major problem in the developing world.

The African country of Sudan has endured food shortages and famine problems due to droughts in the past few decades. In addition, the country's civil conflict since 1980's has intensified and the food shortage crisis left millions of people dead. As the conflict continues, people's displacement and fighting over resources have which in turn exhausted most agricultural resources. Studies showed that environmental factors play a significant role in the start of conflicts, which in turn can lead to fight over resources and cause food shortages.

Agricultural biotechnology will prove to be a key solution to the food shortages problem in Sudan. Introducing the transgenic drought tolerant Sorghum; Sudan main stable crop, into the agricultural sector will alleviate the crop shortages and will help in creating a sustainable economy that will reduce reliance on foreign aid. In addition, the fighting over resources should also decrease.

Implementation of agricultural biotechnology programs in developing countries requires the involvement of many Organizations, such as the UN, WTO and technology developers and owners. To assure that these programs are successful and provide the Sudanese people with the intended results, they need to meet well established ethical standards and regulations.

Neil Seeger (B.S., Biology) is an Assistant Scientist in the BioProcess Development Department at Danisco USA, Inc. His main focus is on relevant microbiological and molecular biological technologies that support research projects, process optimization, customer support, and production issues throughout Danisco. His goal is to develop the increased knowledge and application of new technologies that are essential in a rapidly changing biotechnology industry. Neil looks to build new competencies in business designs for strategies, marketing, and financial projections.

Synbiotics Introduction for Global Human Health and Wellbeing

The last half century has produced advanced medicines, such as antibiotics, along with increased diet modifications that have caused the critical deficiencies in the gastrointestinal microbiota. These deficiencies have great importance for global variability, required beneficial nutrient versus toxin absorption, and have indications for long-term impacts. Some long-term impacts involve the increased risk of colon cancer, decreased immune modulation, and life long illness. Microbial deficiencies have been shown to begin at birth where it is critical to establish the proper gastrointestinal population and environment. Further evidence has shown that with increased aging, the deficiencies occurs naturally, causing life threatening diseases when one is most susceptible. Therefore, it is important to retain, as well as rejuvenate, this critical gastrointestinal environment. To approach this problem, the gastrointestinal tract and microbial environment need to be evaluated for the requirements of a healthy and balanced environment. The methods to address the microbial deficiency involve the introduction of synbiotics. Synbiotics are the combination of probiotics (living, host beneficial microbes) and prebiotics (non-living, probiotic food source and gut environment booster). These components have indicated host benefits by themselves and, more so, combined. Probiotic and prebiotics are considered dietary supplements and have shown mixed reviews in clinical trials and the human health benefit arena. This has been caused by poor regulatory guidelines, false wellness benefit claims, and recently – deaths. Though, with the global socialistic variations, studies and their corresponding results will vary between locations. Therefore, synbiotics have the best potential for mainstream introduction by the combination of multiple probiotic strains and complimentary prebiotics. The mode of administering synbiotics for the gastrointestinal deficiencies will need to be incorporated into daily nutrient consumption habits, such as functional foods. Though, there are concerns and obstacles that need to be addressed before synbiotics and functional foods go mainstream. This will happen when we have: greater understanding of the GI microbiota and metabolic pathways; communication among the science community, global regulatory agencies with matching defined criteria and enforcement, and consumer education; additional human clinical trials; and ultimately through functional foods administered in daily consumed products we will rejuvenate and retain the critical gastrointestinal microbiota environment.

Casey Stankewicz (CLSp(CG), B.S. Biochemistry) is the manager of the Cytogenetics Laboratory at the WiCell Research Institute, where he performs chromosomal analysis of human embryonic stem cell lines. His prior work experience has shown him that a broader understanding of business and operations is necessary for a scientist. His goal in entering the program was to become a more versatile research scientist, with an increased understanding of the business, operations and legal issues that exist beyond the laboratory bench.

The BioWatch Program Through the Generations: Technologies, Requirements, and Rationale for Detection Systems of Aerosolized Bioterrorism Events

Biological agents such as bacteria, viruses, and protein toxins have been used throughout history by states and individuals as weapons of war and terror. The lethality and prior use of biological agent by terrorists against civilian targets, the inability to enforce the Biological Weapons Convention treaty, the difficulty in detecting a biological attack, and the low-cost and relative ease of producing bioweapons increase the likelihood of their future use. The expansion of modern biotechnology has further increased the global risk of bioterrorism with the ability to make classic agents more effective with the simplest of genetic techniques and the potential to create completely new biological weapons through synthetic biology. Although a successful aerosolized biological attack is considered a high-risk, low-probability event that has yet to be realized, there is little doubt that mass casualties, economic disruption, and panic would ensue.

BioWatch is the Department of Homeland Security's environmental monitoring program, initiated rapidly and without much publicity in 2003. The primary goals of the program are early detection of aerosolized bioterrorism events in major cities, transportation hubs, and special events in the United States, enabling the rapid response of effective emergency public health management, and funding the development and implementation of improved biosensors. The Biological Aerosol Sentry and Information System (BASIS) is the first generation BioWatch sensor that is currently deployed in at least 30 of the nation's urban centers. The BASIS system involves the filtering of large volumes of aerosols and then analyzing the filters daily for pathogenic nucleic acid sequences using polymerase chain reaction (PCR). It is an expensive and labor-intensive system that is currently being replaced by the Generation 2 BioWatch sensor, the Autonomous Pathogen Detection System (APDS). The APDS can operate unattended for up to 7 days, detecting both nucleic acid-based organisms and protein toxins with a flow cytometry-based immunoassay, PCR confirmation, and wireless transmission of data to authorities. The APDS is an elegant biodetection system that is the new standard for biosensor development and requirements.

The BASIS and APDS systems have known limitations for widespread and economically feasible deployment which has encouraged the development of Generation 3 biosensors that are more effective, efficient, and inexpensive. The federal government is currently funding, and will begin testing, a variety of Bioagent Autonomous Networked Detectors (BAND) for deployment by 2012. The development of BAND technologies is a collaborative effort between the national laboratories and a number of private biotech companies, including U.S. Genomics, Microfluidic Systems, and IQuum. Future detection platforms require identification and confirmation of numerous biothreat agents, including bacteria, viruses, protein toxins, genetically modified or engineered pathogens, prions, bioregulators and previously uncharacterized agents. In addition, future sensors must be highly autonomous, miniaturized, inexpensive and capable of extremely rapid, sensitive, specific, reproducible, and multiplexed assays directly from complex environmental samples with no false results.

The threat of bioterrorism is real and constantly changing due to advances in biotechnology, historical use of biological weapons, low cost of development, and risk of black market transfer of technology from previous state-sponsored bioweapons programs. As such, the continued development of BioWatch sensor technology, as well as other Homeland Security programs, is required to keep pace with persons, groups and countries with the nefarious intent of using biological weapons to upset the stability and security of the United States of America.

Cynthia Stewart (B.S., Biology Pre-Medicine) is a Clinical Research Associate for Covance Laboratories (Late Stage Development - Princeton, NJ), where she assures that all allocated projects are carried out in strict accordance with the relevant protocols, SOPs, and specified standards of GCP, ICH and CFR. Cynthia's goals include developing knowledge that will help her keep pace with the swift pace of the biotechnology industry and developing the ability to make sound judgments, such as how a company's technology and service meets the clients' needs and wants. Her research experience includes University of Texas Medical Branch, The Methodist Hospital Research Institute, and Baylor College of Medicine during which she managed trials for these medical centers. Additionally, she served as a mentor for those seeking entrance into clinical careers.

Gardasil®.....Should We or Shouldn't We?

TV commercials plug it with the "One Less" theme, the FDA approved it, news highlights tout it, but there are serious concerns about the new vaccine Gardasil® from Merck. How comfortable would you feel receiving or allowing your child to receive a vaccination that has only been on the market barely two years? How effective could this be? Why are there so many unanswered questions? Well, this is the case for Gardasil®, the Merck human papillomavirus (HPV) vaccine. It was introduced and approved for marketing in June 2006. A multitude of issues have arisen due to the new vaccine.

1. The government has proposed to mandate the vaccine in young girls.
2. The vaccine may not last longer than five years.
3. It does not protect against the other 30% of cervical cancer.
4. Skin cancer is also caused by HPV, but in types 5 and 8.
5. The cost of the vaccine is astronomical compared to current vaccines that are mandated.

Although this vaccine is a worthwhile effort, the technology of Gardasil® is a bit complicated given that only four HPV strains are protected. There are over 100 HPV types that have been identified. Some of the types cause various types of cancer. But, because HPV types 16 and 18 are the high risk types of HPV in regards to cervical cancer, which is the second most common cancer among women, these are covered under the newly approved vaccine. Two other types, 6 and 11, are also covered under Gardasil®.

Lee C. Tang (B.S., Biomedical Sciences) has served as a Research Technician for academic labs and has successfully helped a small molecular diagnostic company achieve FDA approval. He has earned second authorship on two papers dealing with drug addiction, both of which were presented at the 2005 Society for Neuroscience Meeting. Lee is currently involved in the CRO business and hopes to apply his M.S. in Biotechnology to further his career in the biotechnology field.

Potential Application of Nanowires from *Shewanella Oneidensis* and Other Dissimilatory Metal Reducing Bacteria in the Management of Municipal Solid Waste and Wastewater

Municipal solid waste and sewage management should be re-evaluated as global population continues to grow and CO₂ emissions continue to be a big threat to the future of earth's survival. Many of the affluent countries have found creative alternatives to solve their waste issues but those solutions have caused other problems. Landfills emit greenhouse gas and leachate. Waste-to-energy incineration may release dioxins and harmful metals and the ash byproduct (that are not reused) still end up at the landfill. Sewage treatment release biosolids as a byproduct and becomes solid waste that could be incinerated or go to landfills. Be it landfills, waste-to-energy incinerators, or sewage treatment plants, all these facilities are incredibly costly to a developing country where they can barely afford any sanitation system.

Microbes have already been in use for sewage treatment. The United State Environmental Protection Agency has supported bioreactor style landfills that are designed to degrade organic waste with microbes. However, these facilities are still expensive to sustain.

There have been great strides made in understanding dissimilatory metal reducing bacteria. Of particular interest is the *Shewanella oneidensis* because it utilizes nanowires for its electron transport system when confronted with electron acceptor limitation. Bacteria have a need to discard electrons as it consumes nutrients or it could lose functionality and die. By utilizing nanowires for electron dumping, *Shewanella oneidensis* can create electrical charges when it is consuming. *Shewanella oneidensis* and other dissimilatory metal reducing bacteria have been potential candidates for microbial fuel cell projects and nano electronics applications. However, a logical potential application for *Shewanella oneidensis* would be to integrate it for municipal solid waste and sewage management.

This solution would be ideal as the microbe will not only be eliminating waste but would be providing energy to help run the process. This feedback loop is the ideal waste-to-energy model as the carbon footprint would be non-existent. This model would provide developing countries a more affordable alternative to existing waste management facilities. Even up and coming superpowers like China could take advantage of a facility that could potential be running off the grid.

It is important to note that harnessing the power of *Shewanella oneidensis* and other dissimilatory metal reducing bacteria is still in its infancy. There are few barriers that must be overcome in order to use *Shewanella oneidensis* in this proposed application of waste management. In order for harness energy through this bacteria and nanowires, the following issues must be addressed:

- *Shewanella oneidensis* cultivation conditions
- Harvesting of pure nanowires and eliminating artifacts
- Scalability of *Shewanella oneidensis* and nanowires
- Increasing the strength of nanowires for industrial use
- Increasing the electrical output
- Control of the consumption rate

It must be understood that microbes are very picky in the way they perform. Cultivation conditions and harvesting refinement should incorporate current bioreactors and filters. Synthetic biology and bioengineering will be needed to address how strong the nanowires are, how much the microbes eat, and how much electricity is produced.

Waste management is not a simple matter of where do we put things left over from our industrialized world. Uncontrolled waste can bring even the most advanced and affluent countries to a standstill. Nature has a natural balance when it comes to handling waste. Using nature to solve humanity's problem is not something novel but something people continue to overlook. Time is working against people to find a feasible solution to eliminate waste without causing more ecological harm or collateral damage. *Shewanella oneidensis* and its nanowires have the ability to convert waste-to-energy where the only byproduct is what the world desperately needs, green energy.

Chelsey Tool (B.S., Biology) is a Research Assistant II at Covance Laboratories. She is responsible for research and method development in the Residue Analysis department. By utilizing Liquid Chromatography/Mass Spectrometry (LCMS) and Gas Chromatography/Mass Spectrometry (GCMS) instrumentation, she aids in the development of methods to analyze different types of foods, agricultural products and nutraceuticals. Her goal after the program is to continue working on research and development in a laboratory setting, but to move into a position of increased leadership and/or management.

Preparations for the Next Influenza Pandemic

The threat of another influenza pandemic like the “Spanish Flu Pandemic” of 1918-1920 is currently on the mind of many scientists, researchers, and government officials around the world. The pandemic of 1918 was said to have caused illnesses in close to one third of the world’s population at the time. [10] Because a threat of this magnitude is lurking around the corner, many countries have developed pandemic preparedness and contingency plans.

Currently there are many alarms or causes for concern that indicate there could be another influenza pandemic, much like the historical ones. First, there are three qualifications that indicate the start of an influenza pandemic. [28a2] They are,

1. Emergence of a virus to which the population will have little or no immunity, and there are currently no existing vaccines available.
2. The new virus is able to replicate in humans and cause disease.
3. The new virus is transmitted efficiently from human-to-human. [28a2]

Presently the first two have been met with the case of avian influenza (H5N1). [5] There may not be sustainable transmission from human to human yet, but there are many factors that could eventually play a role in allowing this to happen.

The influenza virus has the capability to change genetically, either by antigenic shift or drift. [4] One may occur more frequently than the other, but both are cause for concern, because it is by these changes that an avian influenza could one day be the virus of the next great pandemic.

With all these threats facing the world today, many countries are taking the advice of the World Health Organization (WHO) and creating preparedness plans. [28a3] Some plans from different countries are very similar, because most of them use the WHO’s example of WHO Global Influenza Preparedness Plan as a template for developing their own. [28a2, 3] Then there are some that seem to plan out only what they believe is important for their country. [28a2] Either way, it is very important to prepare for the threat of another pandemic, mainly to aid in the decreased spread of morbidity and mortality that an influenza pandemic could cause.

Theresa Weibel (B.A., Biology) is presently a Quality Assurance Specialist with Covance Labs, Inc. in Madison, WI. This position requires a vast understanding of the many types of technology used in the studies conducted at Covance. Her duties include assuring that all studies comply with Good Laboratory Practices (GLP) required for non-clinical studies. Her goal in entering the M.S. in Biotechnology program was to gain a higher level of understanding of technology, while also learning more about the business issues that make life-saving research possible.

A Look at Post Marketing Surveillance: Pharmacovigilance in the Biotechnology World

Every year patients around the world use many pharmaceutical and biotechnology products to improve their quality of life. These products range from simple over the counter drugs to complicated biologics. Drug products can be very benign or have many potential side effects. All of these products have had some form of regulation and development research prior to reaching the patient; however this does not eliminate the possible risks that some patients are facing by using products new to the market. Over the past ten years, there have been a significant number of drugs that have been placed on the market and then pulled off due to FDA required market withdrawals or company induced recalls of products (Kling, 2008). This type of event has brought forth intense criticism of the United States Food and Drug Administration as well as other world organizations, such as the European Medicines Agency, which have jurisdiction to regulate these products. In addition to the

current concerns in the United States, there is also an increase in the use of more advance products throughout the world, where very little information regarding the patients is retained. The result of this is far less information on the effectiveness and side effects of drugs that are being used throughout the world. Because it may take many years for data on the use of a drug to be “seen” it can result in a drug that is causing adverse side effects to stay on the market for a long period of time, when perhaps it should not be used due to safety issues. This all leads to pharmacovigilance (Meyboos et. al, 1999).

Pharmacovigilance is defined by the World Health Organization as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem, in other words, pharmacovigilance is essential ‘drug monitoring’ (WHO, 2008). The term pharmacovigilance is used throughout the world, however in the United States we also discuss the term “post marketing surveillance” to describe this process, which is also referred to as Phase IV clinical trials. It is this process that provides data about a drug product once it is being used by patients through the world. In most cases, the data confirms that the drug is safe and effective for patients and is providing an increased quality life to patients; however there are also cases of drugs causing intense side effects (even death). It is these cases that have caused so much attention to be drawn to the pharmacovigilance process.

Each regulatory body throughout the world has their own process of regulating drug development and clinical trials. Pharmacovigilance is an essential part of these regulations. In the United States this is typically referred to as Phase IV clinical trials. These trials are typically done at the request of the FDA or if there is a known safety concern for a particular product (FDA, 2008). Not all drugs products have a Phase IV trials. In the European countries it is regulated by the European Medicines Agency (EMA). The United States and Europe have established these agencies as the leaders for protecting humans. Other areas of the world do not have organized regulation like these. While there are many countries that do have regulatory agencies (such as Japan, Korea, and many more), there are many more that do not have these infrastructures set up, this is especially true in developing nations. This causes complications to ensuring drug safety in these areas. In the areas where there is lack of drug regulation, the World Health Organization has stepped in to provide guidance and collect data on health related topics, adverse drug events.

In order to ensure that drug safety is a high priority and patients receive the best possible care, it is important to consider the development of a worldwide pharmacovigilance system. While there are many challenges that stand in the way of a program of this magnitude, the possibility of providing safe drugs to the billions of people makes it essential to make an effort to provide surveillance which can help to ensure safety. In order to do this it would be beneficial to have a single system that could be used to report data on adverse drug events. This system would be available to any and all areas of the world that would like to use it. It would provide a way to trend data on high-risk drugs and therefore if an alarming trend were seen, it would be quickly summarize to determine if the product should be removed from the market.