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BCG Welcomes:**Janice M. Wilson, Ph.D., Sr. Consultant****Nebojsa M. Djordjevic, Ph.D., Sr. Consultant**

JANICE M. WILSON, PH.D. <http://www.biologicsconsulting.com/wilson.htm>

Dr. Wilson joined the group in December 2007. She is a quality and compliance executive with over 25 years of global and international experience in the highly regulated bioscience industries. Dr. Wilson was most recently the Global Head of Compliance for Novartis Vaccine and Diagnostics working out of the Emeryville, CA office where she was a member of the executive team providing oversight for the development and implementation of the division's Quality Manual. Her experience includes development, implementation, and directing of sustainable Quality Systems, Quality Assurance programs, and extensive Regulatory Compliance programs for GMP and ISO activities.

Read Announcement:

<http://www.biologicsconsulting.com/announcements/wilsonannouncement.htm>

See Curriculum Vitae

<http://www.biologicsconsulting.com/wilson.htm>

NEBOJSA M. DJORDJEVIC, PH.D. <http://www.biologicsconsulting.com/djordjevic.htm>

Dr. Djordjevic joined BCG in January of 2008. Dr. Djordjevic has over 20 years of experience in Analytical Chemistry utilized in Pharmaceutical and Biopharmaceutical Industry. During this time he has played an active role at virtually every phase of drug development from target identification, lead identification, compound selection and characterization, and pharmaceutical product development. He was most recently the Director of Analytical Chemistry at Cytokinetics Inc., a biopharmaceutical company involved in the discovery and development of oncology and cardiovascular drugs.

Read Announcement:

<http://www.biologicsconsulting.com/announcements/djordjevicannouncement.htm>

See Curriculum Vitae

<http://www.biologicsconsulting.com/djordjevic.htm>

Spotlight on Outsourcing

articles by:

Michael Trapani, MS, MBA, Senior Consultant

<http://www.biologicsconsulting.com/trapani.htm>

David Pepperl, Ph.D., Senior Consultant

<http://www.biologicsconsulting.com/pepperl.htm>

The November issue of RAPS Focus Magazine highlights Outsourcing and includes contributions by both Michael Trapani, MS, MBA and David Pepperl, Ph.D.

Quality & Compliance: The Quality Agreement

Preclinical Outsourcing in 2008: Key Considerations for Study Success

An Early Look at FDA Regulation of Nanotechnology

Article by

Stuart Portnoy, M.D., Sr. Medical Device Consultant

Nanotechnology, broadly defined, is the field of applied science whose unifying theme is the fabrication of materials and products on the atomic and molecular scale -- normally 1 to 100 nanometers (nms). There is currently a wellspring of academic and private sector research and development exploring the myriad potentials for nanotechnology to provide enhanced performance of existing technologies (e.g., improved efficiency of photovoltaic cells) and to offer novel solutions to historically vexing problems (e.g., targeting chemotherapy drugs for release at tumor sites while sparing healthy tissues).

Nanomedicine

Nanomedicine is an area of biomedical research that seeks to use nanoscale tools to improve health. Current medical uses of nanotechnology include sunscreens, dental-bonding agents, novel wound dressings, and liposomal drug delivery platforms.

Nanotechnology products that we should expect to see reach the market during the next few years include the following:

NANOTECHNOLOGY	EXAMPLE NANOMEDICINE APPLICATION
Nanocoatings	Drug Eluting Stents
Nanomaterials	Orthopedic Implants
Nanophotonics	Biosensors
Microneedles	Transdermal Drug Delivery
Microfluidic Devices	Blood Chemistry Lab on a Chip

The Terminology of Scale

There are 3 scales used to broadly categorize the size ranges for macro, micro, and nanotechnologies:

SCALE	SIZE RANGE	TERMINOLOGY	EXAMPLE
MACRO	meters → mms	Conventional Machines	Car Engine
MICRO	0.1 mm → 0.1 μm	Micromachines	Miniature Pump
NANO	100 nm → 1 nm	Nanosystems	Carbon Nanotube

FDA's Nanotechnology Task Force

In August 2006, the FDA initiated the Nanotechnology Task Force (NTF) to help determine appropriate regulatory approaches that would enable the continued development of innovative, safe, and effective FDA-regulated products that use nanoscale materials. As an initial assignment, the NTF was asked to identify and recommend ways to address any knowledge or policy gaps that exist to better enable the agency to evaluate safety aspects of nanomedicine products. The NTF has completed this assignment and released a comprehensive report on July 25, 2007, which recommends among other things, that FDA consider developing guidances and take additional steps to better understand the potential risks and benefits of therapeutics using nanotechnology.

Regulation Strategies

For the most part, FDA and industry experts believe that nanotechnology products present challenges similar to those FDA faces for products of other emerging technologies. The experts also recognize, however, that these challenges may be magnified because product safety and effectiveness might change dramatically as size goes up or down within the micro/nanoscale, thus adding additional complexity to the product review.

FDA expects that many nanotechnology therapeutics will span the regulatory boundaries between drugs, medical devices, and biologics. Initially, nanomedicine will likely be regulated under the rules established for combination products. Consistent with this similar precedent, FDA is expected to have broad latitude to make jurisdictional determinations and to implement preclinical and clinical testing requirements which may be significantly more burdensome for nanoscale products than conventional therapies.

Rather than providing a prospectively specified framework for the regulation of nanotechnology, FDA will likely evaluate each new product on a case-by-case basis. Over time, the agency will presumably attain the necessary understanding of this complex science to develop guidelines covering a wide range of regulatory considerations. This process will probably evolve in a similar manner as with FDA's experience during the past decade with the regulation of combination products.

As an example, consider FDA's development of the critically important paradigm of Primary Mode of Action (PMOA). This science-based concept (which guides the determination of combination product jurisdiction) illustrates how, with the rapid evolution and deeper understanding of the science itself, a clarifying taxonomy emerges which reflects a convergence of thinking among FDA, industry, and the broader scientific community. The taxonomy ultimately serves as a framework for product categorization, thus providing industry and investors with a comforting measure of regulatory predictability.

Safety First -- The Potential for New and Currently Uncharacterized Nanoscale Biological Interactions

Perhaps of greatest relevance to new products regulated by FDA is what the current structures in the nanoscale range is teaching us about biological interactions, especially potential new safety concerns. The scientific literature provides some preliminary approaches to organizing information for risk assessment and risk management of nanoscale materials. It's important to note, however, that while these methods offer some insight into how biological interactions of nanoscale materials might be better understood, nanotechnology experts caution that there may be a fundamental difference in the kind of uncertainties associated with nanoscale products as compared to conventional medical therapies.

For conventional drugs/biologics/devices, there is a relatively long history of product characterization and validated test methods which have provided a robust understanding of the interactions of molecular classes (compounds containing particular structures or functional groups) and also medical device materials with biological systems. For nanomaterials, however, a prudent assumption is that these well-established characterization and testing principles will be subject to new and potentially vigorous skepticism by the FDA.

Important testing and characterization considerations are described in the table below:

ISSUE	POTENTIAL NEW CONSIDERATION
Toxicology	Conventional toxicology screening methods may not be adequate to fully assess toxicologic properties of engineered nanoscale materials. Therefore, new methods may need to be developed to address this critical safety issue.
Pharmacokinetics & Pharmacodynamics	Pharmacokinetics and pharmacodynamics of nanoscale particles are expected to be different from those of larger particles. Existing toxicity screening studies either need to be modified or new methods developed to adequately assess nanoscale therapeutics.
Product Characterization	Characterizing chemical, biological, and/or physical aspects of nanomedicines will likely require exploration of assessment methods for novel product attributes. Sponsors are advised to pay particular attention to the composition and surface characteristics of nanoscale materials and their interactions with biological systems.
Manufacturing & Quality Systems	In parallel with product characterization methodologies, quality systems testing will also need to be revisited to address any new challenges in identifying and developing appropriate test methods

	and specifications to control nanotechnology manufacturing processes.
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Broadly summarizing the above considerations, it will likely be necessary for sponsors to "cast a wide net" in order to sufficiently demonstrate product safety. Unlike conventional therapeutics with a long and well-established safety history, FDA will expect nanomedicines to undergo comprehensive testing designed to rule-out the potential for new types of adverse biological interactions.

FDA Nanotechnology Contacts

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BCG consultants attend numerous conferences every year during which they are available to provide company information or consulting expertise. Below are some conferences that BCG consultants will be attending in the near future. Please feel free to contact the attending consultant either before, or during the conference for company information or to discuss a business opportunity.

Date	Sponsoring Organization	Conference and Presentation Title	BCG Attendee(s)/ Speaker (s)	Location
January 14 - 15, 2008	IBC China	US FDA Biological Approval Process	Lei Zhang, MD, Ph.D. (speaker)	Seoul, South Korea
January 14 - 16, 2008	ALS Association	ALSA Research Workshop	Wilson W. Bryan, M.D. (speaker)	Tampa, FL

January 17 - 18, 2008	IBC China	US FDA Biological Approval Process	Lei Zhang, MD, Ph.D. (speaker)	Taipei, Taiwan
January 21-23, 2008	Institute for International Research	5th Annual Formulation & Forced Degradation "Implementation of a flexible yet cGMP complaint Stability Program for Phase I, II and III Studies"	Nanda Subbaro, Ph.D. (speaker)	San Diego, CA
January 27-30, 2008	CASSS	CMC Strategy Forum Current Practices for Assessing the Comparability and Stability of Gene Therapy Products	Andra Miller, Ph.D. Maritza C. McIntyde, Ph.D. Nadine Ritter, Ph.D. (co-leader) Darin Weber, Ph.D.	Washington, DC
January 27-30, 2008	CASSS	CMC Strategy Forum Extractables and Leachables: Challenges and Strategies in Biopharmaceutical Development	Keith Wells, Ph.D. Ruth Wolff, Ph.D.	Washington, DC
January 27-30, 2008	CASSS	CMC Strategy Forum 12th Annual Symposium on the Interface of Regulatory and Analytical Sciences for Biotechnology Health Products	Nadine Ritter, Ph.D. (speaker) Keith Wells, Ph.D. Ruth Wolff, Ph.D.	Washington, DC

January 28-29, 2008	International Pharamceutical Academy (IPA)	FDA Pre-Approval Inspections "FDA approval processes and combination device and biologics inspections"	John R. Godshalk, MSE, MBA (speaker)	Toronto, Canada
January 28-30, 2008	Phacilitate	Phacilitate Cell & Gene Therapy Forum 2008	Andra Miller, Ph.D. Maritza C. McIntyde, Ph.D. Darin Weber, Ph.D.	Washington DC
February 9-10, 2008	ISCTR (International Society for Cardiovascular Translational Research)	Annual Meeting "Regulatory Considerations for Cell Manufacturing and Cell Delivery"	Darin Weber, Ph.D. (speaker)	San Diego, CA
February 21-22, 2008	Texas Scottish Rite Hospital for Children	30th Annual Carrell-Krusen Neuromuscular Symposium	Wilson W. Bryan, M.D.	Dallas, TX
February 25-29, 2008	Seton Hall Law School	Health Care Compliance Certification Program "Advertising & Promotion of Medical Devices"	Stuart Portnoy, MD (speaker)	Newark, NJ
March 6-7, 2008	ASENT (American Society of Experimental NeuroTherapeutics)	Annual Meeting	Wilson W. Bryan, MD (course co-director)	Washington, DC
March 16-20, 2008	Society of Toxicology	SOT Annual Meeting and Tox Expo	John Jessop, Ph.D., MPH	Seattle, WA
March 28-29, 2008	AABB (American Association of Blood Banks)	Spring Conference 2008 Regulatory Considerations of Using Stem Cells for Cardiac Applications	Ellen M. Areman, MS, SBB (speaker)	Orlando, FL

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