Inhalation Inspiration

“Breath is the bridge which connects life to consciousness, which unites your body to your thoughts.” Thich Nhat Hanh

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The AAPS INTFG Blog by Tammy Shen


The increasing sophistication of orally inhaled and nasal drug product (OINDP) formulations and technologies has augmented the need for standardized characterization metrics, more relevant analytical techniques, and improved processing and analysis of the generated data to better predict the clinical and physiological effects of the aerosolized therapeutics. Solid state therapeutic compound and formulation properties such as crystal polymorphisms, surface roughness, electrostatic charging tendencies, and surface energy can alter drug pharmacokinetic and pharmacological properties and, as a result, the understanding of the solid state properties of inhaled drugs is critical. These physical properties may also significantly affect the aerosol performance and therapeutic index of the drug product; therefore, proper in vitro analytical testing is essential to progressing an OINDP formulation forward.

Compounding the complexity of OINDP development is not only the interplay between the formulation and the delivery platform, but also patient variation and a variety of guidance documents on the characterization of these systems. Thus, bioequivalence and statistical approaches towards quality control of OINDPs from both an industry and regulatory perspective must be aligned to better streamline the development and approval process.

To facilitate discussion and provide valuable feedback to industry and academia on the regulatory landscape and pipeline of OINDPs in the United States and the world market, a comprehensive review of current and future formulation and in vitro testing technology as well as perspectives on quality control programs for OINDPs will be presented in a workshop, Inhaled Drug Products: Current Practices and the Future of In vitro Testing Technologies and Regulation, jointly developed by the AAPS Inhalation and Nasal Technology Focus Group (INTFG), International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS), the United States Pharmacopeial Convention (USP), and the Food and Drug Administration (FDA). This workshop will be held September 9-10, 2013 at the USP Meeting Center in Rockville, Maryland.

More information concerning the joint workshop can be found on pages 4-5 as well as the following website: http://www.aaps.org/IDP.
Emerging Nicotine Delivery Systems: Electronic Cigarettes
By Philip Kuehl

Electronic cigarettes, also known as e-cigarettes or e.cigs, are an emerging device that has shown a dramatic increase in manufacture, marketing and sales. Marketing for e.cigs has been fast and incredibly effective, including print, media and social networking sites. Several specific e.cigs include features that notify the user (by visual and audible methods) that other users or e.cig retailers are nearby. All have these have caused this industry to expand at a very rapid pace. While the specific sales numbers vary depending on the source the global market, it is generally accepted to have been ~ $2 billion in sales in 2011. That figure represented a growth of 30% a year for three years, reflecting success of the novel marketing strategies.

In general e.cigs generate their aerosols (typically called vapor) of nicotine from a solution of nicotine in propylene glycol, glycerin or other surfactant. The ‘vapor’ is generated by a heated nebulizer. The heated nebulizer is activated by the users puff which triggers a sensor that activates the heated nebulizer. Many of the devices are designed to look and feel like a real cigarette; several even have a light that glows on the tip when the nebulizer is activated.

Despite this rapid growth little is known about these products, the formulation of the nicotine, or the composition of the aerosol that is generated. Even with minimal peer reviewed literature any of these products are marketed or designed to reduce harm or risk when compared to burn down cigarettes. In fact, many of the advertisements call out that the products generate water vapor.

At the current time the US FDA has not regulated many of these products, although they do have the authority to do so. This may in part be caused by the infant nature of the industry and the testing methods. Several of the peer reviewed publications have highlighted that mainstream vapor form e.cigs are known to contain nicotine, propylene glycol, glycerin derivatives and volatile organic compounds. In addition several studies have indicated that formaldehyde may be present in the mainstream vapor of e.cigs. Albeit the majority of all constituents (except nicotine) reports are typically lower than comparable burn down cigarettes.

Overall the e.cig industry shows no sign of slowing down in the near future. Many of the testing methods that aerosol scientists utilize every day for aerosol characterization, particle size distribution and tolerance will likely be adapted in the months and years to come to fully characterize e.cigs.
Upcoming Meetings

In vitro Testing and Technologies for OINDPs; Joint AAPS, IPAC-RS, FDA and USP Workshop  
ERS Annual Congress  
ERS Annual Congress  
Amer. Asoc. Aero. Research  
AAPS Annual Meeting  
Drug Delivery to the Lung  
IPAC-RS  
Respiratory Drug Delivery  
ISAM – 20th Congress

INTFG Inhalation Insider Article Series by Tammy Shen

This article series was started to give INTFG graduate students and postdocs an inside look at what goes on in industry, particularly in respiratory research and development. Scientists from a broad spectrum of companies were interviewed and topics ranged from interview experiences to day-to-day responsibilities to characteristics the company looks for in a new hire. Links to these interviews will be posted on the INTFG LinkedIn Discussion Group as well as on the AAPS INTFG Forum.

I am still looking to spotlight several more inhalation scientists. If you or a colleague would be willing to be interviewed please email me at twshen@outlook.com. (You may also remain anonymous if you so choose.)

Industry News & Highlights

• In June 2013 Pearl Therapeutics was purchased by AstraZeneca to gain access to their proprietary metered dose inhaler technology platform. This includes Pearl's PT003 glycopyrrolate/formoterol fumarate LAMA/LABA inhaler currently in Phase III studies. This product is intended to treat patients suffering from COPD.

• Teva purchased MicroDose Therapeutx in June 2013 for their proprietary multi-dose dry powder inhaler. Inhalers designed to treat respiratory syncytial virus (RSV; MDT-637) and asthma/COPD are currently under development.
Monday, September 9, 2013, 8:00 am–5:00 pm


Morning Session:

Welcome to the Workshop and Overview of INTFG
Samiran De, Ph.D., Next Breath

New OGD Guidances: Bioequivalence Requirements for Inhaled Products
Robert Lionberger, Ph.D., (invited), U.S. Food and Drug Administration

Delivered Dose Uniformity: Statistical Approaches for Quality Control Programs, FDA Perspective
Yi Tsong, Ph.D., (invited), U.S. Food and Drug Administration

Delivered Dose Uniformity: Statistical Approaches for Quality Control Programs, Industry Perspective
J. David Christopher, Ph.D., Merck & Co., Inc.

Current and Future Statistical Approaches for Cascade Impactor Studies for Inhalation Products
Sau (Larry) Lee, Ph.D., (invited), U.S. Food and Drug Administration

Lunch

Afternoon Session:

Population Bioequivalence Studies (PBE) for Nasal and Inhalation Product In Vitro BE Study Analysis
Bing Li, Ph.D., (invited), U.S. Food and Drug Administration

Quality by Design (QbD) Studies for Nasal and Inhalation Product In Vitro BE Study Analysis
Bita Mirzai Azarm, Ph.D., (invited), U.S. Food and Drug Administration

Dissolution Approaches for Inhalation Drugs: QC versus Clinical Relevance
Guenther Hochhaus, Ph.D., University of Florida

Direct Measure of Particle Size Equivalence: A Review of Raman Spectroscopy Combined with Optical Microscopy Technique
William H. Doub, Ph.D., (invited), U.S. Food and Drug Administration

Session I Panel Discussion

Evening Reception
Session II: In Vitro Testing of OINDPs: A USP Perspective on Current Practices and Future Thinking

Morning Session:

An Overview of the Aerosols Subcommittee's Future Activities
Anthony Hickey, Ph.D., Research Triangle Institute

Analytical Methods for Orally Inhaled Products
Paul Curry, Ph.D., Abbott Laboratories

Good Cascade Impactor Practices—An Evolving USP View
Jolyon Mitchell, Ph.D., Trudell Medical

General Chapter <1XXX> Spacers and Holding Chambers, Guidance from the USP
Jolyon Mitchell, Ph.D., Trudell Medical

Session II Panel Discussion

Session III: Solid State Characterization for Inhaled Therapeutics

Quality by Design for Inhalation Products
Lawrence Yu, Ph.D. (invited), U.S. Food and Drug Administration

Terahertz Spectroscopy for the Solid State Characterization of Lactose
Chanda Yonzon, Ph.D., Merck & Co., Inc.

Lunch

Afternoon session:

Optimizing Dry Powder Inhaler Performance through Understanding of Particle-particle and Particle-device Interactions in Dry Powder Mixtures
Speaker to be Announced

Solid-state Characterization and Nanotechnology in Inhalation Aerosol Formulation Development
Heidi M. Mansour, Ph.D., University of Arizona-Tucson

DPI Modeling
Jag Shur, Ph.D., University of Bath

Session III Panel Discussion and Closing of the Workshop