FORMULATION & DELIVERY

SERIES US 2020

Pre-Event Newsletter Feb 2020

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AND MUCH MORE!

HILTON SAN DIEGO MISSION VALLEY

17 - 18 MARCH 2020 | SAN DIEGO, US

OXFORD GLOBAL CONFERENCES

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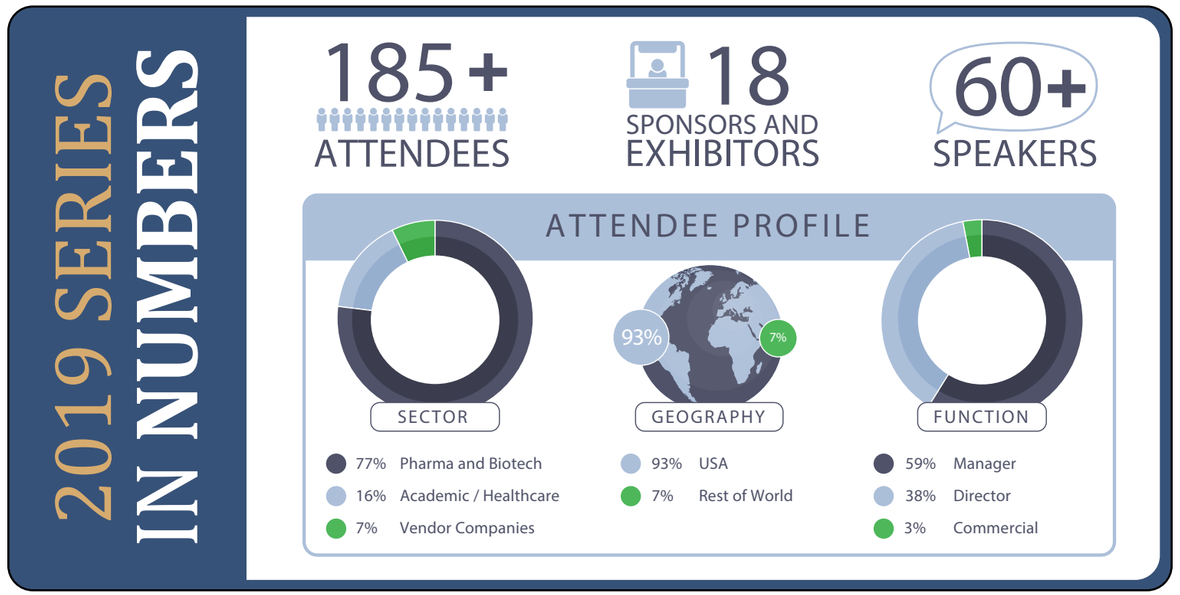

WELCOME TO OXFORD GLOBAL'S FORMULATION & DELIVERY SERIES US PRE-EVENT NEWSLETTER!

With the 3rd Formulation & Drug Delivery USA Congress and co-located Inhalation & Drug Delivery USA Congress taking place in March 2020 in San Diego, I am delighted to take a look back at the 2019 event and provide some exciting details on some of the key features and new additions for the 2020 congress.

Featuring over 60 presentations from leading figures within the industry and key sponsors offering relevant solutions & services, the 2019 event brought together over 180 attendees to discuss updates and innovations in small and large molecule drug formulation and delivery. It also examined the development & formulation of inhaled therapies as well as novel inhalation devices and analytics. 2019 saw the addition of two new featured streams focusing on the delivery for RNA therapies and nano-formulation and delivery. We welcomed the resounding feedback from attendees commenting that they were very pleased with the seniority of the audience and the number of high-level scientific presentations on the programme. It's always great to hear that the forum provides a beneficial and highly effective networking environment.

The Formulation & Drug Delivery 2020 Congress will again ensure delegates gain invaluable insights into both small and large molecule formulation development as well as drug delivery. The 2019 streams proved very popular and will remain. New for this year's agenda, we are excited to announce the expansion of the programme to include a more in-depth review of continuous manufacturing, CMC and process development strategies, and featured streams on bioanalysis, characterisation and stabilisation updates. At the 3rd Inhalation & Respiratory Drug Delivery Congress, alongside the popular 2019 topics in novel inhalation and devices, in line with current industry trends, our 2020 event will have case studies on alternative therapeutic fields and in-depth presentations on pioneering technological advancements in digital health.

As always, we look forward to welcoming known and new faces to the 2020 congress, with over 200 attendees from leading US based pharma & biotech companies for high-level discussions on the latest innovations for biopharmaceutical development. We hope you can join us!

- Hayley Watson, Portfolio Director

HILTON SAN DIEGO MISSION VALLEY

17 - 18 MARCH 2020 | SAN DIEGO

3RD ANNUAL
FORMULATION & DRUG DELIVERY
USA CONGRESS

co-located with

3RD ANNUAL
INHALATION & RESPIRATORY DRUG DELIVERY
USA CONGRESS

WHO IS ATTENDING?

For the full attendee list please contact
marketing@oxfordglobal.co.uk

- **200+ senior level attendees** from leading pharmaceutical, biopharmaceutical, biotechnology, diagnostics, CRO and solution provider companies.
- **Professors, Directors and Heads** of formulation development and drug delivery, biologics developments, inhalation drug delivery, respiratory pharmacology, inhalation process development, inhaled dosage forms, pulmonary disease, respiratory therapeutics.
- **Highly esteemed members** of academic and government institutions.

These companies and many more:

Glenmark – A new way for a new world
Boehringer Ingelheim
AstraZeneca
Takeda
teva
NOVARTIS
MERCK
Celgene
Roche
Allergan
Lilly
AMGEN
Genentech – A Member of the Roche Group
INCARDA Therapeutics, Inc.
Pfizer

GOLD
Recipharm

SILVER
Lonza
Pharma & Biotech
Cambrex

BRONZE
Aptar CSP Technologies
EMERGO a UL company
MedPharm Breaking through boundaries
Pfanstiehl
CAS A DIVISION OF THE AMERICAN CHEMICAL SOCIETY
EXPERIC
MERXIN
WYATT TECHNOLOGY

NETWORK AND PROGRAMME
Celanese
ADARE Pharmaceuticals
ZERION
INTEC PHARMA
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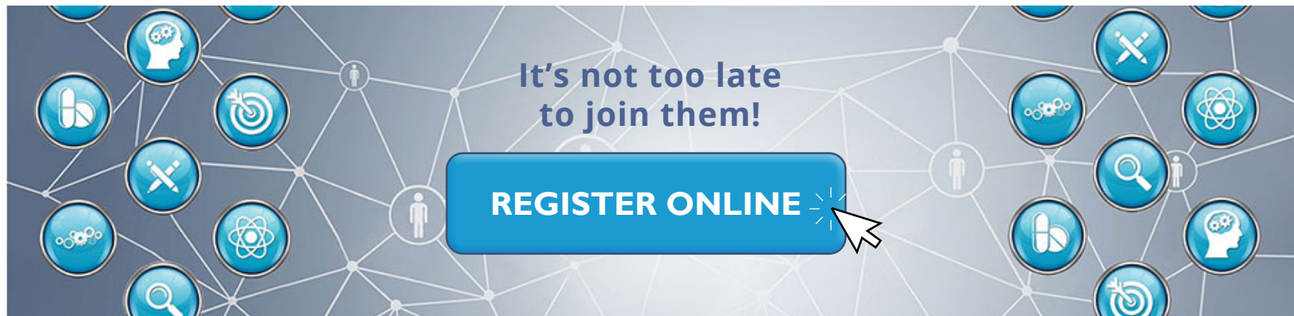
BASF We create chemistry
Pii PHARMACEUTICS KNOW-HOW
Quotient Sciences
Harro Höfliger
leon NANODRUGS
MUNIT WE ARE MICRONIZATION
halo labs



LONG ACTING INJECTABLES: CHALLENGES AND POTENTIAL
JOEL RICHARD

A serious difficulty when working with fragile pharmaceuticals is delivering the formulation to the patient in a safe and effective manner. Thankfully, industryleading experts such as Joel Richard, of MedInCell are progressing technologies that allow for easy and ready-to-use long-acting injectable therapeutics by adjusting the drug-release profile. Joel discusses his work and the potentials for development with delivering fragile molecules for the future.

What are you working on currently?

I am currently working on the development of Long Acting Injectables (LAIs), using the proprietary BEPO technology of MedinCell. I am leading all the product development, non-clinical, regulatory and clinical activities for the whole portfolio of projects of the company. This is a very versatile technology based on the association of biodegradable, amphiphilic, block copolymers, where the formulation scientist can play with many different parameters to adjust the drug release profile and get duration of action between a few days to up to 6 months, with a limited burst release. In addition, the BEPO technology makes it possible to produce ready-to-use liquid formulations in pre-filled syringes, easy to administer through small Gauge needles without any preliminary constitution step, and able to form a subcutaneous polymer implant after injection, due to a solvent exchange mechanism.

What are the major challenges with Long Acting Injectables?

One of the major challenges with LAIs is related to the control of the burst release which may lead to high circulating concentration of drugs and potential associated safety concerns. BEPO technology actually allows for a very good control of the burst effect, based on specific diblock and triblock copolymer compositions. Another key challenge is related to the delivery of fragile, hydrophilic molecules like peptides and proteins. As regards peptides, long acting injectable formulations based on biodegradable microspheres have been available on the market since more than 20 years ago, but most of the time these are not ready-to-use (RTU) formulations, and they need extemporaneous reconstitution before administration. Preformed solid implants made of biodegradable polymers are also available, but need the use of large Gauge needles (16-18 Gauge) which results in very invasive, painful and stressful injections for patients. The in situ implant forming BEPO technology would bring the unique combination of a RTU liquid product (solution or suspension) associated with a patient-friendly injection procedure with the possibility to control the burst and the release duration between days and months.

Joel Richard, Head of Technical & Pharmaceutical Operations, MedinCell

Dr Joël Richard is currently Head of Technical & Pharmaceutical Operations at MedinCell (Montpellier, France). He is leading all the pharmaceutical development and non-clinical pharmaco/toxico-kinetic activities of the company, specialized in the development of Long-Acting Injectables. (LAIs), using the proprietary technology BEPO®. Dr Richard has 30 years of experience in chemistry and biopharmaceutical R&D, including several global senior positions in various Biotech and Pharma companies, such as: Ipsen, Merck Serono, Ethypharm and Mainelab (France), a drug delivery company he co-founded, which was specialized in developing solvent-free processes for protein delivery systems. Since 1996, Dr Richard has focused his research activity on new formulation technologies and drug delivery systems (such as microspheres, nanosystems, gelling systems, chemically-modified proteins, supercritical fluid technology), especially for injectable peptide and protein formulations. Dr Richard has graduated from Ecole Normale Supérieure (Cachan, France). He has got a PhD in Materials Science from University of Paris, France, and the "Habilitation à Diriger les Recherches" degree in Chemistry from University of Bordeaux I. He has published 68 peer-reviewed scientific papers, 8 book chapters and 2 review editorials in various fields (colloids and interfaces, drug delivery systems, supercritical fluids, protein formulations, nanoparticles). He is the author of more than 140 international communications and 55 patent families.

> *"Novel LA formulations will likely show a very favorable benefit/risk balance in patients with chronic, highly life-impacting conditions"*

What do you see as the most interesting developments in the field?

There is likely a strong interest from the market to deliver fragile biotechnology products, like engineered antibodies or antibody fragments, since these very promising drug candidates show short plasma half life. In this context, a recent work has shown that BEPO technology makes it possible to deliver small bispecific antibody for immunotherapy in prostate cancer, binding both Prostate Specific Membrane Antigen (PSMA) and the T-cell receptor CD3 over several weeks after injection, improving half life and subcutaneous bioavailability of the bispecific antibody, while keeping bioactivity and high anti-tumor efficacy in animal models. This is a very promising result that shows the great potential of BEPO technology for long acting (LA) delivery of engineered antibodies.

What do you see as the major therapeutic areas for development with novel formulations?

Novel LA formulations will likely show a very favorable benefit/risk balance in patients with chronic, highly life-impacting conditions, in particular in the field of treatment of central nervous system, cancers, auto-immune diseases, and diabetes. A greater interest may even be found when the depot formed by the injected solution of block copolymers make it possible to keep the drug released in a specific local area of the body (like e.g. a joint, or a solid tumor, etc...), limiting potential systemic toxicity of the drug and improving its efficacy locally.

What do you look to achieve at the Formulation & Drug Delivery Congress?

As for me, attending the Formulation & Drug Delivery Congress means meeting the best experts in the field, confronting ideas and having high level scientific inputs from experienced leaders. I feel really excited to have the opportunity to learn from my peers, I am convinced that these conversations will generate new ideas to design the next innovative drug delivery systems that patients are expecting.

TOPICAL DELIVERY OF OPHTHALMIC DRUGS

HOVHANNES J. GUKASYAN

Hovhannes J. Gukasyan (Hovik), Associate Director, Early Pharmaceutical Development, Allergan plc

In 1999 Hovik received a BS in Chemistry from the University of Southern California (USC) with an academic minor in Biological Sciences. In 2003 he received a PhD in Pharmaceutical Sciences from USC School of Pharmacy under the supervision of Prof. Vincent H.L. Lee. He has authored 39 peer-reviewed papers, including 2 book chapters, 2 guest-edited topical thematic collections, and 87 abstract presentations as posters or invited talks. One patent/invention. 16 years of pharmaceutical industry experience, currently and Associate Director in Pharmaceutical Development Allergan Plc (prior experience at Pfizer Inc and Anadys Pharmaceuticals Inc). He is Adjunct Professor at the University of Southern California and Keck Graduate Institute Schools of Pharmacy, lecturer at UCSD School of Engineering. Serves on PhD thesis committee of graduate students at University of Arizona School of Pharmacy. Graduate and Healthcare Professional level course taught include Pharmaceutics, Regulatory Sciences, and Medical Devices.

What is your current role? What drew you to Allergan?

I am an Associate Director of Early Pharmaceutical Development (PharmDev) at Allergan plc. Allergan runs an Open Science R&D model, which is something very progressive and attracted me to the organization.

What are you currently working on?

In Early PhrmDev I get to work across all the major therapeutic areas at Allergan; Eye Care, CNS, GI, and Medical Aesthetics. We provide drug-product development support for a variety of molecular modalities and routes of administration, for initial safety and proof-of-concept testing.

What are the biggest challenges when working with delivery to the eye?

Eye care has a special place in my heart; ocular drug delivery and physiology are areas of long term research interest and expertise for me. There are several challenges unique to this field and I'll mention two of current interest which I'll discuss with the audience: first is a shift towards predictive modelling and simulation tools to understand and design ophthalmic drug delivery systems, and second is a long standing grand challenge of efficient topical delivery of drugs to the retina.

What do you see as the future for this exciting area of research and development?

There will be a paradigm shift in several areas from research to development, as well as regulatory guidance. In R&D, we may see patient centric innovations in wet AMD management, breakthroughs for dry AMD, and a curative solution for glaucoma. The FDA has been doing a lot of innovative research in ophthalmic drug product bioequivalence studies, with promising early analyses of published results. I hope to see continued engagement with the agency in this area.

What would you like to achieve at the Formulation & Drug Delivery congress?

This is a great networking opportunity to engage in precompetitive and collaborative scientific discussions; as well as look for business opportunities especially in novel combinations of small or large molecule drugs with the right drug delivery technology.

IMPROVING PATIENT'S LIVES WITH COMBINATION PRODUCT DRUG DELIVERY

JAMES LEAMON

James Leamon,
Director of Biologics Device Development,
Jazz Pharmaceuticals

Jim is a medical device and drug device combination product development leader, an engineering director, and a manufacturing manager. He is experienced in working across functions and business groups in varying organizations. Jim has successfully brought new and effective products to market throughout the world and has developed and implemented new engineering, quality control and manufacturing processes. Jim continues to lead product development, and contract engineering teams while working at Jazz Pharmaceuticals. He is highly experienced and proficient in CMC drug-device combination product leadership as well as strategic planning, design engineering, manufacturing engineering and new product and process development. Jim is also a community leader in social justice and feeding the hungry. As treasurer of a non-profit organization, he has used his strategic planning and financial management skills to help people in need. This correlates well with his career drive to improve the lives of cancer patients and those with other life-threatening diseases.

What is your current role, and what drew you to the role/Jazz Pharma?

I am the director of biologics device development at Jazz Pharmaceuticals; I have always wanted to provide device development leadership in a biotech company that has a portfolio of products for treatment cancer patients. You could say it is a realized goal.

What are you currently working on?

We are working on a novel combination product to deliver a large bolus of drug to the patient in a short period of time. It is challenging and cutting edge; very exciting!

What do you see as the latest challenges and developments in combination products?

Anytime a company takes on a new combination product development there are many challenges and risks. From Quality Systems to Manufacturing Execution, leadership must plan appropriately and monitor the progress. Even the regulatory authorities are learning and advising as the combination product industry expands to meet the needs of a wider range of patients. There are challenges in traversing the EU and US regulatory landscape as a medium sized pharmaceutical/biotech company. While Jazz and many other companies have integrated combination products into their pipelines, there remains a steep learning curve for both device and pharmaceutical or biologics and developers must both listen and teach. I appreciate those who are able to do both and I take it as a challenge as Jazz moves into the combination product space.

What do you see as the future for drug delivery and novel device technologies?

I see no end to innovation! Of course, innovative delivery products as well as drug products must be safe and effective, but the treatment experiences are getting easier for patients and more convenient. I'm sure some day the treatment will be as easy as the treatments Dr. Bones performed on *Star Trek*; hold a device on the patient's skin and press a button. Some of today's innovative products are almost there. Subcutaneous drug/biologic delivery is preferred over intravenous delivery and companies are listening to their stakeholders and patients.

What are you looking to achieve at the Formulation & Drug Delivery congress?

Learn, learn and learn some more. I'd like to meet those colleagues who are doing similar developments in their respective corners of the world. I have a few colleagues coming to meet with me there and I'm sure I'll get introduced to a few more. I'd also like to learn more about new innovative drugs and process from the presenters.

Q&A WITH RECIPHARM'S **LEI MAO**

Lei Mao, Director of Inhalation Science and Product Development at Recipharm Laboratories

Lei Mao is the Director of Inhalation Science and Product Development at Recipharm Laboratories. With over twenty years of experience, Lei has a wealth of knowledge in formulation and inhalation product development within the pharmaceutical industry. He started a career working as a senior scientist, where he developed particulate formulations for inhalation applications and has since held managerial positions for big pharma companies. He also holds a Ph.D. in Pharmaceutical Sciences and a degree in pharmacy.

Describe your current focus within inhalation science.

As a leading contract development and manufacturing organisation (CDMO), our goal at Recipharm is to support pharma companies with the development and manufacturing of inhaled products, including metered dose inhalers (MDIs), dry powder inhalers (DPIs) and nasal sprays, in line with regulatory requirements. It is well known that inhalation dosage forms are unique and technically more challenging compared to other dosage forms. Inhalable products require specialist expertise from development through to manufacturing, meaning our core focus is utilising our development team's expertise and scientific knowledge to fully support the needs of our clients' projects. The majority of our customers come to us for an end-to-end service. At the beginning of 2019, we launched Recipharm Inhalation Solutions™ which provides an integrated service from development, scale-up and clinical supply to commercial manufacturing to meet this demand.

What are your main priorities within the inhalation field and how do these compare to the priorities of the industry as a whole?

Advances in science and technology mean that a key area for growth is trying to deliver medicines for unmet patient needs. In order to cater for evolving patient needs, it is important that CDMOs deliver high quality products that can progress to market as quickly as possible. CDMOs offering integrated services are able to better expedite the process and achieve this goal, as they facilitate projects from development to commercial manufacturing. In recent years, we have been continuously investing in our inhalation business in terms of both capabilities and capacities. For example, the acquisition of Sanofi's former inhalation product manufacturing facility at Holmes Chapel provided us with specialist technologies for MDIs and nasal sprays. It also afforded the team with equipment for the development, scale up and commercial manufacture of inhalation products. In acquiring access to specialist development suites at the facility, Recipharm can contribute to the advances in inhalation science and launch new patient-centric products that can improve the lives of people living with conditions like asthma and other prevalent respiratory diseases. To better satisfy customer needs, we continue our investment in building new MDI and nasal spray production lines as well as expanding dry powder filling capability at our manufacturing site.

What has been the biggest recent advancement for Recipharm within inhalation?

In a bid to continue to expand our development and manufacturing offering for inhalation and nasal dosage forms including MDIs, DPIs, soft mist inhalers, nebulizers, nasal sprays and nasal powders, we are continuing our M&A strategy. As part of this, we are looking at different capabilities to add to our offering, including the onboarding of medical devices, to support our growth in the inhalation market.

From a technical perspective, we invested in a SprayVIEW system at our Research Triangle Park (RTP), US facility along with a newly built aerosol collection lab and modified development process lab. This strengthens our capability in supporting both inhalation and nasal product development and we expect more investment to take place in the coming months/years.

Outline the current challenges that Recipharm is working to overcome in the development of inhalation products?

At Recipharm, we are actively seeking to develop dual and triple API inhalation products. Although the development of these products is highly complex, they present pharma companies with an opportunity to deliver more patient centric medicines and gain a competitive edge, as they will remain patent protected for a long-term period.

Selecting the best dosage form is also a challenge that we work with our customers to overcome. For example, in the early phase development of new chemical entities for inhalation, providing a quality clinical supply is critical to reduce the development cycle. Recipharm supports and recommends selection of dosage forms and the delivery platform for first in human studies. This can include DPIs or nebulised solutions based on the desired dose, physicochemical properties including solubility and stability of the compounds.

Also, helping customers to understand drug development and clinical costs associated with inhalation drug products is also a key challenge. Due to their complexity, these products often involve a costly development process which is not fully recognised by customers. As an example, we have seen an increase in requests for drug products involving cannabidiol (CBD) and minimising costs for these types of projects is a key focus.

> *"Technology in the inhalation space has significantly evolved"*

What future innovations within inhaled formulations and devices do you expect to see over the next year? What impact will these advancements have upon the inhalation industry?

While inhalation therapy has a long history, it has been adopted more since the launch of the first nebuliser during the nineteenth century. Following the invention of the first MDI and DPI in the midst of the twentieth century, technology in the inhalation space has significantly evolved. Each advancement in inhalation sciences and technology has generated a large volume of products to patients. For example, the introduction of hydrofluoroalkane (HFA) propellants delivered numerous MDI products to patients in the early 1990s. In addition, the invention of the soft mist inhaler device has enabled the launch of four inhaler products since the beginning of the 21st century.

More recently, successful development of the Ellipta DPI device and application of PulmoSphere™ particles made triple combination products accessible to patients with respiratory diseases.

Looking to the year ahead, we expect to see continuous advances in technologies and applications in the inhalation field. These include, but are not limited to, the following areas:

- New user and environment-friendly formulation and devices. For example, new DPIs make formulations more compatible for multiple compound products. We have seen more portable nebulizers under development and vaporised inhalers, which could offer potential advantages.
- Application of new particle technology in DPIs following the launch of MDIs based on the same technology will bring more products to the market.
- Smart inhalers will continue to grow.
- There is a potential need to explore more environment-friendly propellants for MDIs.
- New molecules, especially biologicals for inhalation, will start to appear which will require specific formulation technologies and delivery platforms.
- Dual or multiple compound inhalers for controlling chronic obstructive pulmonary disease (COPD) and severe asthma are in increasing demand.
- Inhaled drugs for new applications or the same application via inhalation or nasal routes through 505(b)2 regulatory path will bring more products to the market

In addition, developing generic inhalation products will continue to be a keen interest to reduce the burden of healthcare costs.

All these advances require scientists to take initiative and shorten the development cycle, whilst not compromising on product quality. The employment of new approaches, such as understanding in vitro and in vivo correlation of inhaled products, quality by design (QbD) throughout development, subsequent product life cycle management and working closely with regulatory agents will likely become routine in the inhalation industry, ultimately bringing more quality products to patients.

THE DEVELOPMENT OF DRY POWDER INHALERS FOR LARGE DRUG PAYLOADS

PAVAN MUTTIL

We have made significant progress toward delivering therapeutics to the lung in the last half-century.

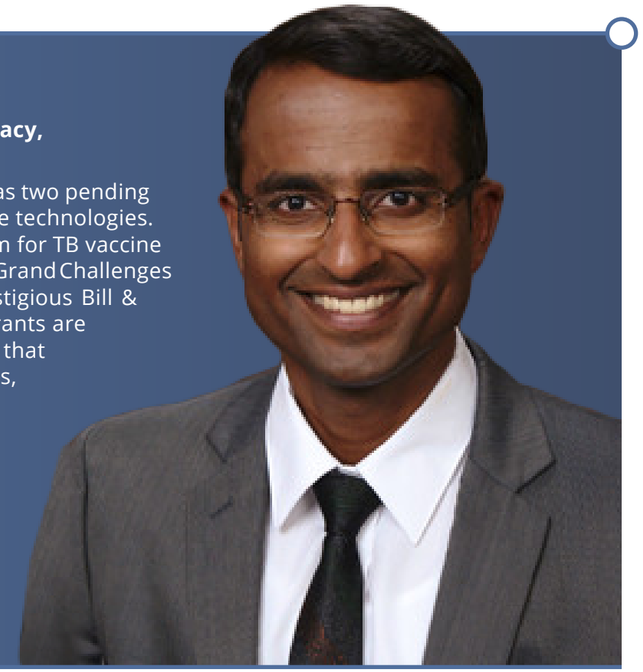
Therapeutics are delivered using devices such as pressurized metered-dose inhalers (pMDIs), nebulizers, and dry powder inhalers (DPIs); however, all these devices require different formulation approaches to deliver the therapeutics reproducibly to the lung. In recent years, DPIs have gained popularity as a pulmonary therapeutic delivery option because of the consistency in lung dosing, ease of patient use, short delivery time, and the improved stability that is inherent to dry powder formulations. The range of diseases that are being treated using DPIs have expanded tremendously from asthma and chronic obstructive pulmonary disease (COPD) to infectious diseases; this is reflected in the total sales for DPIs in 2014 alone was more than $17 billion, higher than the combined revenues generated for pMDIs and nebulizers (IQVIA Inc. (Durham, NH). MIDAS®, 2016)[1]. Dry powders for use with DPIs have historically been formulated using 'top-down' approaches such as milling. However, milling technique has challenges such as requiring inactive lactose carrier particles to ensure proper powder de-aggregation in the device, and variable powder performance due to poorly understood effect of milling on powder properties[2]; these are critical formulation properties for DPIs to have consistent performance. In the last two decades, powders for inhalation have been formulated using 'bottom-up' approaches such as spray drying (SD) due to its superiority over 'top-down' manufacturing processes. SD allows powders to be engineered in the respirable size range, is a continuous manufacturing process that allows easy scalability, and permits the use different excipients to have better control over powder properties and hence formulation-device performance; the evaluation of formulation-device combination is a mandatory requirement by regulatory agencies such as the FDA. Such an evaluation would also ensure that the various inhaler components are compatible with the dry powder. SD also generates low-density powders that can easily de-aggregate and could potentially exclude the use of carrier particles. One potential drawback of SD powders, however, is their amorphous nature that is prone to degradation during storage; therefore, SD powders will require protective packaging to ensure product stability during its shelf life.

There has been a recent interest in treating lung infections by delivering 'low potency' antibiotics by the pulmonary route; these antibiotics require a milligram-to-gram range of powder dosing to achieve therapeutic efficacy[3]. In 2013, Novartis received FDA approval for the Tobi Podhaler for treating lung infections associated with cystic fibrosis. This product showed, for the first time, the feasibility of delivering high powder doses using DPIs. The Tobi Podhaler contains powders developed using the PulmoSphere™ technology that has porous characteristics with improved flow and dispersion properties, and are manufactured using an emulsion-based SD process[4]. One of the drawbacks of using Podhaler is the requirement of multiple capsules to achieve high powder dosing (28 mg power per capsule- 4 capsules total); this could lead to an increase in patient error during multiple inhalation maneuvers and potentially lack of patient compliance[5]. Further, the overall inhaled powder volume increases due to the highly porous nature of PulmoSphere™ powders. Therefore, the development of novel formulations is required such as those containing little or no excipients to minimize multiple inhalation maneuvers and improve patient compliance. SD technology allows for fine control over multiple process parameters that can alter a wide range of particle properties such as density, size distribution, surface morphology (smooth or rough), water content, particle shape, etc.

Pavan Muttil, Associate Professor, Dept. of Pharmaceutical Sciences, College of Pharmacy, University of New Mexico

Dr. Muttil has disclosed nine inventions and has two pending patent applications for his inhaled/oral vaccine technologies. Dr. Muttil's dry powder inhaled delivery system for TB vaccine BCG received a $100,000 Phase I grant from the Grand Challenges Explorations, an initiative funded by the prestigious Bill & Melinda Gates Foundation. The Foundation grants are awarded for the most innovative research that targets solutions to major health problems, particularly in developing countries.

Dr. Muttil's technologies are focused on developing novel dry powders for inhaled/oral vaccines and drugs against various infectious diseases and cancers. These dry powders are prepared using a spray drying technology and are ultimately evaluated in different animal models for their efficacy.



> *"SD also generates low-density powders that can easily de-aggregate and could potentially exclude the use of carrier particles"*

Next-generation DPIs are being developed to accommodate the high dose dry powder delivery. Existing DPIs for asthma and COPD treatment have used carrier particles to achieve better flow and dispersion characteristics for powders with high cohesive properties. However, the use of carrier particles for high payload drugs is not feasible due to the reasons outlined above. Future DPIs need to be more powerful to disperse the powders efficiently and reproducibly, and to provide consistent lung dosing. This can be achieved by studying the role of active vs passive DPIs (dependence on the inspiratory flow rate from patients) to maximize aerosolization performance from the device. It is also critical to evaluate DPIs that use either capsules or cartridges to store and aerosolize powders. Capsule-based DPIs will require a higher flow rate to discharge powders for aerosolization due to their relatively small internal surface area and pin-sized perforations. On the other hand, cartridges could benefit from having a higher surface area and will provide better protection for dry powder formulations against moisture uptake[3].

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ADVANCING INHALATION DRUG DELIVERY
SUSAN HOE

SUSAN HOE, Associate Director, Inhalation Product Development, **AstraZeneca**

Susan Hoe is an Associate Director for Inhalation Product Development at AstraZeneca, located in South San Francisco, CA. She currently leads preclinical and early phase development of inhaled biologics, and spray dried formulation platform development within the company. Since joining Pearl Therapeutics (now AstraZeneca) in 2014, Susan has supported product development for Bevespi Aerosphere, Breztri Aerosphere, and PT027 programs, in addition to her work driving the establishment of an inhaled biologics pipeline within AstraZeneca.

Prior to 2014, Susan conducted postdoctoral research into inhaled bacteriophage therapy, and spray dried formulation design via predictive in silico modelling, at the University of Alberta, Canada under Professor Reinhard Vehring. She holds a PhD in Pharmaceutical Science and Bachelor of Pharmacy from the University of Sydney, Australia.

What are your current priorities within biopharmaceutical development for inhalation drug delivery?

The current priority is to advance as many new modalities as quickly as possible through clinical development, to 'validate' these molecules against their target and via this route of administration, and gather enough data early on to make some initial decisions on what types of modalities are suitable for inhalation and which need more work and can be deprioritized. There is still much to learn and understand about the DMPK and PD of these biomolecules, and the inhalation safety profile of these molecules for patients with pre-existing respiratory disease is still in question.

Another priority is executing an appropriate device and manufacturing strategy for these new modalities. These biomolecules necessitate an investment in infrastructure to potentially support entire franchises at the commercial scale, infrastructure which is currently lacking within most pharmaceutical companies and is in question for CMOs specializing in inhalation. There is also a need to rethink device design, as these molecules are being formulated in ways that have additional requirements that current devices cannot or struggle to deliver (e.g. moisture protection, high payload delivery).

What have been the biggest challenges that you have had to overcome within this field?

The major challenge has been to define the development strategy in this area that has limited regulatory guidance and very little published safety data. The most conservative approach is to adopt appropriate requirements from both inhalation product development and large molecule injectables development, however this creates an immense amount of work to generate data, some of which is potentially unnecessary. It also significantly limits avenues for inhalation product development, which in turn may lead to molecules being terminated prematurely, however patient safety is paramount and

application of injectable biomolecule requirements mitigates business and patient risk. This is an area that continues to be debated, and without conclusive patient safety and tolerability data it is difficult to assess the risk level.

What are some priorities for your work within this field over the next year?

Similar answer to Question 1 - Progressing several biomolecules to Phase 1 and generate safety and tolerability data not only for the biomolecules, but also for the formulations, which contain novel excipients for the inhalation route.

Another priority is to expand our understanding of particle formation models and drying kinetics to spray dried formulations containing biomolecules, and how this correlates to the physical properties of the subsequent powder. Properties such as moisture sensitivity, hygroscopicity, aerosol performance, powder density, and so on are key to drug product performance. Since the device and manufacturing strategies are currently in design or open to redesign, there is a lot of interplay between how a formulation is selected and the viability of the biomolecule as a commercial product. There is no defined decision tree that says modality X has to use formulation Y, and device Z, in order to be acceptable. The aim is not to create something like this, but rather to create a general set of guidelines for each modality. Reinvestigating particle formation modeling, how the biomolecules are distributed on the particle surface, and what impact this has on the final drug product, is a key priority.

> *"Improvements in animal models predicting the safety, efficacy, and DMPK of inhaled biomolecules will have a major impact on the progress of inhaled biomolecules development."*

Looking forward, what future innovations do you anticipate that will progress inhaled therapy development?

The industry is primarily focused on monoclonal antibodies, but we are already seeing new classes of engineered proteins entering pre-clinical or early clinical development with certain liabilities mutated out of the protein sequence (e.g. for molecular stability, improved binding affinity, improved specificity, improved manufacturability). Given that the formulation options for inhalation are still rather limited, protein engineering innovations are a key aspect to consider in deriving a viable inhaled drug product.

This may be more of a wish than an anticipation, but improvements in animal models predicting the safety, efficacy, and DMPK of inhaled biomolecules will have a major impact on the progress of inhaled biomolecules development. De-risking pre-clinical development will open up the biomolecules pipeline.

How do you expect goals of carbon footprint reduction may affect manufacturing and strategy within this industry?

For the inhalation industry as a whole, carbon footprint reduction is an issue already affecting strategy. Global warming concerns within the general population has been discussed as a potential reason for doctors to prescribe DPIs over pMDIs. There has been a recent announcement by Chiesi to transition to lower global warming potential propellants in their pMDIs. The total carbon footprint of pharmaceutical-grade propellants are dwarfed by the footprint of other industries, however as regulations on propellant manufacture tighten, the use of HFA-134a and HFA-227ea propellants may rapidly become cost-prohibitive and the supply chain strategy could also weaken should suppliers choose to exit the market.

Another aspect that I don't see discussed much is how the development of biomolecules in dry powder format could potentially achieve carbon footprint reduction by eliminating the cold chain. Spray drying, freeze drying, are energy intensive processes, but are transient. Biomolecules in liquid require refrigeration and/or freezing from beginning to end (drug substance to fill-finish, storage in warehouses, shipment, storage in hospitals or at home).

Susan Hoe will be speaking on "*Challenges and Opportunities with Excipients in Inhalation Drug Product Development*" on Day 1 of our 3rd Annual Inhalation & Respiratory Drug Delivery USA Congress, 17 – 18 March 2020, San Diego USA in the stream Development & Formulation of Inhaled Therapies.

OXFORD GLOBAL CONFERENCES

FORTHCOMING EVENTS

OXFORD GLOBAL CONFERENCES

Biologics Series

UK

13th Annual Proteins & Antibodies Congress
27 - 29 April 2020 | London, UK

7th Annual Peptides & Oligonucleotides Congress
27 - 29 April 2020 | London, UK

2nd Annual Bispecifics in Discovery & Development Congress
27 - 29 April 2020 | London, UK

Co-located Events

Biomarkers Series

UK

15th Annual Biomarkers Congress
18 - 20 February 2020 | Manchester, UK

Genomic Markers Congress
18 - 20 February 2020 | Manchester, UK

Co-located Events

US

5th Annual Biomarkers & Precision Medicine USA Congress
October 2020 | San Diego, USA

Cell Series

UK

9th Annual Cell Culture & Bioprocessing Congress
06 - 07 October 2020 | London, UK

7th Annual Regenerative Medicine & Advanced Therapy Development Congress
06 - 07 October 2020 | London, UK

6th Annual Cell & Gene Therapy Manufacturing Congress
06 - 07 October 2020 | London, UK

Co-located Events

Formulation & Delivery Series

UK

6th Annual Formulation & Drug Delivery Congress
22 - 23 April 2020 | London, UK

5th Annual Inhalation & Respiratory Drug Delivery Congress
22 - 23 April 2020 | London, UK

Biomanufacturing Congress
22 - 23 April 2020 | London, UK

Co-located Events

US

3rd Annual Formulation & Drug Delivery USA Congress
17 - 18 March 2020 | San Diego, USA

3rd Annual Inhalation & Respiratory Drug Delivery USA Congress
17 - 18 March 2020 | San Diego, USA

Co-located Events

Immuno Series

UK

5th Annual Advances in Immuno-Oncology Congress
21 - 22 May 2020 | London, UK

Autoimmunity & Immunology Congress
21 - 22 May 2020 | London, UK

Co-located Events

US

3rd Annual Advances in Immuno-Oncology USA Congress
October 2020 | San Diego, USA

PharmaTec Series

UK

18th Annual Pharmaceutical IT & Data Congress
24 - 25 September 2020 | London, UK

4th Annual Artificial Intelligence in Drug Development Congress
24 - 25 September 2020 | London, UK

2nd Annual SmartLabs & Laboratory Informatics Congress
24 - 25 September 2020 | London, UK

Co-located Events

R&D Series

EU

21st Annual Drug Discovery Summit
26 - 27 May 2020 | Berlin, Germany

8th Annual Drug Design and Medicinal Chemistry Congress
26 - 27 May 2020 | Berlin, Germany

2nd Annual Neuroscience Drug Discovery Congress
26 - 27 May 2020 | Berlin, Germany

Co-located Events

NextGen Omics Series

UK

12th Annual Next Generation Sequencing & Clinical Diagnostics Congress
05 - 06 November 2020 | London, UK

8th Annual Single Cell Analysis Congress
05 - 06 November 2020 | London, UK

6th Annual Genome Editing Congress
05 - 06 November 2020 | London, UK

2nd Annual Digital PCR Congress
05 - 06 November 2020 | London, UK

Co-located Events

US

6th Annual Next Generation Sequencing USA Congress
07 - 08 April 2020 | Boston, USA

6th Annual Single Cell Analysis USA Congress
07 - 08 April 2020 | Boston, USA

4th Annual Genome Editing USA Congress
07 - 08 April 2020 | Boston, USA

Co-located Events

Register your interest, e-mail us:

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