CASE STUDY REPORT

Enhancing Drug Stability & Exploring Novel Formulation Strategies

A Concise Report Featuring Insights From The Prominent Thought Leaders Of Formulation & Delivery UK 2024

Introduction

The pharmaceutical sector is undergoing rapid change due to continuous innovation and unprecedented technological growth. Research into new therapies and improved treatment modalities is highly encouraging. The global drug formulation market was estimated to be valued at $1.64 trillion USD in 2022 and it is estimated to be worth $2.95 trillion USD by 2032, with an impressive CAGR of 6.05% during the forecast period. At the centre of this market report lies three key themes that encapsulate the milestones and challenges within drug formulation and delivery.

Innovative Drug Delivery Systems

Technological advancements are improving injectable drug delivery formulation products, enhancing their efficacy and adaptability across multiple industries. Transdermal drug delivery in particular plays a key role in the growth of the market due to its advantages including non-invasive administration, sustained release, and improved patient compliance. Due to the ease of uptake, the oral drug delivery segment is the most preferred method of administration. Insights from industry experts in this market report show that ocular and pulmonary drug delivery segments are also widely considered for the pharmaceutical market products.

Challenges & Opportunities in Drug Manufacturing and Stability

Ensuring the stability of novel therapeutics particularly biologics was a recurring theme in this market report. The case studies demonstrate that rigorous stability testing and analytical requirements for monoclonal antibodies is important. While small molecule drugs are easier and cheaper to manufacture, the interest around developing and manufacturing biologics has exploded in the last few years post COVID-19.

Computational and Mechanistic Modelling in Drug Development

Computational methods can predict material behaviour thus optimising drug formulation and manufacturing procedures. In-silico modelling and high throughput screening can foster rapid formulation development to enhance drug solubility, displaying the effect of computational approaches in accelerating drug development.

This market report draws upon of insights from the recent Formulation & Delivery 2024 event, a meeting of over the 400 key opinion leaders committed to reshaping formulation strategies and drug delivery methods. Through an in-depth analysis of presentations, data and expert opinions, this report aims to offer a refined understanding of the current paradigm, strategic challenges, and emerging opportunities in drug formulation and delivery.

Lucia Simmen,
Digital Content Assistant, Oxford Global

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Key Speakers Include

Ijeoma Uchegbu ,
Professor ,
University College London

Declan Lowney ,
Director of Stability Sciences, Janssen

Stephen Pham
Senior Vice President
Avalyn Pharma

Key Speakers Include

Chrsitopher Locher
CEO, Versatope Therapeutics

Jérôme Mantanus,
Associate Director ,
UCB

Ildiko Terebesi,
Managing Director,
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Key Speakers Include

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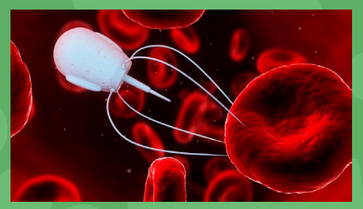
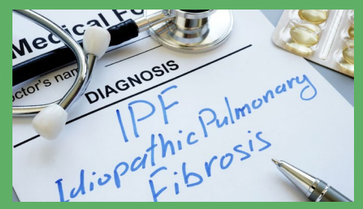
- RNA beyond the liver: challenges in non-liver RNA therapeutic delivery





Innovative Drug Delivery Systems

The global drug delivery system is projected to grow from USD $46.23 billion in 2024 to USD $96.34 billion by 2032. Market growth is propelled by the increased adoption of self-administered devices among patients. Furthermore, the digitalisation of medical devices has improved awareness of advanced products among patients.

Source: Fortune Business Insights

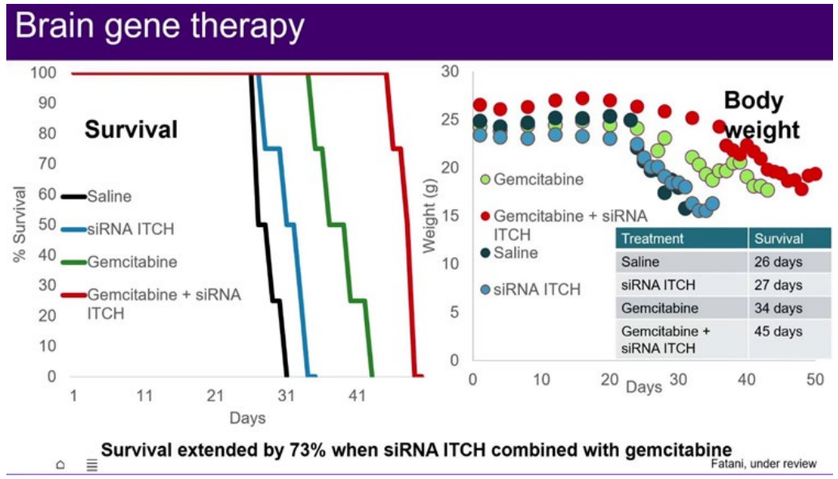
Controlling In Vivo Drug Transport Using Nanotechnology

Ijeoma Uchegbu (Professor, UCL) discussed UCL's new oncology platform and UCL's work in brain drug delivery. Uchegbu gave a brief overview of drug discovery and drug development processes and highlighted the expensive, inefficient, and risky nature of drug development. She mentioned that a key contributor to these failures is having poor drug exposure at the target site.

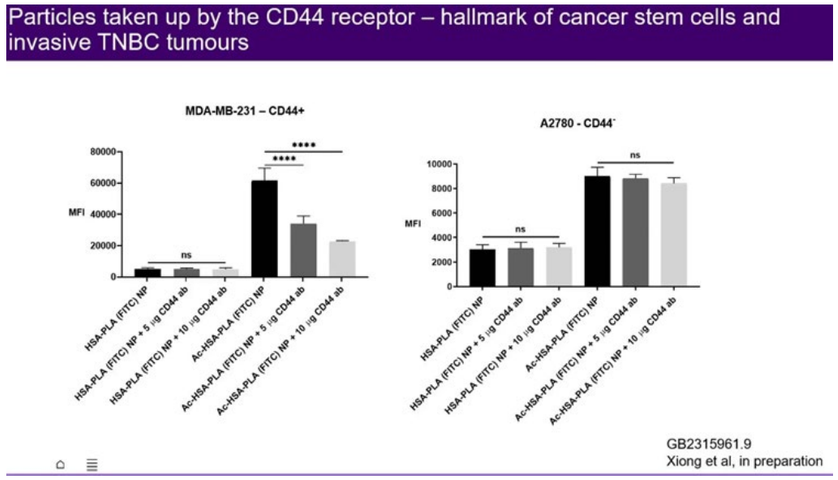
Patients with chronic conditions sometimes don't take their prescribed medication due to fear of side effects. UCL aims to repurpose medication using nanotechnology. UCL has had success in delivering nucleic acid into the brain. Nucleic acids differ from nanoparticles in terms of structure and size. Uchegbu highlighted the importance of brain delivery, it is a highly unmet need and the treatment of CNS diseases has been hindered by the blood brain barrier.

Uchegbu and her team aimed to deliver genes to the brain through the nose. The higher the dose the higher the response in the mouse models, the study showed that there was expression in the olfactory bulb, cortex, and striatum. The study also aimed to demonstrate whether silencing the ITCH gene would lead to apoptosis. The ITCH gene targets p73 protein for degradation.

The anti-ITCH RNA turns off the ITCH gene leading to over expression of p73, thus better cell kill. However upregulating p73 in the presence of gemcitabine proved to be highly effective. The study showed that nucleic acids could be delivered to the brain and the nucleic acids had a pharmacological effect.



UCL also developed an oncology platform for triple negative breast cancer. Metastatic triple negative breast cancer has a very poor survival rate of just 12%. Using nanoparticles, targeted delivery to cancer stem cells via CD44 receptors was achieved leading to significant tumour regression in mouse models.



Uchegbu also briefly highlighted the commercialisation efforts conducted by her company, Nanomerics. Nanomerics have developed an active excipient-based approach, aiming to enhance drug targeting and bioavailability. She gave a brief overview of Nanaomerics's current pipeline.

Overall, Uchegbu summarised by reiterating the importance of delivering nucleic acids to the brain and she indicated the usefulness of UCL's oncology platform in targeting cancer cells.

nanoVAST: Non-Viral Cell Membrane Fusogenic Vesicles For Nucleic Acid Delivery

Panasome is a startup biotech that is currently developing a platform for nucleic acid delivery. Dimitra Stamkopoulou (Scientist, Panosome) introduced Panosome's delivery

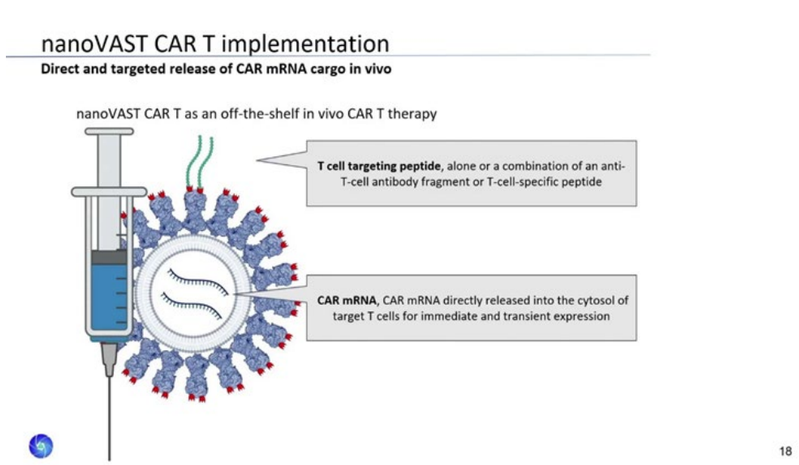
technology, nanoVAST. nanoVAST are extracellular vesicles produced by trypanosome membranes.

The aim of this therapeutic delivery is to overcome the three main challenges associated with cell-specific payload delivery: delivering specifically to target cells, releasing cargo into cytoplasm and manufacturing to scale. VAST technology makes variant surface glycoproteins (VSGs) targetable to any molecule of choice. This platform was developed for small molecule VSG.

nanoVAST could target specific cells and efficiently deliver cargo. nanoVAST deliver cargo directly to the cytoplasm by fusion. Furthermore, nanoVAST is continuously optimised to deliver diverse cargo. The unique fusion mechanism of nanoVAST allows cargo delivery and is a key differentiator and provides a way of avoiding the endosomal pathway.

From a manufacturing standpoint, nanoVAST production is a quick process yielding highly homogenous material. The trypanosome culture goes through sonification, purification and sortagging. Stamkopoulou mentions that her company aim to upscale this process.

Currently they aim to implement this technology in in-vivo CAR T cell therapy. Since CAR T cell therapy involves extracting the cells from the patient to be modified and then inserted back into the patient's bloodstream, researchers are looking to save time by looking into in-vivo processes. NanoVAST could fit into this demand by direct and targeted release of CAR mRNA cargo in vivo.



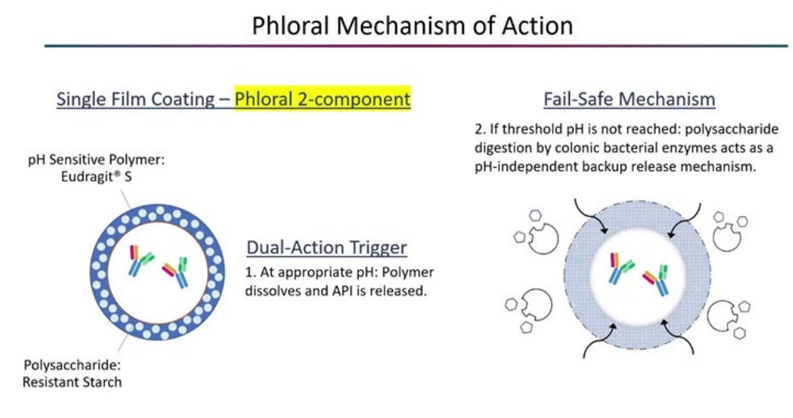
Development of Drug Delivery Tecnologies For Oral Biologics

Maurits Kleijnen (Head of Research, Intract Pharma) highlighted the expertise and capabilities of Intract Pharma, a spinout from UCL School of Pharmacy formed in 2016. The focus of their work lies in the delivery of small molecules and large protein biotherapeutics. Kleijnen outlined their proficiency in several areas, including coating technologies for targeted delivery to the gastrointestinal (GI) tract, payload stabilisation and protection, and strategies for enhancing payload uptake.

Intract Pharma offers various ex vivo GI models to test stability and tissue uptake, as well as small animal studies for pharmacokinetic (PK) and pharmacodynamic (PD) assessments. They described their involvement in the development of formulations for large animal experiments and their role in scaling up formulations for tech transfer to GMP manufacturing.

Their technology development efforts centre around three main areas: improving targeting of active pharmaceutical ingredients (APIs) to the GI tract, enhancing API protection and preservation in the harsh GI environment, and improving payload uptake into tissue and systemic circulation.

One of their key technologies discussed was the Phloral pill coating, which enables pH-dependent release of payload in the GI tract. They also introduced Soteria, a formulation designed to protect protein therapeutics from degradation in the GI tract, thereby improving their bioavailability**.**



Kleijnen elaborated on the rationale for delivering monoclonal antibodies orally, particularly in the context of inflammatory bowel diseases (IBD), where the compromised epithelial barrier allows for antibody uptake into the tissue. They discussed the potential advantages of oral delivery, including achieving high local concentrations at the target site and potentially reducing toxicity and off-target effects compared to intravenous administration.

In their pursuit of improving antibody uptake across the healthy GI epithelium, Intract Pharma is actively researching formulation permeation enhancers and active transport mechanisms. They introduced a novel technology involving engineered fusion proteins that uses pancreatic lipase-mediated transcytosis to facilitate antibody transport across epithelial cells.

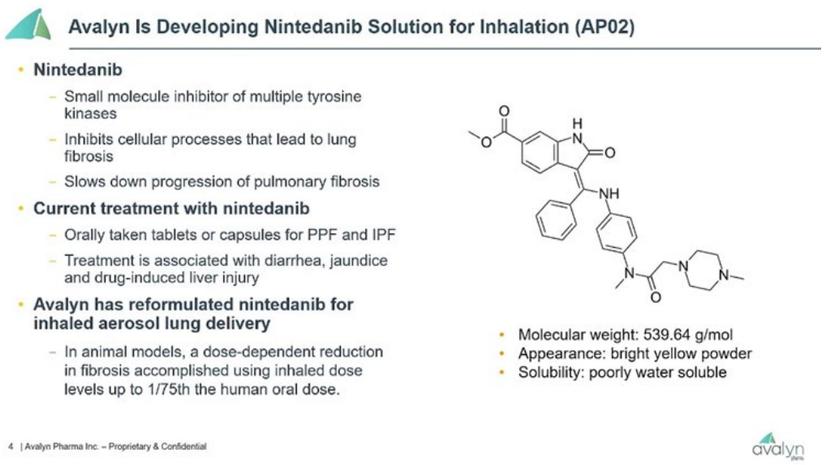
Overall, Kleijnen's talk showcased Intract Pharma's comprehensive approach to drug delivery, encompassing targeting strategies, protection technologies, and innovative approaches to enhancing payload uptake, with a focus on improving therapeutic outcomes for patients with GI-related conditions.

Kleijnen's presentation shows his team's comprehensive expertise in GI drug delivery, their innovative solutions to overcome existing challenges, and their commitment to advancing pharmaceutical technologies**.**

Challenges In The Development Of Inhaled Nintedanib for IPF and PPF

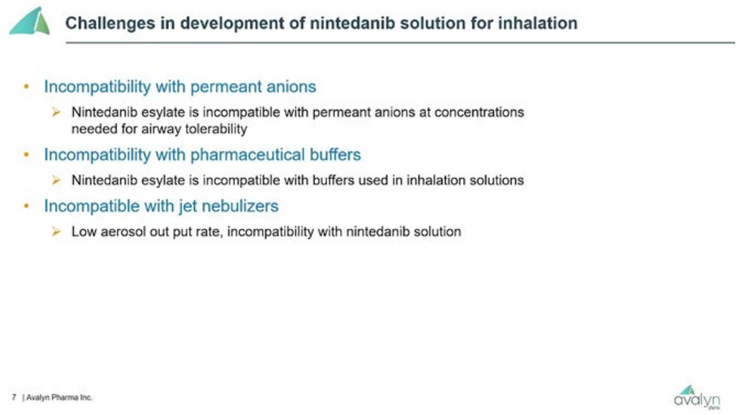
Stephen Pham (Senior Vice President, Avalyn Pharma) provided an outline of the challenges involved in developing inhaled and intended IV formulations for treating progressive lung diseases such as idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF). He began by acknowledging the brutal nature of these diseases, characterised by the gradual scarring of lung tissue, leading to a loss of lung function over time and ultimately resulting in respiratory failure and death. Pham claimed that the lack of effective treatments for these conditions, underlining the pressing need for innovative therapeutic approaches.

The presentation focused on Avalyn Pharma's efforts to address these challenges by delivering existing drugs directly to the lungs through inhalation, aiming to improve drug efficacy while minimising systemic side effects. Pham introduced Nintedanib, a small molecule inhibitor of multiple tyrosine kinases, as a potential candidate for inhalation therapy. He explained that while Nintedanib is currently available in oral tablet or capsule form, its systemic administration is associated with significant side effects, including gastrointestinal issues and drug-induced liver injury.



To overcome these limitations, Avalyn Pharma sought to develop an inhaled formulation of Nintedanib, with the goal of increasing lung exposure and reducing systemic exposure. Pham discussed the formulation challenges involved in this process, such as achieving the optimal pH, osmolality, and chloride ion concentration to ensure airway tolerability and prevent coughing during inhalation. He also highlighted the importance of selecting appropriate excipients and buffers compatible with the intended route of administration.

The fast path to toxicological assessment and clinical evaluation and the overall suitability for PPF and IPF patients were the main justifications for selecting nebulization as a route of administration. Furthermore, Pham discussed the challenges related to nebulization, including the selection of suitable nebulizers capable of producing the desired aerosol output rate and particle size distribution. He described the company's efforts to identify compatible nebulizers and optimize the drug formulation for effective delivery to the lungs.



Despite these challenges, Pham highlighted the promising results of phase I studies, which demonstrated the safety and tolerability of the inhaled Nintedanib formulation in 38 participants healthy volunteers and IPF patients. The lack of side effects in the volunteers shows that the formulation is promising. He outlined plans to advance the program to phase two, with the goal of further evaluating the efficacy of the treatment in larger patient populations.

In conclusion, Pham's presentation provided valuable insights into the development of inhaled therapies for progressive lung diseases, highlighting the importance of overcoming formulation and delivery challenges to improve patient outcomes.

Novel DDS For Neonatal Respiratory Distress Syndrome Treatment

Neonatal respiratory distress syndrome (nRDS) is disease of lung surfactant deficiency, meaning patients struggle to breathe and this leads to high rates of mortality and morbidity. Current treatment options include non-invasive ventilation support and lung surfactant intratracheal administration. However, these methods have limitations including invasiveness and uneven distribution of surfactants in the lungs.

James Min (Senior Scientist, Pfizer) proposed using microbubbles in aerosols to improve lung penetration and distribution of surfactants. Microbubbles were hypothesized to reduce aerosol density, thereby enhancing penetration into the small nasal airways of preterm infants. The study used a setup mimicking clinical conditions, including non-invasive mechanical ventilation support and a 3D-printed model of a preterm baby's airways.

Results showed that incorporating microbubbles into aerosols reduced aerodynamic diameter and increased the number of aerosols with sizes below one micrometre. Moreover, microbubble aerosols demonstrated improved lung penetration compared to conventional aerosols in the preterm neonate model.

Limitations of the study included its reliance on a single 3D-printed model and the lack of exhalation mechanism in the model. Further investigation is needed to confirm the role of submicron aerosols in lung penetration.

In conclusion, the study suggested that microbubbles could enhance the effectiveness of nebulized lung surfactant therapy in preterm infants by improving aerosol penetration into the lungs.

Challenges & Opportunities in Drug Manufacturing and Stability

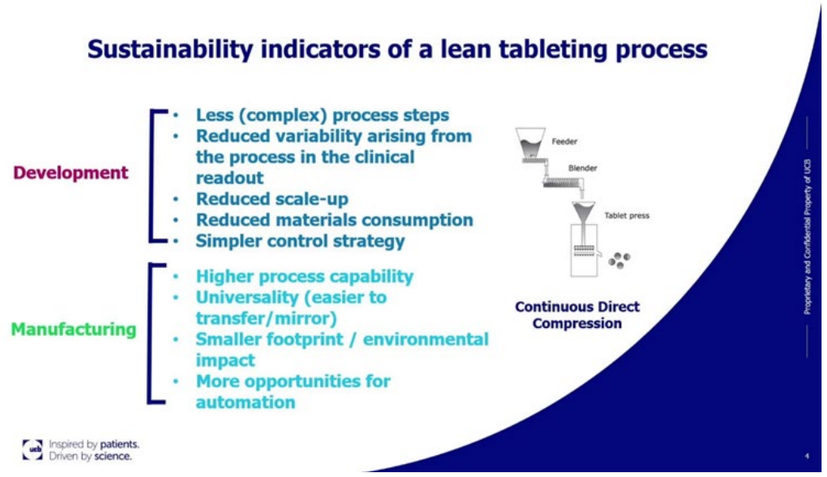
Accoring to European Pharmaceutical Review In 2022, 40% of US Food and Drug Administration (FDA) approved drugs were biologics. There is a projected compound annual growth rate (CAGR) of 9.5%% through 2027. Furthermore, this growth is occurring alongside a significant number of clinical trials, with nearly 20,000 active investigations involving approximately 9,500 new biologic treatments. This reiterates that the biologics market is booming and there are endless opportunities for scientists to tap into the area of biologics formulation and development.

Source: GMInsights

Designing Sustainability Into Drug Product Manufacturing – A Particle Engineering Story

Jérôme Mantanus (Associate Director, Head of Materials UCB) focused on the importance of the properties of active pharmaceutical ingredients (APIs) and formulation screening and how this influences commercialisation. He started by introducing tableted oral solid dosage forms (OSDs) and their main advantages including long shelf-life, accurate dosing, convenience, and patient-centricity.

At UCB anticipating sustainability by design affects the commercial picture related to Drug Product Manufacturing. Designing sustainable methods when developing and manufacturing OSDs is important. Mantanus highlights these sustainability indicators.



The continuous direct compression (CDC) stands as a critical sustainable scenario for DP manufacturing. CDC requires specific API particle and powder properties. Particle engineering involves optimising the nanoparticles via crystallisation and formulation screening. Crystallisation improves the particle properties by improving their MCS score and their potential to switch from wet to dry processing.

Mantanus explains how advances in technology, such as computational modelling and simulation, aid in material selection and formulation development for direct compression.

CDC is also affected by drug loading, compromising on the drug loading can facilitate drug development. The smaller the RSD the better the tablet.

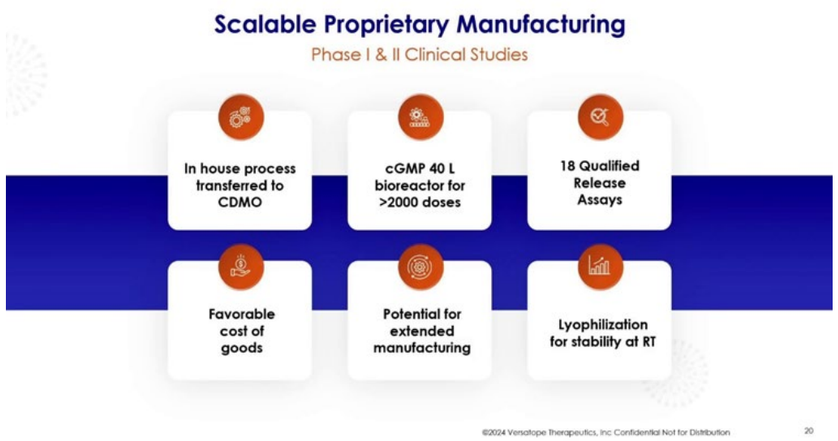
By fostering collaboration across disciplines within CMC (Chemistry, Manufacturing & Controls) and leveraging innovative methodologies like continuous direct compression, Mantanus shows the importance of integrating sustainability into every stage of drug product development.

Cell Specific Targeting Of Therapeutics Using Nanovesicles

Christopher Locher (CEO, Versatope Therapeutics) introduced the nanovesicles' therapeutic characteristics. He mentioned their safety profile, surface display of antibodies and cell-targeting affibodies and scale up with adapted bioreactor processes. Manufacturing nanovesicles is notoriously challenging but Versatope Therapeutics has developed a cGMP process for scale up and purification.

Versatope's rET-Vs attributes include tissue penetration to deliver payloads, specific cell targeting, potential for oral delivery and carriers of RNA for re-programming. By genetically engineering lipo-polysaccharides, scientists can improve tolerance and reduce reactogenicity. Versatope's vesicles can help kill cancer cells by cross-priming of CD8+ cells.

By using targeting technology vesicles can reach the tumour environment much quicker than free vesicles which tend to move and bind to the liver. Locher highlighted that Versatope Therapeutics has developed a scalable proprietary manufacturing process.



Locher stated the importance of getting good quality product which requires optimisation. 100 bioreactor runs were performed to achieve the top-quality product. A good quality vesicle is determined using SDS-PAGE densitometry. Nanoparticle tracking analysis gives insight into particle size.

Overall, Locher concluded by reiterating that the hurdles of reactogenicity can be managed by genetic engineering. Moreover, scale up and purification is feasible and there are multiple routes of administration.

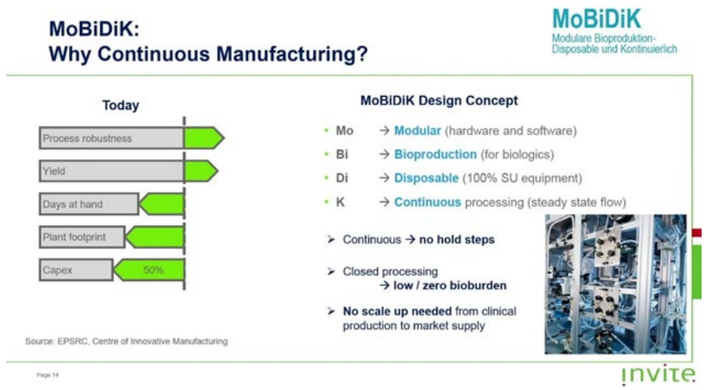
High Dose Formulation & Continuous Manufacturing Processes For Biologicals

Ildiko Terebesi, (Managing Director, Invite Research), provided insights into two projects during her talk. Invite Research is a public-private partnership located in Cologne, Germany, focusing on innovative production technologies for the pharmaceutical industry. Terebesi stressed the collaborative nature of their work, involving academia, industry, and pharmaceutical partners.

Their Drug Delivery Innovation Center (DDIC) is an open consortium with academic and industrial partners for pre-competitive research on drug delivery. The overall aim is to bridge the gap between academic research and industry.

The first project focused on high-dose formulations and quantum manufacturing processes for biologicals. Collaborating with universities in Dortmund and Munich, the project aimed to address stability issues associated with high-concentration protein formulations. By evaluating solubility, colloidal stability, and conformational stability, they identified optimal excipient mixtures using a modelling approach based on thermodynamic considerations. Their findings suggested that certain amino acids, like arginine and histidine, were most suitable for improving solubility and stability.

The second project, named MoBiDIK, aimed to develop modular and continuous manufacturing processes for biologics. This project emphasized the need for robust, efficient, and scalable production methods. Through a large consortium involving academic and industrial partners, Terebesi successfully demonstrated a single-use closed system for continuous bioprocessing, showcasing its robustness and scalability compared to traditional batch processes.



Overall, Terebesi pointed out the importance of collaborative research and innovative approaches to address challenges in pharmaceutical manufacturing, particularly in the development of high-dose formulations and advanced manufacturing processes for biologicals.

Stability Considerations For Protein Therapeutics

Declan Lowney (Director of Stability Sciences, Janssen) discussed the distinctions between monoclonal antibodies (mAbs) and other therapeutic proteins, as well as the analytical methods and regulatory requirements involved in ensuring their stability and quality.

He highlighted that mAbs are derived from biological systems, such as recombinant DNA or non-recombinant cell culture systems, which distinguishes them from products produced by chemical synthesis. mAbs highly purified and characterized nature, along with their medium size (around 150 kilodaltons), sets them apart from polyclonal antibodies and other therapeutic proteins.

Lowney discussed the complexities involved in the production of biopharmaceuticals, including variability arising from fermentation processes and purification methods. In contrast, chemically synthesized products have discrete manufacturing steps and alternative synthetic routes.

Analytically, mAbs require accurate and sensitive methods to ensure their quality attributes, including identity, strength, purity, and stability. Techniques such as UV absorbance, capillary electrophoresis, mass spectrometry, and particle monitoring are employed to assess these attributes and detect degradation pathways like aggregation.

Stability testing, crucial for regulatory compliance, involves evaluating how the quality of the drug substance or product changes over time under various environmental conditions. Lowney outlined the regulatory guidelines for stability testing, emphasising the need for long-term real-time stability studies for mAbs, unlike small molecules where accelerated studies may suffice.

He also unpacked the challenges in stability study design, including the selection of representative batches, container closures, and storage conditions. Additionally, he highlighted the importance of considering factors like glass transition temperature, container compatibility, and temperature excursions in stability studies.

In summary, Lowney emphasized the additional challenges involved in stability testing for mAbs compared to small molecules, including the need for representative batch selection, complex analytical methods, and stringent regulatory requirements.

Unlocking the Potential of Continuous Pharmaceutical Spray Drying

Sune Andersen's (Principal Scientist, Janssen) talk discussed the potential of continuous pharmaceutical spray drying He began by discussing the dSdp manufacturing classification system. He suggested that balancing drug substance and drug product processes is crucial for optimal product development. He highlighted the need to navigate risk and guide towards success in both areas.

While the food industry has made significant advancements in spray drying, the pharmaceutical industry faces unique challenges due to smaller scale production, cost considerations, and sustainability concerns.

The talk then delved into the components of continuous spray drying, including solution preparation and filtration, spray drying itself, and secondary drying. While solution preparation and filtration are feasible for continuous production, secondary drying remains predominantly batch-oriented. Challenges in secondary drying include long drying times, solvent diffusion through particle shells, and the need to meet stringent solvent content requirements.

Andersen discussed examples of continuous spray drying setups in other industries. In the pharmaceutical industry, a batch-oriented setup with multiple reactors is commonly used to maximize efficiency while acknowledging the limitations of continuous secondary drying.

In summary, continuous pharmaceutical spray drying involves three unit operations: feed preparation and filtration, spray drying, and secondary drying. While the first two operations lend themselves well to continuous production, secondary drying remains a challenge, often requiring a batch-oriented approach. Integrating secondary drying techniques from other industries and leveraging new data on particle properties can help optimise spray drying processes in the pharmaceutical industry.

Computational & Mechanistic Modelling in Drug Development

Applications Of Mechanistic Modelling And Machine Learning In Pharmaceutical Product Development

Charely Wu (Professor, Chemical Engineering, University of Surrey) focused on the importance of product development. He raised the question of whether scientists can develop a digital tool that can assess the performance, process-ability and product properties of identified drug molecules. He addresses the product development challenges.

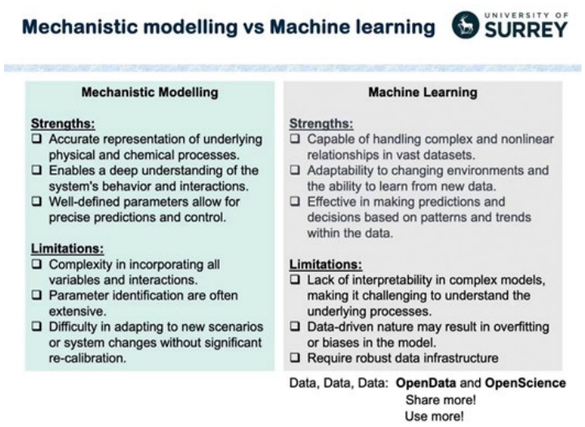
Can we predict the behaviour of API and excipients in formulation and manufacturing? Wu touched on the two computational approaches that could be used to predict this behaviour: mechanistic modelling and machine learning.

Wu's talk focused on using computational methods in product development, particularly in the context of solid dosage forms such as tablets. He discussed the challenges of predicting material behaviour in manufacturing processes and presented two computational approaches: mechanistic modelling and machine learning.

Mechanistic modelling is based on underlying physics, chemistry, or biology and involves formulating mathematical or numerical models to capture material behaviour. Wu illustrated various techniques, including discrete element modelling and computational fluid dynamics, to simulate powder behaviour and process dynamics.

On the other hand, machine learning involves training computers to learn from data and build predictive models. Wu demonstrated how machine learning algorithms can identify critical material attributes and process parameters, aiding in formulation optimisation and process control.

He highlighted the pros and cons of each approach, noting that mechanistic modelling provides a deeper understanding of processes but can be complex, while machine learning is data-driven and efficient but may lack mechanistic insight. Wu suggested the potential for hybrid models that integrate both approaches to leverage their respective strengths.



Overall, Wu's presentation summarised the role of computational methods in accelerating product development and optimising manufacturing processes in the pharmaceutical industry.

Transport Agitations Stress Model Systems For Biologics And Novel Lab-Scale Transport Simulation

Florian Rosenthal (Senior Scientist, Roche) provided a summary of the challenges and methodologies involved in validating the transport of pharmaceutical products, particularly focusing on liquid biologics. He explored the criticality of process validation, including shipping qualification, to ensure the safety and efficacy of drug products after commercial distribution. This set the context for his exploration into the complexities of assessing vibrations during transport and its impact on product quality.

One of the key challenges highlighted was the lack of representative testing methods for simulating real-world transport conditions in the laboratory. While lab simulation testing is a common practice across industries, it often falls short of accurately replicating the stress conditions experienced during actual transport. Rosenthal pointed out that certain health authorities do not fully accept lab simulation testing, necessitating the need for alternative approaches.

To address this challenge, Rosenthal and his team adopted a bottom-up approach, starting from a formulation perspective. He hypothesized that long-term vibrations during transport could lead to splashing and wave formation, potentially causing degradation of the protein in liquid products. This hypothesis formed the basis for their investigation into understanding input stress conditions and liquid behaviour during transport.

The presentation outlined the methodology employed, including computational fluid dynamics (CFD) modelling to describe liquid behaviour under vibrational excitation. This mechanistic modelling approach aimed to elucidate the effects of vibrations on liquid products, providing insights into potential degradation mechanisms.

Moreover, Rosenthal introduced a novel transportation checking system developed in collaboration with Zurich University of Applied Sciences. This system aimed to bridge the gap between lab simulations and real-world conditions by providing a more representative model for process validation. Through high-frequency data collection and analysis, Rosenthal's team was able to characterise vibrations in commercial shipping lanes and develop testing profiles that closely mimic real-world conditions.

Results from protein degradation studies using this system highlighted the importance of accurately simulating transport conditions. They observed visible particle formation and sub-visible particle formation when subjected to liquid splashing, highlighting the need for robust testing methodologies to ensure product stability.

In conclusion, Rosenthal stressed the importance of clearer guidelines and standards from health authorities to facilitate more effective transport validation studies in the pharmaceutical industry. By addressing these challenges and advancing methodologies for transport validation, Rosenthal and his team aimed to ensure the safety and efficacy of pharmaceutical products throughout their lifecycle.

The Response Of Inhaled Aerosols To High Humidity

Jonathan Reid (Professor, University of Bristol) explored the dynamics of pharmaceutical aerosols as they are delivered to the lungs through various inhalation devices, such as dry powder inhalers (DPIs), metered-dose inhalers (MDIs), and nebulizers. He highlighted the importance of understanding how aerosols behave during the inhalation process and how their characteristics can be altered to optimise drug delivery to specific regions of the lungs.

Reid explained the differences in aerosol generation among DPIs, MDIs, and nebulizers, noting that the source of the aerosol varies depending on the technique used. For example, DPIs produce dry powder, MDIs produce aerosols containing propellant coupled with ethanol, and nebulizers produce mist mainly composed of water, salt, and drug particles.

Aerosols undergo changes in size and water content as they travel through the respiratory tract. The increase in humidity within the lungs causes aerosols to take up water, leading

to changes in their size distribution. Reid emphasised that these changes in aerosol characteristics during inhalation affect where the drug dose is ultimately deposited in the lungs.

Reid introduced the concept of hygroscopic growth, which describes the increase in size of aerosol particles as they absorb water from the surrounding environment. He discussed how the hygroscopic properties of aerosols can be manipulated using excipient-enhanced growth techniques or enhanced condensation growth techniques to influence drug deposition in the lungs.

The talk also briefly touched on single-particle analysis techniques, such as using electronic balances to measure the evaporation dynamics of individual droplets, and how these techniques can be used to model aerosol behaviour during inhalation. Reid explained how understanding the dynamics of aerosol size change as a function of humidity can help predict where the drug dose will be delivered in the lungs.

Furthermore, Reid discussed the complexities of aerosol plume dynamics, particularly in soft mist inhalers. He highlighted research efforts to understand how plume behaviour affects drug delivery. He also presented data showing the evolution of aerosol size distribution over time and how changes in humidity can influence the mass concentration of aerosols in different lung regions.

In conclusion, it is important to integrate single-particle analysis techniques with plume dynamics studies to gain a comprehensive understanding of aerosol behaviour during inhalation. This knowledge can be used to optimise drug delivery strategies and improve therapeutic outcomes for patients with respiratory conditions

Report Summary

Overall, this case study report gives a comprehensive overview of the latest challenges and technologies in drug formulation and drug delivery. Experts in this report provided insights into the key technologies being adopted in drug formulation and delivery and they explained how scientists can leverage these tools to improve therapeutic outcomes.

Several projects in this report focused on harnessing nanotechnology for targeted drug delivery, particularly to the brain. Insights from the experts discussed delivering nucleic acids and repurposing medications using nanotechnology. Furthermore challenges like delivering across the BBB and poor drug exposure at target sites were addressed.

It has been widely acknowledged the biologics market is expanding but due to their size biologics present hurdles upon their delivery. However, scientists have risen to the challenge and are focusing on developing delivery technologies for oral biologics. There have been rigorous efforts concentrating on improving the targeting, protection, and uptake of active pharmaceutical ingredients (APIs) in the gastrointestinal (GI) tract. The phloral pill and soteria formulation aim to enable pH-dependent release and protect protein therapeutics from degradation in the GI tract, thus enhancing bioavailability.

In the latter half of this market report, key opinion leaders discussed the potential of continuous manufacturing processes that can address stability issues associated with high-concentration protein formulations and develop scalable production. Through collaboration, innovative approaches such as modular continuous bioprocessing improve efficiency and scalability in pharmaceutical manufacturing.

While there have been impressive advancements in formulation and delivery technologies, this market report also touches on the challenges that are facing the field. For example, regarding pharmaceutical spray drying, there are challenges in achieving continuous processing for secondary drying. Solution preparation and filtration can easily be adapted for continuous production, but secondary drying remains predominantly batch oriented due to factors like long drying times and strict solvent content requirements.

Furthermore, there are analytical challenges in characterising medium-sized and large molecules including regulatory requirements and the complex structural constraints of these molecules. Although there have been improvements in analytical methods like NMR and mass spectrometry, identifying impurities and understanding molecular structures remain challenging due to the molecules' unique characteristics.

To achieve optimal formulation conditions, factors such as pH, osmolality and ion concentration must be considered to ensure airway tolerability and prevent coughing during inhalation. This is a challenging endeavour so selecting the most suitable nebulisers and optimising drug formulations for effective delivery to the lungs requires balancing drug efficacy while minimising systemic side effects.

This report provided an overview of the latest trends and technologies being adopted in the drug formulation and delivery field. The experts pointed out the importance of implementing computational tools at various stages in drug development. Moreover, it is critical to explore ways of formulating and delivering biologics given their significant therapeutic potential.