TRANSFORMING DRUG DELIVERY WITH SYNERGISTIC WORKING

Here, Bas van Driel, Chief Executive Officer of DFE Pharma, discusses how expert collaborations can help develop a knowledge base to transform drug delivery and manufacturing. He shares how recent collaborative research projects involving lactose-based dry powder inhalation formulations, with and without magnesium stearate and lactose as an excipient in 3D tablet printing, have done just that.

The covid-19 pandemic has seen an unprecedented rate of innovation in the pharmaceutical industry. However, to continue this pace, the industry must harness the potential of collaborative working. It must recognise the value that committed stakeholders from industry, government, academia and patient advocacy groups can create by working together closely.

Successful partnerships can provide access to new technologies, provide valuable data-driven insights, help unlock new funding and contribute to delivering treatments for patients' unmet needs. Cross-sector working has already helped accomplish a great deal – proactive players in the market are keen to engage further in order to maintain and deepen their dialogues, as well as push the boundaries of what they can achieve (Figure 1).

Here are some recent examples of DFE Pharma's collaborations that are helping to transform the knowledge base for drug delivery and manufacturing.

Figure 1: A DFE Pharma manufacturing site in Germany.

Bas van Driel
Chief Executive Officer

DFE Pharma
Klever Strasse 187
47568 Goch
Germany

www.dfepharma.com

IMPROVING DPI FORMULATION STABILITY WITH MAGNESIUM STEARATE

Lactose-based dry powder inhaler (DPI) formulations are well established in the market for the treatment of asthma and chronic obstructive pulmonary disease (COPD). Recently, they have also been used in the treatment of covid-19. There is now a growing trend towards developing DPI formulations that are ternary mixtures that include magnesium stearate as well as lactose and the API. However, the successful delivery of the API into the lungs depends on numerous interconnected factors during the production process – the smallest formulation changes can have a major effect on the end result.

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Drug developers need to know how different qualities and combinations of excipients affect their final formulation, and what kind of equipment and technologies are best suited to their project. They need very specific details, such as which grade of lactose to use, and how magnesium stearate will affect their end product, however, that information is often simply not available. As such, development work is often a matter of trial and error, leading to lengthy and costly delays in the process. Therefore it is essential for partners across the processing industry to work together to grow the evidence base and provide data-driven insights that could accelerate progress.

CROSS-INDUSTRY WORKING

Putting these principles into practice, DFE Pharma has worked collaboratively with fellow processing companies Hosokawa Micron (Runcorn, UK), a powder processing technology manufacturer, and Harro Höfliger (Allmersbach im Tal, Germany), a machine and technology expert, to examine the industry's understanding of lactose-based DPI formulations with and without magnesium stearate. With three leading companies joining forces in this way it became possible to conduct a unique multidisciplinary study that resulted in valuable practical insights.

By testing various formulations of magnesium stearate-coated lactose in the blending and filling process, valuable data-driven insights were gained, enabling DFE Pharma and its collaborators to offer even better advice and support to their pharmaceutical customers. The collaboration has not stopped there – phase two of the study will present information on the magnesium stearate coating used to coat the lactose formulation and analysis of the flow properties and filling. In phase three, the results of adding the API and analysis of the stability of the formulation will be shared.

By sharing knowledge and expertise, this cross-industry, multidisciplinary team has generated insights that could give generic players a head start in the development process, enabling them to reduce their costs and shorten their time to market.

3D POWDER BED PRINTED TABLETS

Currently, a key area of innovation in medicine production to reduce development time and cut costs is 3D printing. As such, it is one of the main innovation areas within DFE Pharma. This technology offers great opportunities around dose flexibility, taste masking, solubility enhancement, shape modifications and producing pills with multiple APIs. 3D-printed tablets can also be created on demand in local healthcare settings, opening up a new era of personalised medicines.

What's more, the 3D printing of medications can potentially accelerate the scaling up of manufacturing and offer global security of supply (Figure 2) – a need highlighted during covid-19. However, to make the most of these opportunities, experts must pool resources and knowledge between industry, innovators and academia.

There is limited literature available on excipient selection for 3D printing, and the only marketed 3D-printed drug is prepared with powder bed printing. It is key to understand powder blend characteristics in relation to tablet features when using pharmaceutical 3D printing in order to obtain tablets that comply with pharmaceutical specifications.

The whole sector would benefit from the creation of a centralised database on 3D-printed tablet research. This database should bring together all key players, from pharmaceutical companies to researchers and academia. Bridging the data gap as to how different excipients impact the powder parameters central to the success of the 3D printing process is vital. This will help us learn which materials or techniques are appropriate for each case.

DFE Pharma envisages a repository including data on excipient usability and applicability and their impact on powder and tablet parameters. This would provide investigators with an invaluable tool and bring the industry together in the common aim of providing patient-centred care.

COLLABORATING IN 3D

It was with this goal in mind that DFE Pharma research teams recently carried out a project on the use of lactose as an excipient for 3D tablet printing in collaboration with The Netherlands Organisation for Applied Scientific Research (TNO). The primary objective was to develop a lactose-based blend with sufficient flowability, wettability and binding to be used effectively in powder bed 3D tablet printing.

Figure 2: Security of supply is a critical issue for formulators.

The research resulted in 3D-printed products with properties that, while not yet equal to traditional tablets, were approaching the industry standard for hardness and friability. Ultimately, lactose works. This joint project is the first step towards creating a centralised dataset that could accelerate progress throughout the industry and encourage future collaborative input.

INTERNATIONAL, MULTIDISCIPLINARY NETWORKS

To truly embrace collaborative working, it is key to have an international outlook. The Drug Delivery Innovation Center (DDIC), recently joined by DFE Pharma, is an international centre of excellence based on partnership and close collaboration between academia, industry and public stakeholders. By fostering international, multidisciplinary networks in the research area of drug delivery and manufacturing, DDIC is helping to promote pharmaceutical science along the value chain.

Another valuable knowledge sharing partnership looking to maximise technology opportunities within the medicines supply chain is the UK-based Medicines Manufacturing Innovation Centre. This centre, now also joined by DFE Pharma, is a collaboration between CPI, the University of Strathclyde and founding industry partners GSK and AstraZeneca, with funding provided by Scottish Enterprise and UK Research and Innovation. It aims to advance emergent and disruptive technologies through a series of flagship "Grand Challenge" projects to increase productivity in the pharmaceutical industry and improve patient outcomes. DFE Pharma's new partnership will focus on Grand Challenge 1, which aims to develop a novel digitally twinned continuous direct compression (CDC) platform to reduce waste and cut costs during the manufacture of oral dosage medicines.

As a leading global excipient manufacturer, DFE Pharma will help accelerate phase one of Grand Challenge 1, as well as minimise associated costs and risks. The partnership builds on the company's existing contributions to Grand Challenge 1, including the supply of direct compression excipients that have been particle engineered for the CDC platform. These unique data insights could significantly reduce the number of trials needed to develop the CDC platform.

ACADEMIA – A KEY PLAYER FOR INNOVATION

Knowledge from academia plays a key role in innovation – collaborating with these institutions can boost progress in the drug delivery and manufacturing industry. To further expand these collaborations, DFE Pharma supports a four-year PhD at the University of Groningen in the Netherlands, focusing on increasing the understanding of how biologic APIs and DFE Pharma's excipients can be combined into stable formulations. This research contributes towards a global push to create new, functional, stable and safe biologic formulations for patients.

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NOW IS THE TIME FOR PARTNERSHIPS

Expert collaborations and synergistic work are helping to develop knowledge bases which will drive the next innovations in drug delivery and manufacturing. Those who strike early and establish partnerships will be able to take advantage of post-covid-19 growth.

DFE Pharma is committed to using innovation to further medical research and providing premium excipients and services. The company believes that partnering and collaborating with top science organisations is the best way to achieve this. Sharing knowledge and expertise can allow pharmaceutical players to gain new data insights, embrace new technologies, lower costs and improve patient outcomes.

ABOUT THE COMPANY

DFE Pharma is a global leader in pharmaceutical excipient solutions. The company strives to develop, produce and supply the highest quality functional excipients for use in the pharmaceutical, biopharmaceutical and nutraceutical industries for respiratory, oral solid dose (OSD), ophthalmic and parenteral formulations. DFE Pharma's excipients play an essential role as fillers, binders and disintegrants, as well as in stabilising active ingredients for release in a predictable and effective manner into the patient's system. With over a century of experience and more than 400 people worldwide in over 100 countries serving more than 5,000 customers, DFE Pharma is committed to supporting (bio)pharmaceutical and nutraceutical companies in their journey to improve patients' lives.

ABOUT THE AUTHOR

Bas van Driel is Chief Executive Officer at DFE Pharma. He joined the company from Royal FrieslandCampina (Amersfoort, the Netherlands), where he held a number of commercial management positions. Mr van Driel brings vast experience in the field of marketing, sales and key account management and also a wealth of knowledge in general management. He holds a master's degree in Business Administration, Strategic and Financial Management.