EXPERTISE IN DEVELOPMENT, MANUFACTURING AND COMMERCIALISATION CONTRIBUTE TO SINGLE-CYCLE REVIEW FOR NOVEL MDI

In this case study, 3M Drug Delivery Systems reports on how its deep expertise in the development of MDIs enabled it to overcome a significant formulation challenge, achieve a single cycle FDA review, introduce a brand new dose-counter, and align and integrate manufacturing across two sites in different countries.

It takes significant expertise and outstanding management to launch a novel metered-dose inhaler (MDI) with a single-cycle US FDA review. 3M Drug Delivery Systems recently achieved this feat, not only formulating, scaling-up and commercialising a new product, but also introducing a patient-friendly dose-counter technology.

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AN INNOVATIVE FORMULATION

The development process for the new combination MDI product began with a significant formulation challenge. One of the compounds in the product had previously been developed for use in a dry-powder inhaler, but never for an MDI. The surface energy of the compound is such that particles are attracted to each other and get larger over time. The resulting shift in particle size distribution makes this compound unstable at first glance. However, after experimentation, 3M's experts were able to devise a solution which involved the introduction of a 3M proprietary manufacturing process. Post-implementation testing showed that the product was very stable and consistent.

"This was a unique and innovative project," said Richard Beesley, New Business Development Manager at 3M Drug Delivery Systems. "When we develop products, we recognise that the stability of the active pharmaceutical ingredient is key. In this case, our understanding of the particle engineering – the science of the particles and micronisation of the drug – allowed us to make some predictions about particular formulations and pick a winning one. In this industry that is unique; nobody else does that."

ENSURING A SMOOTH TRANSITION TO COMMERCIALISATION

Once the project moved out of R&D into commercialisation, 3M's expertise again proved invaluable, with the team working to ensure a smooth transition into manufacturing at its Loughborough, UK plant. Several modifications were required at the manufac-

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turing facility to accommodate the new product. First, because the product used a different propellant from many other MDIs, 3M worked with its engineering team to install a system to store this new propellant and pump it to the manufacturing lines. Additionally, the new manufacturing process required further concentrate manufacturing equipment and associated facilities to be installed.

ADDING VALUE WITH A DOSE COUNTER

Concurrently, 3M was also working to develop and manufacture a brand new dose counter to be incorporated into the inhaler. The 3M™ Integrated Dose by Dose Counter (see Figure 1) is designed to eliminate under-counting and over-counting, and has a familiar look and clear display so patients can use it with little or no training. This MDI product represented an ideal opportunity to introduce this specific dose counter to the market.

The dose counter was being manufactured in Germany, necessitating careful management from afar to align its production smoothly with the manufacturing in Loughborough.

"It can be quite difficult managing a supply chain that's at a distance from you, and it was also the first time 3M had used this dose counter technology," said Christine Hart, Project Manager for 3M Drug Delivery Systems. "However, managing global supply chains is a strength for 3M and something we have significant experience in, so we were able to call on that experience in the manufacturing of the dose counter, and ultimately, the final product."

A GLOBAL PLAN

Figure 1: MDI incorporating the 3M™ Integrated Dose Counter, manufactured by 3M Drug Delivery Systems.

Hart explained that the client's global launch plan demanded seamless co-ordination between countries, as the client planned to package the product at sites in both the US and in Ireland for its markets around the world.

"We worked with our client's supply chain to make sure those sites were lined up with shipping documentation, quality documentation, certificates of analysis, and more," she said. "You have to get it right, otherwise you may encounter interruptions at customs."

SINGLE-CYCLE SUCCESS

3M also readied its facility and processes for the FDA's pre-approval inspection (PAI) audit, and trained staff extensively to prepare for the handover from development to operations teams. With its long experience in the MDI market and its expertise in the regulatory process, 3M was able to achieve a single-cycle review for the new product, accelerating its speed to the market and optimising revenues for the client.

"Clients lose time when the FDA comes back with questions or says the package is inadequate for the review cycle," said Hart. "We leverage a very sound regulatory department with good expertise – we know what is required and anticipate needs in these reviews. When the FDA does an audit, they are on-site for a period of time and it's a very heavy review of all the documentation, the production line, batches made in the past and more. There was not an issue raised in our PAI audit; it was a green light from start to finish, so at the end, there were no snags and we achieved a single-cycle review."

In fact, 3M's expertise in MDIs is so in-depth that it is the only company that has been involved with every FDA MDI submission during the past five years – all of which have achieve a single-cycle review.

"This was the most complex product we've taken to launch. Not only the development, the dose counter and the single-cycle review, but also working through multiple customer touch points, from feasibility groups to supply chain management," said Hart. "It was certainly a challenge, but we successfully walked the path together and helped commercialise our client's product."

RESULTS

This project represents the latest in a long line of commercialisation successes from 3M's product commercialisation team. Not only did 3M develop, scale-up and commercialise a new formulation, it also developed and scaled-up a significant piece of additional technology at the same time – the 3M™ Integrated Dose by Dose Counter. With its ability to manage a complex supply chain, including multiple new suppliers, 3M never missed a milestone, and dedicated commercialisation managers provided a single point of contact for the client. With outstanding collaboration and a long history in MDI development and commercialisation, 3M was able to help its client effectively introduce a successful new product.

KEY SUCCESSES

- Achieving a single-cycle review for new-to-the-world product
- Solving formulation challenges that puzzled pharmaceutical companies in the past
- Introducing the 3M™ Integrated Dose by Dose Counter
- Managing complex global supply chains and schedules
- Building a stronger working relationship with our client.

To learn more about 3M Drug Delivery Systems' solutions and services, visit www.3M.com/InhalationExpertise or call +1 800 643 8086.

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We put no limits on curiosity

Imagination and curiosity are the starting points for 3M innovation – the kind of curiosity that leads to innovative solutions for real world problems – such as creating the first metered dose inhaler, enabling patient-centric transdermal technology and converting microreplication technology to microneedle delivery systems. From development, to scale up and commercialization, let the curious minds at 3M Drug Delivery Systems provide innovative solutions to your drug delivery challenges.

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