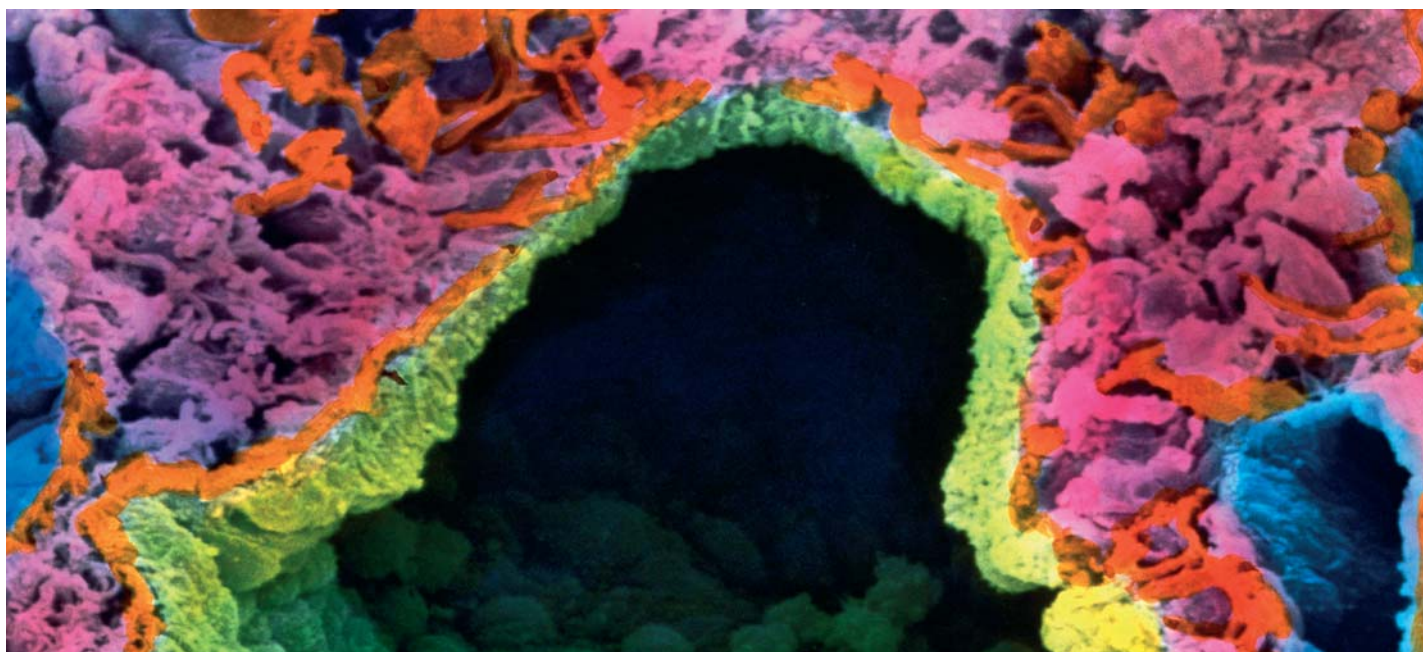


Novel inhaler devices: balancing innovation against price is important

In the seventh article in our series looking at developments in drug technologies, **Jenny Bryan** describes the development of novel inhaler devices for delivery of drugs for asthma and chronic obstructive pulmonary disease



Professor P. Mottar/SPL

The lungs are a lucrative target for pharmaceutical companies developing novel drug delivery systems for asthma and COPD

If you are designing a new inhaler for lung disease, do you put your money on dry powder or metered-dose inhalers, more accurate dosing or more efficient deposition, innovative mechanism or tried and tested reliability, patient friendliness or just plain old price? If you thought the inhaler market was already too overcrowded to be asking such questions, think again. In a market worth around £3bn, at least a dozen big and small name pharmaceutical companies are developing drug delivery systems for asthma and chronic obstructive pulmonary disease which could soon be coming to your pharmacy.

“In Europe there’s been a push towards dry powder devices, and MDIs took a big knock because of the environmental issues, but they’ve still got the advantage that they’re so robust,” says Glyn Taylor, senior lecturer at the Welsh School of Pharmacy in Cardiff.

However, he sees cost as a continuing and major hurdle for companies intent on designing something truly novel.

“The regulatory agencies see devices and drugs in different budgets, and they take a narrow view of what devices they will pay for. But there could be huge savings to be

made from reduced hospital admissions for asthma and COPD patients if you can show that a device gives you better drug deposition or patients are using it more effectively,” adds Dr Taylor.

Others debate the importance of better drug deposition for asthma and COPD. There is little disagreement about the need to get 70 per cent of a dose deep into the lung for treatment of systemic diseases, such as diabetes (see *PJ*, 31 July 2004, pp161–2), but some consider that the 10–40 per cent achieved with the highly potent steroids and bronchodilators currently used to treat asthma and COPD may be enough. Even so, in certain situations, such as treatment of lung infections with antibiotics or, in the future, cystic fibrosis with gene therapy, high dose delivery may be desirable.

At the University of Bath, Paul Young and his colleagues in the Pharmaceutical Technology Research Group, in the Department of Pharmacy and Pharmacology, recently showed that it is possible to achieve 70 per cent efficiency in delivering a high dose treatment, such as surfactant, into the lung, using pressurised gas to aerosolise dry powder in a hand-held inhaler.¹

Another novel inhaler that has moved away from tried-and-tested delivery systems is Boehringer Ingelheim’s Respimat Soft Mist

Inhaler (SMI). Already on the market in Germany as a delivery device for the combination of fenoterol and ipratropium bromide, Respimat is a propellant-free, liquid-based device which produces a slow moving mist of drug.

According to Boehringer Ingelheim, the soft mist travels more slowly and lasts much longer than aerosol clouds from traditional devices, and scintigraphic studies show that this leads to more drug deposited in the lungs and less in the mouth and throat than with an MDI. A recent review of clinical trials suggests that it may be possible to reduce the dose of ipratropium/fenoterol required, for the same efficacy than when treatment is inhaled through a chlorofluorocarbon MDI.² Patient preference studies, presented by the company at last year’s European Respiratory Society conference in Glasgow, showed that patients preferred Respimat over conventional devices. But no date has been set for a UK launch.

SkyeHaler — a dry powder inhaler developed by drug delivery specialists SkyePharma — has received EU approval for use with Novartis’s formoterol, and is expected to receive individual country approvals this year. It uses magnesium stearate to protect dry powder drugs from moisture and, in the case of formoterol, to help bulk-up the low doses

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that are required, so that flow and deposition can be improved.

Magnesium stearate is also being used in SkyePharma's hydrofluoroalkane MDI, not only as a bulking agent, but also as a lubricant to reduce valve wear and tear — a common cause of inhaler failure with HFA devices.

Completing the company's range of novel inhalers is an HFA MDI which uses sodium cromoglicate, not as an active ingredient, but as an excipient to scavenge moisture.

"We looked at a lot of different drugs and excipients and it turned out that sodium cromoglicate was the most hygroscopic compound we tested. So given its safety record, we decided to use it in our MDI," explains Geraldine Venthoye, business unit lead, aerosol and inhalation at SkyePharma.

The Achilles heel of many dry powder devices is the energy which patients need to generate to get the drugs into their lungs, and companies, such as SkyePharma and Nektar Therapeutics, are quick to show how they have overcome this problem. For example, the Nektar Pulmonary Inhaler is powered by a bolus of compressed air to make drug delivery independent of inspiratory air flow, and powder is dispersed into a holding chamber from which the patient inhales.³

Like many of the new generation of inhalers, the Nektar device includes an indi-

cator to show when a dose has been taken. Better feedback to patients about how well they are using their inhaler is another area of interest among developers of novel inhalers.

Perhaps the most adventurous attempt at getting asthma patients to take more interest in the way they use their inhalers is SmartMist — a microprocessor controlled device which allows actuation of an MDI at a preprogrammed point during inspiration, with a traffic light system to signal when patients have inhaled correctly. It also measures lung function, with a downloadable record of results.^{4,5}

But innovation alone is not enough to get the pharmaceutical industry to pay serious money to take a novel inhaler through to market. For those making and selling millions of inhalers every year to service a worldwide market, device reliability is even more important than innovation. A failure rate of just 0.1 per cent can mean hundreds of thousands of treatment failures — and complaints — and is not acceptable to the big league. But device reliability is hard to prove when all you have is a prototype.

Pulmonary product development company, Vectura, appears to be responding to real-world need for low cost, reliable devices rather than innovation, with its new 60-dose, dry powder Gyrohaler. It boasts the simplicity of its new device, which has fewer than 10

simple mouldings, and, it says, is smaller, lighter and likely to be less expensive than other dry powder devices.

Whether it can compete with the success of another small devices company, Meridica, remains to be seen. So impressed was Pfizer with Meridica's inhalation technology that it recently bought the company — for a reported \$125m. Small pharmaceutical companies undoubtedly know there is money still to be made from novel inhalers — as long as they can balance innovation against price.

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