DELIVERING INJECTABLES:

FORMULATIONS, AUTO-INJECTORS AND NEEDLE-FREE

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"Delivering injectables: formulations, auto-injectors and needle-free"

This edition is one in a series of sponsored themed publications from ONdrugDelivery Ltd. Each issue focuses on a specific topic within the field of drug delivery, and is supported by industry leaders in that field. Full contact information appears alongside each article. Contributing companies would be delighted to hear from interested readers directly. ONdrugDelivery would also be very pleased to pass on to authors, or answer as appropriate, any queries you might have in relation to this publication or others in the series.

During 2008 we will be covering the following topics:

February: Transdermal Drug Delivery
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Front cover image "Hydrated liquid crystal depots in water, FluidCrystal®" reproduced with kind permission from Camurus AB.

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INTRODUCTION

Welcome to ONdrugDelivery's first issue of 2008, and our third publication focusing on the topic "delivering injectables". Inside, I am pleased to present a selection of articles tackling issues from across the range of injectable drug delivery. At the "small" end of the spectrum, we discover advanced nanoparticles which self assemble *in vivo* to form drug carriers. Zooming-out to look at the bigger picture, we explore market trends in the area of advanced injection devices.

From the patient's perspective, needle-based injection is seldom the most attractive route of administration, but it is often the only viable option. There was a period of hopeful optimism during the last decade when scores of non-invasive alternatives were promised; some even seemed to hint at the end of the needle and syringe altogether. In reality, of course, drug delivery has not succeeded in banishing the hypodermic needle to the history books, but it would not be at all fair to suggest that the quest to do so has achieved nothing. Important lessons have been learnt along the way.

Although there is not a needleless alternative for every currently injected product, considerable progress has been made. Numerous technologies offering non-invasive alternatives to injection have been developed and many products using these systems have reached the market.

The nasal route of administration is one which has proven successful at bearing viable alternatives to injections. Although not without its own challenges and problems, nasal delivery has several attributes, including rapid onset of action which is crucial in the context of replacing an injection. Systemic nasal products such as nicotine, sumatriptan, nafarelin and calcitonin, as well as nasal vaccines such as the live influenza vaccine, FluMist, have been launched in recent years, with numerous other products coming through the pipeline.

On page 20 of this issue, Matthias Birkhoff of Pfeiffer (Randolfzell, Germany) comments further on the commercial success that nasal drug delivery has had in offering an alternative to injection. He draws particular attention to lifestyle drugs – a $23 billion global market enjoying double digit annual growth – as an important growth area for nasal products.

An interesting point that Pfeiffer makes is that its devices are Drug Master File supported and all materials used are known and approved by the US FDA. In terms of regulatory scrutiny of material contact, this brings their nasal spray products into the same league as injectable products.

A NEW TAKE ON NEEDLE-FREE

If the example of nasal drug delivery can be linked with realistic product opportunities for alternatives to injection, many people might hold up needle-free injection as an example of a sector that, while chasing attractive dreams, has yet to achieve market success. Personally I have always believed that the needle-free sector has much to offer and that commercial success – although hampered by misfortune and bad press – would eventually arrive.

And then along came a man with an elegant new approach to needle-free injection that decisively changed the question hanging over the commercial success of needle-free injector from an "if" into a "when" and then into a "how soon". His name is Charles Potter, founder and chief executive of Glide Pharma (Abingdon, UK).

I am particularly pleased to present in this issue an article from Glide Pharma. It describes the company's Glide SDI technology which, instead of accelerating a liquid jet across the skin like other needle-free injectors (NFIs), uses a solid dose. With innovative ideas such as this progressing through development, perhaps the needle-free sector will blossom a little sooner than we previously imagined.

NEEDLES ARE STILL NEEDED

We have learnt how better to identify the instances where it really is possible to substitute the needle for a non-invasive delivery system and, as described above, technology is moving on apace. However, crucially, the industry has also learnt to spot those instances where it is not yet possible to avoid injection. This latter point is significant because being realistic about the limits of non-invasive delivery allows proper attention to be given to developing the best possible needle-based injectable delivery systems.

The injectables market continues to expand, particularly with advances in subcutaneous self-injection technology moving injections from the professional clinical setting into the home, and thus edging into the market that non-invasive delivery systems have not been able to fill.

Those involved in developing improved injection delivery systems will be looking in detail at all aspects of the device or the formulation, with the aim of optimising:

- Needle safety
- Comfort
- Cost-effectiveness
- Ease of use
- Manufacturability
- Stability
- Storage
- Frequency of injection
- Applicability across different types of compound
- Applicability across therapeutic categories
- Product differentiation
- IP position

In his article on page 15, Ian Thompson, Head of Business Development at Ypsomed (Burgdorf, Switzerland), gives an excellent overview of factors influencing the injection device market, and the criteria for selecting different types of device, or combinations of device characteristics – pen or auto-injector; standard prefilled syringe or safety-enhanced syringe; dual chamber or single chamber; mono-dose disposable or multi-dose reusable. He describes some of the recent technology developments, such as the emergence of the mono-dose disposable dual chamber injector for lyophilised products.

Turning from devices to injectable formulation technology, Camurus (Lund, Sweden), is developing self assembling lipid liquid crystal and nanoparticle systems which overcome some of the limitations commonly encountered by formulation approaches such as liposomes, emulsions and micro-emulsions. A summary of the advantages of self assembling lipid liquid crystal formulations – in terms of patient benefits, pharmaceutical benefits and technical/commercial benefits – can be found in the boxed text on page nine.

One fascinating characteristic of the systems Camurus is developing stems from the fact that they self assemble *in vivo* on contact with aqueous fluid inside the body. This means that the single formulation can exist in effect in two different conformations – pre-delivery and post-delivery. Thus the formulation can be designed optimally to fulfil the requirements on it before delivery (storage, high drug payload, no need to re-constitute, low viscosity etc). Then, once inside the body the pre-delivery requirements no longer apply, so the formulation can change its structure and related functional properties for the optimal timed and/or targeted *in vivo* drug release profile.

From needle-based injection devices and formulations to needle-free and nasal alternatives, I hope that this publication provides you with an interesting and informative insight into the world of injectable drug delivery.

Our next injectables-related publication is out in April 2008 and focuses in on the topic of prefilled syringes.

Guy Furness
Publisher

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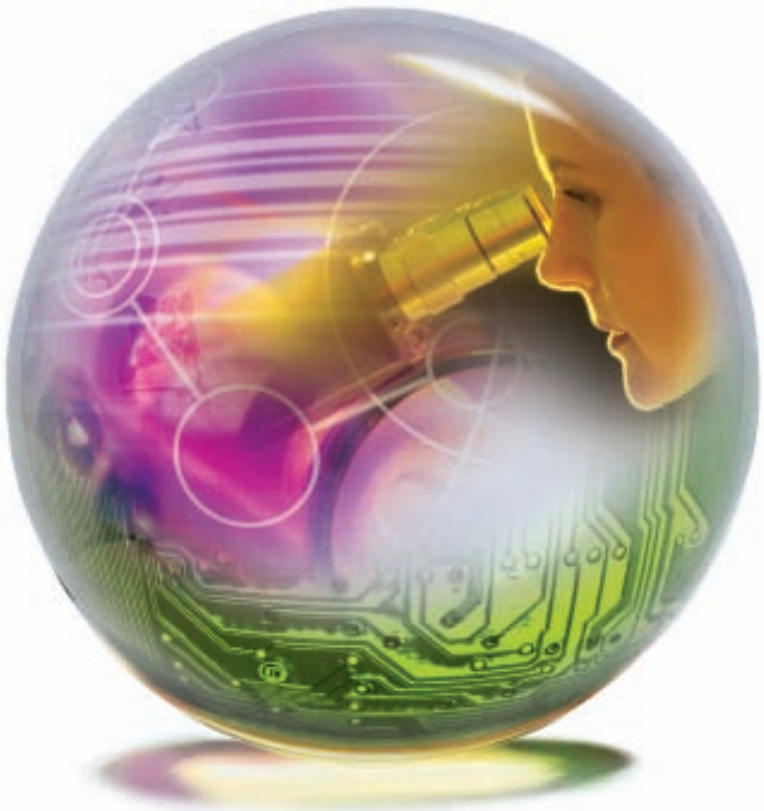

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