

# New Drug Delivery Remove the "Ouch" While

When it comes to prescribing medication, physicians have many concerns: drug interactions, side effects and efficacy, to name a few. Patients may think about all these things, but if the method of drug delivery is injection there is one thought uppermost in mind: *pain*. This is especially true for children, the frail elderly and, let's face it, those of us who cringe at the sheer thought of a needle stick.

Of course, while finding pain-free and convenient drug delivery methods are paramount for R&D-focused companies, efficacy is also top of mind.

There are various different drugs that, in the past, had to be delivered in a certain way because of the way the body processes them, explained Dr. Warren Levy, CEO of Unigene, maker of inhaled osteoporosis drug Fortical.

Diabetics, for example, have relied on multiple daily injections of life-sustaining insulin. Protein-based pharmaceuticals, such as insulin, interferon and interleukins, had to be injected. A transdermal patch couldn't work because the insulin couldn't get absorbed through the skin and a pill would get

digested by the enzymes in the stomach before it hit the blood stream.

***But times, as they say, are a-changin' in the world of drug delivery.***

One visit to the local drug store and it's easy to track down a host of prescription and over-the-counter products offering myriad delivery options. There are eye drops to treat non-eye-related ailments and inhaled products for non-nasal related problems (Unigene's osteoporosis drug, for example.) There are patches, strips that melt on the tongue, creams, and instant-dissolve pills (that taste good!)

Drug delivery is big business. Everyone from small boutique biotechs to Big Pharma is in on the action. And, more than the issue of finding pain-free approaches to drug delivery, these companies are looking for a way to solve the physician's No. 1 concern: compliance.

"One of the big problems in medicine today is that people stop taking their medicine for a variety of reasons. They forget to take pills as prescribed. They don't like the

## Aspects of Non-Invasive Drug Therapy – a Technology Viewpoint

By: Russ Somma, Ph.D



The need for self-administered, non-invasive drug therapies is growing due to the decreased time patients remain in hospitals and to an increased array of large molecule or new medications brought about through the use of biotechnology. When developing dosage forms, researchers need to consider several key factors that drive the degree of "invasiveness" of drug therapies: patient's cultural

differences, chemistry of the drug substance, disease state of the patient, target site or location where the medication is to take effect, and desired mode of action of the medication.

### Cultural Differences

Scientists must be cognizant of patient demographics and cultural preferences when developing new dosage forms. For example, suppositories are a very effective method of drug delivery, but they are not popular in some cultures, particularly in the U.S. Oral administration is preferred because it is thought

of as minimally invasive. However, not all drugs may be delivered via popular dosage forms. A particular drug's chemistry drives or limits these types of options.

### Chemistry of the Drug Substance

Many medications are not absorbed very well into the biological system when taken orally due to the unstable nature of the drug in stomach acid. Proteins and many biotechnology-based medications such as insulin fall into this area. Other medications become less effective because they are quickly broken down or metabolized. Suppositories are a good solution to bypass this problem, which is commonly known as first pass effect. A low volume injection given just below the skin or subcutaneous is another viable solution. Unfortunately, these solutions do not appeal to patients and for the most part are considered invasive.

### Disease State

Many factors must be balanced against the intrinsic properties of the medication such as its physical chemistry and the pharmacokinetic details of its absorption into the system. These will be different in each sub set of patients due to health, age and ethnicity.

Routes of administration may need to be modified to account for each individual

# Every Methods Promoting Compliance

By Bari Faye Siegel

side effects. They feel better so they don't finish the prescription. There are difficult-to-follow instructions. And, of course, they don't like to inject themselves," Dr. Levy said. "And there are a variety of problems that come with not taking – or finishing – a prescribed medication."

Take birth control pills, for example. If you miss one, you run the risk of a complete lack of effectiveness for the entire month.

Fosamax, a medication for osteoporosis, must be taken first thing in the morning and the patient must remain upright and can't eat for two hours after taking the drug. If a diabetic doesn't take the required amount of insulin on a daily basis, the consequences could be disastrous.

And, while people typically prefer a pill more than any other method drug delivery, there are many who can't swallow a pill: children and some elderly. Plus, this method is not without its downsides for the general

patient. For example, patients who are ambulatory will require different forms than those who are hospitalized. The reduction of hospital stays require that dosage forms provide for ease of use since "self care" has become common place. The need for self-administered dosage forms obviates the more common drug development options open to researchers, such as intravenous or IV administration. This drives the need for novel, "easy to use" and less invasive dosage forms.

## Target Site

The industry is moving toward medications that are "customized" to create a clinical effect at selective areas. Many of these New Chemical Entities (NCEs) have properties that presently require some form of invasive or uncomfortable route of administration. This new watershed of candidates will drive the need for more technology to achieve their intended clinical effect. More conventional forms of NCEs may take on this site selectivity by applying various types of dosage form technology.

Conventional NCEs may be formulated into systems that look common place for the patient (i.e. tablets, capsules) but are internally a new generation of oral form. Or, a "small injection" may appear as an adhesive bandage or "patch" to the patient. Like the oral forms, the internal technology for these "patches" has entered into a new generation of design and functionality. While transdermal or patch systems have been a part of the array of dosage forms

population. Sure, there is no pain and there is the convenience factor of being able to carry it with you – but you need something to drink to swallow the pill. And, there's that pesky compliance issue again. You have to *remember* to take a pill for it to be effective.

Scott Fleming, senior vice president of marketing for MicroDose, explained that the company is developing the first-ever totally electronic dry powder inhaler for both local and systemic delivery. The device is breath-activated (i.e. coordination independent) and is also flowrate-independent, meaning asthma and COPD patients who can't breathe deeply at a time when they need the medicine most, will have two to three times better efficacy than other dry powder inhalers currently on the market.

And, Fleming added, MicroDose's device just finished phase 1 clinical trials for an inhaled insulin product. "We know that most biotech products like insulin have to be injected. But, a non-invasive system would be incredibly marketable."

The MicroDose Dry Powder Inhaler is just that. With an efficacy rate 60 to 80 percent, the device is hand-held, portable and easy-to-use. (The company's main competition, Pfizer's Exubera, the first and only inhaled insulin device on the market,) is "too big and requires too many steps to use."

It's clear that companies that have entered the drug delivery race are in it to win it. They know that any drug that can be administered safer, smarter, faster and cheaper will be preferred by patients. And, if the patients like it better, the doctors are more likely to prescribe it.

"For a company, this is a low risk side of product development," Dr. Levy said. "Any time you can take an existing drug with known efficacies and known side effects and find a new way to delivery it is a lot less risky from the corporate perspective."

available, newer and more selective technologies have been developed. These technologies allow larger molecules like proteins to be transported across the protective epidermis layer of the skin and into the capillary blood vessel system. It is these systems that may be used to administer medication at selected areas or replace the small injection.

## Desired Mode of Action

Some dosage forms help the patient by maintaining a constant plasma level of the medication. This in turn controls a medical condition or prevents the recurrence of severe or "break through" events. These events are in many cases linked to a reduction in the drug's plasma concentration. New dosage methods help patients maintain a continual plasma level for longer periods, obviating the need for frequent oral dosing.

While many of the small molecule NCEs may be formulated into a controlled release oral form, these technologies will not accommodate all the promising new drug candidates. This is particularly apparent when we look to the growth in vaccine development. These medications will not survive gastric transit in most cases. Transdermal application using the newer generation of "patch" will permit inoculation without the less popular injection route. New drug delivery systems that allow for dosing on an as-needed basis or that can be controlled using a small onboard microchip may better help manage pain suppression. Localized control of joint pain using topical application of medication has been a common approach, but with modifications, a more pronounced effect may be seen. A good example of this progress is nitroglycerine, which had been used as a topical paste and evolved into a nitroglycerine patch.

Russ Somma, Ph.D. is president of SommaTech, LLC.