Established via hypodermic syringe in the 1850s, intramuscular and subcutaneous injections have a long-standing history and are still used today by millions around the world. However, an estimated 10% of all Americans are needle-phobic, and an even higher percentage of individuals claim their dislike of needles as the reason for foregoing medical treatment (1). In addition, conventional syringes are also challenged by the potential of an accidental needlestick injury to the dose administrator, or limitations – in some cases – of administration by a clinician rather than in a patient's home setting.

A common alternative to intramuscular and subcutaneous injections for those looking to avoid needles is transdermal delivery, which uses an adhesive patch to deliver medication. This form of delivery presents advantages over oral methods too, including improved efficacy due to its ability to avoid first-pass metabolism. Additionally, it can reduce...
side-effects in certain therapeutic areas and maintain a steady blood level of medication.

A number of advancements have been made since the transdermal patch’s introduction in 1975, but this delivery method still has limitations. The natural barrier properties of skin can be an issue itself. Most transdermal drugs must be lipophilic, but also possess some hydrophilic character, in order to permeate through the lipid cell layers and deeper into the skin where interstitial fluid is present.

**Microneedle Capabilities**

Intradermal delivery via microneedle technology may expand the range of large molecules that could otherwise prove difficult to deliver. Microneedle technology actively transports drugs through the outer stratum corneum to the dermis. The needles are narrower and shorter than a pen injector, putting them out of the range of many nerve endings. The smaller needles result in a more patient-friendly administration method.

There are several technologies in development intended for intradermal delivery. 3M’s hollow microneedle delivery system, for example, is designed for intradermal delivery of liquid formulations, including biologics and other small molecules. This technology has the flexibility to deliver up to hundreds of milligrams of high-value formulations of proteins, resulting in direct absorption of the drug into the systemic circulation, by-passing the digestive and hepatic portal systems (2). Capable of holding a high volume of formulation, it should be supported by an appropriate solution cartridge, where the formulation sits prior to delivery (see Figure 1). 3M’s hollow microstructured transdermal system (hMTS) consists of a drug reservoir and flow path between the reservoir and the hollow microneedles. It also includes the means to pressurise the drug reservoir and insert the microneedles, due to the microneedle density (see Figure 2) (3).

**Key Points**

When considering intradermal delivery, there are a few factors pharmaceutical and biotech companies should keep in mind:

- Formulation compatibility with an intradermal delivery method – this can be tested during early feasibility studies
- Desired volume of the delivered formulation – some intradermal delivery systems can only deliver between 0.5mL and 1mL of the liquid formulation, although 3M’s hollow microneedle system is intended for delivery up to 2mL
- Strength of the microneedles upon delivery
- Required drug delivery timeframe
- Overall performance and additional benefits – such as a pharmacokinetics profile or improved bioavailability, compared with subcutaneous or intravenous routes of administration

**Competitive Landscape**

The expanded delivery range of biologics has challenged companies to be innovative in developing new drug administration methods. With the advancements made thus far, it is hard to believe that only a few years ago, the first intradermal injector to reach the market was introduced by Becton Dickinson: BD Soluvia™ Microinjection System. It is a microinjection system for intradermal delivery, consisting of a single needle coupled with a prefillaflowi injection system for vaccines or drugs (3). The device is capable of injecting about 0.1mL of flu vaccine.
For treatments suitable for self-administration, switching from intravenous administration to intradermal delivery could mean avoiding an extra trip to a doctor’s office for an injection or outpatient hospital facility for intravenous therapy.

Other companies are also continuing to work towards developing and commercialising hollow microneedle technology, including NanoPass, Debiotech and 3M:

- The MicronJet Needle™, developed by NanoPass, is a single-use microneedle-based device that is intended for use with a standard syringe and may be compatible to inject biologicals, vaccines or small molecules.
- The DebioJect, launched by Debiotech, is a single needle or three-needle device with silicon microneedle arrays, and has a sharp tip with a side hole for rapid injection of 0.5mL volume (4).
- 3M’s hMTS is designed for self-administration of liquid formulations. The device is comprised of 12 polymer microneedles in an array that is intended for delivery of between 0.5mL and 2mL of fluid.

These options give biopharma companies looking for the most suitable intradermal delivery method a basis of comparison to determine which delivery option best meets their needs.

Patient Preference
In addition to formulation-design advancements, microneedles offer a patient-friendly alternative for the administration of injectable therapies. Easy handling for self-administration may increase the patient’s convenience and potentially reduce associated healthcare costs from the necessity of administering a drug in a clinical setting. As an example, the hMTS features a textured grip which is designed for patients with dexterity issues.

For treatments suitable for self-administration, switching from intravenous administration to intradermal delivery could mean avoiding an extra trip to a doctor’s office for an injection or outpatient hospital facility for intravenous therapy. This provides convenience for the patient, along with the potential to offer additional pharmaco-economic benefits.

New Alternative
As pharma companies continue to explore alternatives to traditional injections, microneedle technology is ideally suited for intradermal delivery, addressing the need for effective administration of biologics, including proteins and peptides.

Notes
BD Soluvia is a trademark and product of Becton Dickinson.
MicronJet is a trademark and product of NanoPass.
HUMIRA is a registered trademark and product of AbbVie.

References
5. Dohmeier D, Microneedle-based drug delivery: Clinical data and manufacturing readiness, Lecture from the International Conference on Microneedles, Baltimore, Maryland, May 2014