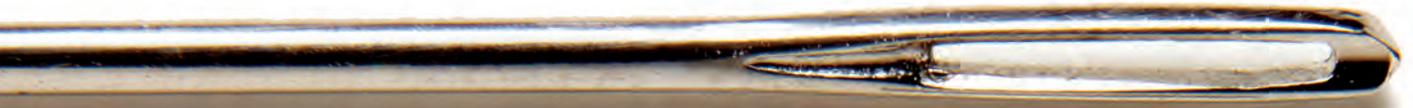


Phillips Plastics Corporation®

INTERFACE

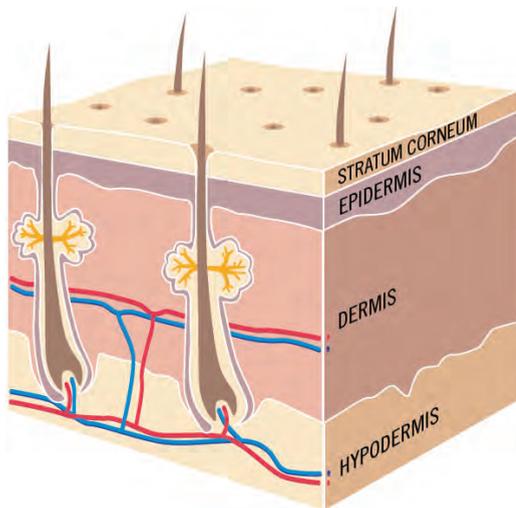
Phillips Plastics Redefines
Microneedles for
Drug Delivery



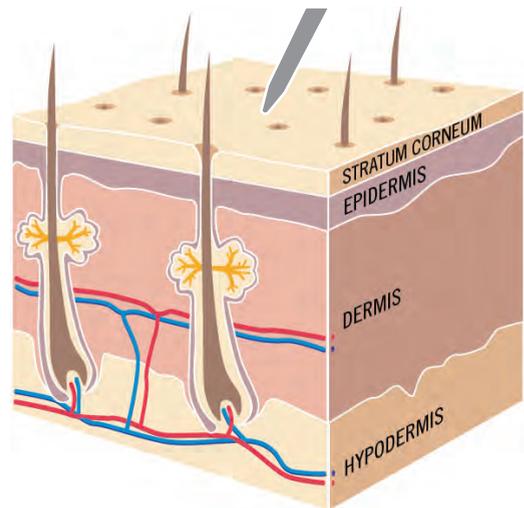
Traditionally, large-molecule drugs, such as vaccines, are administered via hypodermic needle injection, deep into the skin or directly into the bloodstream.
But who likes shots?



Demand for a painless method of delivering macromolecular compounds is on the rise. However, large-molecule drugs typically cannot be administered in the oral tablet form patients and doctors prefer. In addition to the molecular weight being too high to enter the bloodstream from tablet ingestion, the body's digestion process would dilute the drug potency to a level of inefficacy.



The objective of microneedle drug delivery is to administer medicines or vaccines to the epidermis and dermis. However the thin top layer of skin, the stratum corneum, provides a significant and difficult barrier for the medicines to overcome. Large-molecule drugs can't successfully bypass the protective layer of packed, dead skin cells without help. An innovative, active method of drug delivery is required.



Microneedles can range from 100 to 1000 μm in length, with a tip diameter of 15 μm to 400 μm in diameter at the base. They can be solid or hollow, and configured in NxN arrays as required. The stratum corneum layer of skin is approximately 15-20 μm in thickness. Microneedle drug delivery systems are designed to penetrate the stratum corneum to facilitate delivery of both small- and large-molecule drugs. Upon entering the skin, the compounds can rapidly diffuse through deeper tissue before absorbing into underlying capillaries. Since microneedles don't impinge on the nerve fibers and blood vessels in the dermal layer, they don't cause the anxiety, pain or bleeding associated with IVs or syringe injections that can adversely affect compliance among patients requiring frequent injections.

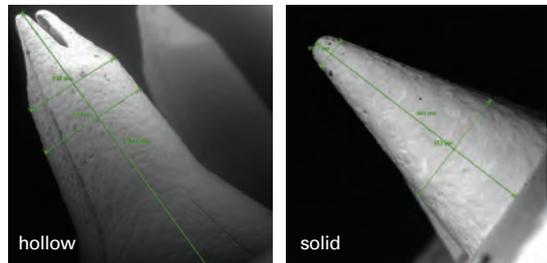
Microneedle Drug Delivery Systems

Microneedle drug delivery systems feature microneedles that can painlessly penetrate the uppermost layer of the skin called the stratum corneum. Capillaries and blood vessels then absorb the macromolecular drug for distribution throughout the body. Jeff Spaulding, New Technologies Sales Manager, Phillips Plastics, explains, “We have followed the studies, which show that delivering vaccines just below the stratum corneum layer to the epidermal Langerhans and dermal dendritic cells have a stronger immune response at lower doses than deeper injections. This can be a significant benefit, especially for older patients.”

The use of microneedles in drug-delivery systems is presently under review by the Food and Drug Administration (FDA). Once approved, microneedle drug delivery systems could potentially combine the effectiveness of delivery associated with syringe injections with the comfort and convenience of a less invasive delivery method. The technology shows promise in allowing for:

- Less pain, as the needles that are micro in scale do not penetrate past the epidermis
- Simple medication administration, possibly by patients themselves, which enhances patient comfort, compliance and quality of life
- Enhanced drug efficacy, resulting in reduced drug usage
- Enhanced treatment safety, simplicity, and cost effectiveness
- Less bio-hazardous sharp medical waste

In addition to administering medication, possible microneedle applications include vaccines, such as flu shots, and potentially interstitial fluid sampling for blood glucose monitoring.



Microneedle drug delivery systems may include either solid or hollow microneedles. Microneedle materials can range from metals to ceramics, or engineered plastics. Solid microneedles are typically coated with powder forms of drugs for absorption into the dermis. Hollow microneedles, in contrast, are capable of delivering liquid drug formulations.

Micro Molding Microneedles

Pharmaceutical and manufacturing companies are investing millions of dollars to design and develop effective methods of bypassing the top layer of skin – as well as the supporting manufacturing machinery and technology – to enhance drug delivery.

There are several competing solutions for manufacturing microneedles under development in the marketplace, such as laser etching and deposition modeling. Phillips Plastics Corporation saw potential in the process of micro injection molding (micro molding) microneedles.

According to Spaulding, micro molding technology is changing at a rapid pace. Phillips Plastics has the ability to make geometries today that were not manufacturable as little as two years ago.

“Our customers continually challenge our micro molding engineers to make smaller and smaller parts. In combination with advanced-engineered polymers, new tooling developments and our design center, we continue to define what is possible when it

comes to micro molding. Our ability to mold microneedles using polymers, ceramic, and metal compounds is a good example of what can be accomplished,” says Spaulding.

Micro molding allows for accurate and easy-to-manufacture devices that are scalable for small- to large-volume production. It also opens the door for small, complex, and innovative geometries.

For example, microneedles could be cone or wedge shaped, have varied surfaces and features within the flat sides, or incorporate unique tip geometries.



Magnified seven times.

“All these ideas can become possible with micro molding. We are encouraged that our first iteration of the solid microneedle using micro molding techniques proved effective in recent lab tests. This success is important because it revealed that micro molding could be considered a viable option for manufacturing microneedles,” Spaulding says.

The Microneedle Micro Molding Process

Microneedle design, development and manufacturing are integrated processes. “Simulating how the material will flow into the mold allows us to uncover potential issues and make recommendations with respect to design requirements before starting on the tool,” says Spaulding.

Once designs are optimized for manufacture, they’re ready for finite element analysis (FEA), which helps determine whether the part is strong enough to meet the demands of its intended function. Finally, microneedle prototype tools – and the parts themselves – can be created in small volume for testing before multi-cavity types of production tools are made for high-volume microneedle manufacturing.