ADARE® PHARMA SOLUTIONS

3D SCREEN PRINTING

ENABLING A NEW GENERATION OF COMPLEX FORMULATIONS

By overcoming key challenges, 3D screen printing is unlocking new possibilities in drug development and manufacturing

by Steven Facer, Adare Pharma Solutions, & Klaus Kühne, Laxxon Medical

The pharmaceutical industry has been acquainted with the promise of 3D printing for some time now, with many large pharma companies exploring the possibilities of the technology. However, 3D-printed pharmaceuticals have been largely relegated to niche markets and prototyping due to limited scalability and reliance on manufacturing processes that could potentially damage APIs.

But now a new technology, 3D screen printing, is shattering those constraints and opening new frontiers in drug formulation and manufacture.

Unlocking The Full Potential of 3D Printing

Most 3D-printed pharmaceuticals have been based on laser technologies or extrusion via nozzles. These technologies lack effective scalability and feature aggressive production processes that limit their applications to areas like prototyping and pilot production.

Therefore, the general perception of 3D-printed pharmaceuticals has been that they are very niche, expensive, and incapable of fulfilling market demand even for smaller applications. However, drug delivery system provider Laxxon Medical uses a 3D pharmaceutical printing technology that stands apart from other systems by utilizing additive manufacturing based on a flatbed screen printing process widely used in electronic, automotive, and aerospace industries.

Introducing SPID® Technology

Laxxon Medical's proprietary Screen-Printed Innovative Drug (SPID®) Technology is a cold-process 3D screen printing platform that unlocks technical and clinical advancements for a wide range of pharmaceutical therapies. Materials are combined into a semi-solid paste, which is then applied in layers ranging from 10 µm to 150 µm to produce tablets.

Unique release profiles and combinations that are difficult or impossible using traditional pill-pressing can be easily achieved using 3D screen printing. It allows for near-endless possibilities in the geometric shaping of dosage forms, including multi-function, multi-compartment tablets and microtablets as small as 200 µm. SPID Technology can produce oral, transdermal, and implantable dosage forms, enabling heterogeneous distribution of active ingredients.

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SPID Technology enables drug delivery systems with optimized pharmacokinetics and pharmacodynamics, leading to improved clinical outcomes, reduced side effects, and lower API requirements compared to conventional drug delivery methods. Additionally, it is not API-specific, allowing for broad application across pharmaceutical therapies.

With 3D screen printing, it's easy to achieve unique release profiles that are difficult or impossible using traditional pill-pressing

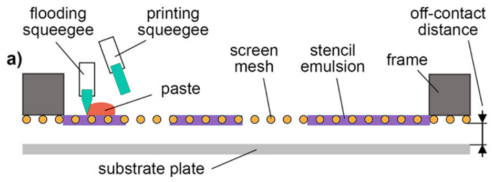
3D screen printing is inherently scalable from R&D to commercial production. It supports low-quantity API use – requiring only a few tablets' worth for R&D – while also enabling seamless scaleup to mass production of up to 1.5 million units per day without significant changes to the manufacturing process. Unlike other 3D printing technologies, which are limited by the number of printing heads, 3D screen printing allows for the simultaneous production of a significantly greater number of tablets. The process eliminates unnecessary material waste, enhancing both cost-effectiveness and sustainability.

Finally, 3D screen printing presents opportunities for IP and patent protection supporting Section 505(b)(2) registration by enabling dosage systems that increase patient benefit or distinguish from generic products on the market.

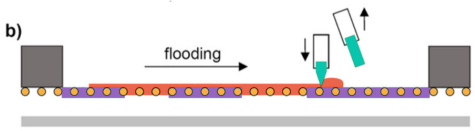
The 3D Screen Printing Process

A semi-solid paste containing the API and excipients is prepared using a vacuum dissolver, ensuring homogeneous mixing. This mixture is dispensed onto a screen and "squeegeed" into fine layers using a flow process. Individually printed layers are gauged and controlled by a laser detector to ensure exact thickness and to detect any shaping failures. During the printing process no pressure is applied, and water content in the individual printed layers is precisely monitored and controlled.

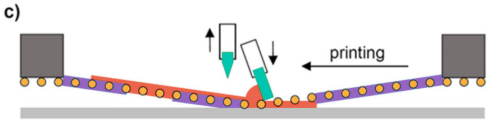
After application to the printing plate, the wet layer is dried in a convectional and temperature-controlled process (between 30°C and 100°C), then is returned to the printing area. The printing screen lifts to the appropriate level for application of the next layer, and the process repeats until the run is complete.



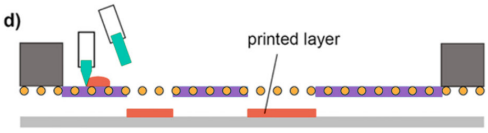
Paste dosing: The formulated API containing paste is applied on the screen.



Flooding: The paste is spread on the screen by a squeegee filling the mesh.



Printing: The squeegee forces the paste through the stencil onto a printing surface.



Screen adjustment: The substrate plate returns to the printing station, where the printing screen is lifted by the thickness of the printed layer. The printed layer is dried by convection. This cycle is repeated until the desired tablet height is reached.

Thicker layers may take longer to dry or may require some longer application of heat, but those determinations are based on the material's sensitivity. Unlike traditional 3D printing approaches, which use a polymeric heat system that can negatively impact the molecular structure of API or excipients, 3D screen printing's "cold" process is very gentle in formulation and manufacture as well as drying.

Temperature is monitored and controlled throughout the process, since rotating and convective drying of the layers may raise ambient temperature. Thus, the technology automatically provides cooling when necessary to ensure the printing plate always returns to the printing station under the same temperature and starting conditions as the previous layer.

This process is self-contained and limits printing unit contamination potential. General cleaning typically comprises removal of the screen and the plate; however, the machine design facilitates this procedure and single-use pipe work can be used between the paste-dispensing cartridge and the screen. Additionally, the printing process occurs separately from paste/suspension production, avoiding the microdust generation seen during encapsulation or tablet pressing. This eliminates the need for microdust cleanup as part of line operation.

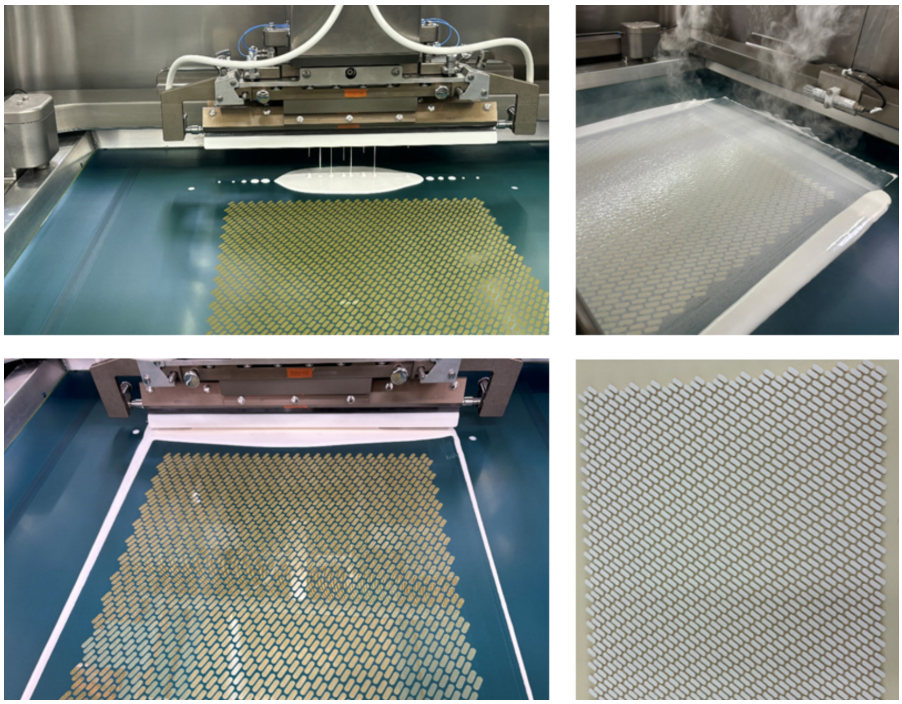
Adare's cGMP 3D printer installed in Pessano, Italy

Unparalleled Control Over Release Profiles

One of the greatest advantages of 3D screen printing technology is the precise control of release profiles via tablets containing multiple drugs that are either layered or one within another.

3D screen printing technology builds a tablet in layers, and each layer can comprise its own pharmaceutical function, such as immediate release, extended release, deferred or sequential release. Layers can also have no API content, which facilitates deferred release from a deeper layer or compartment layer. The technology is extremely flexible in the structures it can create, and this flexibility does not impact the time or cost-effectiveness of the manufacturing process.

Traditional tableting technology can technically achieve this layering, but it's difficult to control the layers and typically no more than two layers can be produced. No standard tableting technology offers the precise interlayer thickness control as 3D screen printing, and layering is much more challenging to achieve with other tableting technologies.



Adare's 3D printer installation in Pessano, Italy. Clockwise from top left: paste dosing, drying, completed tablets, and a flooded/squeegeed screen

In other methods, layering can be achieved by drilling a tablet with a laser to create space for an API, but this process is complex and has the potential for numerous failure points. With 3D screen printing technology, there's no need for drilling; the tablet is simply created and filled using the same process to provide much more consistent quality.

Scalable from R&D to commercial production without significant changes to the manufacturing process

Additionally, in traditional tablet manufacturing, adding any other additional function typically interrupts one manufacturing process for transfers to another, several times in some cases. But 3D screen printing consolidates every step into a single streamlined manufacturing process.

Revolutionizing Formulation Development

SPID Technology can be used to help formulate difficult-to-manufacture molecules, such as those that cause powder to clump or contain an API that is difficult to compress. Various sizes and shapes of printing mesh are available as well. Twenty different tablet shapes could be produced on a screen quickly and inexpensively to support feasibility work like dose-finding studies. To achieve the same on a standard tablet press would require the creation of twenty individual punches.

3D screen printing technology allows for the inclusion of permeation enhancers needed to increase bioavailability. Peptides, even for oral intake, are difficult to produce in standard tablet and

capsule forms, but the gentle SPID Technology process can build very stable tablets essentially free of variability and abrasions, making them ideal carriers and offering numerous possibilities in both injectable and oral delivery forms.

Adare Pharma Solutions and Laxxon Medical: Breaking Barriers in Drug Formulation

Adare offers customers SPID Technology 3D screen printing from its Pessano facility in Milan, Italy, which houses a flexible cGMP suite that permits direct scaling from laboratory quantities through to clinical trial material volumes. Adare's Vandalia facility in Ohio, USA will soon be upgraded with 3D screen printing equipment and capabilities as well. Commercial-scale equipment will be added at a later date.

Adare and Laxxon have entered into a multifaceted partnership to serve customers who can leverage 3D screen printing to its fullest potential. SPID Technology may present a viable path forward for projects requiring controlled release, delayed release, and taste masking solutions, especially if they are difficult or impossible to accomplish with conventional drug formulations and manufacturing technologies.

Building Toward a Brighter Future

SPID Technology is an exciting innovation in the world of formulation because it reduces the challenges that hamper other technologies, such as the production of complex shapes or the combination of layers and different APIs. While each of these capabilities was technically possible individually in the past, they were difficult to produce and nearly impossible to combine. But now, 3D screen printing has made such endeavors easy, fast, and cost-effective.

By expanding the horizons of drug development, 3D screen printing is paving the way for tailored, patient-centric therapies that were previously out of reach. This marks the beginning of a new era of opportunity for pharmaceutical innovation, and Adare is proud to collaborate with Laxxon at the forefront of this exciting journey.

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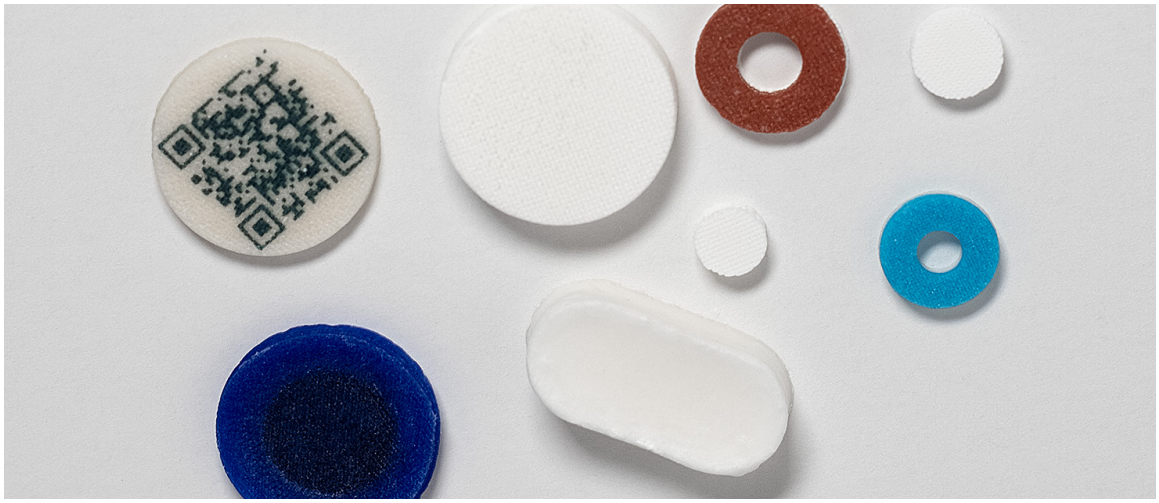

About The Authors

Steven Facer is Senior Vice President of Global Sales and Marketing at Adare Pharma Solutions. With over 30 years of global experience in pharmaceuticals and healthcare, he has held leadership roles at Thermo Fisher Scientific, ACG Worldwide, Capsugel, Catalent Pharma Solutions, and Colorcon. Facer is committed to advancing pharmaceutical solutions that improve patient health and well-being, finding purpose in contributing to the industry's positive impact on global healthcare. He holds a Bachelor of Science honors degree in Materials Science & Technology from Swansea University.

Klaus Kühne is Chief Operations Officer at Laxxon Medical. A lawyer with over 25 years of experience in the pharmaceutical industry, Kühne has an expertise in managing product development, global commercialization, marketing, and operations. He started Laxxon Medical in 2017 when he and business partners Helmut Kerschbaumer and Dr. Achim Schneeberger acquired the license for the pharmaceutical application of SPID Technology, an additive manufacturing platform technology that utilizes 3D screen printing to produce advanced drug delivery forms. Today this technology is backed by more than 200 patents and patent applications with more than 5,000 patent claims.

Adare Pharma Solutions is a global technology-driven CDMO providing end-to-end integrated services, from product development through commercial manufacturing and packaging, with small molecule expertise focusing on oral dosage forms. Adare's specialized technology platforms provide taste masking, customized release, solubility enhancement, and patient-centric dosing solutions. With a proven history in drug delivery, Adare's seven facilities in the US and Europe have developed and manufactured more than 65 products sold by customers worldwide.

Laxxon Medical is a leading pharma-technology company and global leader of 3D screen printing in the pharmaceutical industry, pioneering a new generation of advanced oral drug delivery forms designed to optimize drug delivery and maximize patient success through SPID Technology, Laxxon's proprietary 3D screen printing platform. SPID Technology unlocks innovative drug delivery advancements paired with fast-tracked market access and extensive IP protection to yield disruptive opportunities in drug development and commercialization.