From Disruption to Reinvention: The Story of API-in-Capsule Technology and Its Future

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WHEN INNOVATION SHOOK THE PILL BOTTLE: THE ORIGINS OF API-IN-CAPSULE TECHNOLOGY

Some innovations enhance established processes. Others redefine them entirely. API-in-capsule (AIC) technology doesn't just improve existing methods; it offers a new path forward by removing traditional formulation steps and delivering API directly to the patient.

The story begins with Meridica Ltd., a British drug delivery company founded in 1999 with a mission to rethink pharmaceutical development. By 2002, Meridica had designed and built the first prototype of what would later be known as the Xcelodose® system. Unlike conventional methods requiring granulation and excipient blends, Xcelodose enables precise microdosing of API directly into capsules using gravimetric feedback and vibration-based feed technology. The design was elegant in its simplicity, but that simplicity masked a range of complex challenges.

In 2004, Meridica entered a co-marketing partnership with Sartorius, officially bringing the Xcelodose system to market (Meridica & Sartorius, 2004). Interest in the technology grew quickly thanks to its faster timelines, minimal API use, and a streamlined regulatory pathway for first-in-human (FIH) studies. The platform could deliver doses as low as 100 micrograms, with fill weights accurate to within a few percentage points thanks to its gravimetric control system and real-time weight monitoring.

THE LEAP OF FAITH THAT STARTED IT ALL

The launch of Xcelodose was a leap of faith. The team behind it invested heavily into development without conducting a formal market study. Regulatory pathways were hazy, and the industry's appetite for disruption was limited. Despite initial interest from companies like Pfizer, commercial traction did not come quickly (Laboratory Talk, 2004). For the first year, there were no batches produced, and no revenue generated. There was no traction in the market. Nonetheless, the industry was paying attention, and the technology began generating meaningful discussions.

PROOF OF CONCEPT IN 200 MICROGRAMS

In August 2006, the first low-fill batches were finally produced. They measured 200 micrograms per capsule, with throughput hovering around 300 to 400 capsules per hour and fill accuracy at 98% (McGilvery et al., 2004). While the system lacked speed and scalability, it demonstrated technical feasibility and accuracy that proved its value. When the right molecule came along, the development model made perfect sense.

RESISTANCE, PUCKS, AND THE PRICE OF DISRUPTION

This disruption rippled across the formulation landscape. Conventional formulation workflows became irrelevant, and stability testing had to be rethought. Some early customers pushed back, and QA departments grew wary due to the departure from typical protocols. In particular, the absence of a traditional drug product matrix raised questions about whether a drug product assay was still required if an API assay was already validated. This debate often slowed development timelines when conservative interpretations prevailed.

The equipment was also very expensive and sometimes difficult to justify. At one point, clients were paying over $5,000 for a single puck used to hold the capsule in place. Vibration tables required specialized balancing and environmental controls. The skepticism was understandable, but so was the potential.

Then, Pfizer acquired Meridica and folded Xcelodose into its broader drug delivery platform cementing the credibility of the technology. The Xcelodose platform later changed hands again, landing at Capsugel and then finally at Lonza (Thombre, 2004). During this time, internal debates emerged: should the business approach focus on selling the machines, or pivot to a services model? Lonza chose the latter, creating a vacuum in the market. Without a standalone equipment provider, demand didn't vanish, it simply had nowhere to go.

A NEW CHAPTER BEGINS: ENTER 3P INNOVATION'S FILL2WEIGHT TECHNOLOGY

The gap left by Xcelodose paved the way for reinvention. 3P innovation, the UK's leading supplier of aseptic fill-finish, was already advancing it's own Fill2Weight technology, and recognized an opportunity to expand its impact.
3P innovation's API-in-capsule technology uses modern automation, analytics, and scalable design. Their Fill2Weightplatform, addresses the limitations of earlier

systems while setting a new standard in precision powder dosing. Fill2Weight delivers what the original Xcelodose systems could not: reliable performance across a broader range of powders, faster throughput, and exceptional accuracy. While legacy systems often struggled with cohesive or electrostatically charged powders and limited throughput, 3P's modern platforms such as the R500 and R1000 can now fill up to 1,000 capsules per hour with sub-milligram precision and real-time control for a wide variety of powders.

At the core of Fill2Weight is an advanced dual-phase gravimetric dosing algorithm. This two-step control strategy is guided by real-time feedback from high-sensitivity weigh cells and supported by in process control and finely tuned piezoelectric vibration, which provides ultra-precise dosing.

As a result, the system dynamically adjusts to changes in powder characteristics, including flow behavior, density, and electrostatic charge; factors that traditionally disrupt consistency in capsule filling.
Doses can range from sub-1 mg to 5 g without the need for hardware changeovers, a major advantage for clinical and adaptive trial settings. Additionally, 3P's "top-up" algorithm enhances yield by correcting slight underfills on the fly, rather than rejecting capsules outright. This feature is particularly impactful when working with low-

yield or expensive compounds where every milligram counts.

From a process integration standpoint, Fill2Weight offers a GMP-ready, modular design that fits easily into lab-, pilot-, and commercial-scale fill-finish lines. The equipment can be incorporated into containment isolators or biosafety cabinets, making it suitable for potent compounds and biologics requiring high levels of environmental control.

PRECISION WITHOUT THE WAIT

At AustinPx, we have fully embraced the advantages of next-generation API-in-capsule technology by integrating 3P Innovation's Fill2Weight system into our Quick to Clinic offering. This strategic investment enables us to help clients reach the clinic with unprecedented speed, precision, and flexibility especially when working with small API quantities or complex powder properties.

With minimal API amounts, we can conduct rapid feasibility assessments, giving sponsors early confidence in their development path. From there, our streamlined operations and automated capsule filling workflows can support manufacturing and release of clinical trial materials in as little as 12 weeks from API receipt.
By leveraging 3P's gravimetric Fill2Weight technology, we deliver:

- High-precision dosing with 100% weight verification
- Minimal API consumption, reducing cost and conserving valuable material
- Exceptional powder handling, accommodating even the most challenging materials such as micronized APIs, lyophilized solids, spray-dried powders, engineered particles, and highly cohesive or electrostatically charged APIs

This capability has been transformational for small and emerging biotech companies aiming to generate rapid clinical data without the burden of lengthy formulation development. The need to spend months refining excipient compatibility, blend uniformity, or manufacturing parameters has been replaced with a flexible system that meets product needs from the start.

For clients looking to bridge the gap between molecule nomination and first-in-human studies, AustinPx's API-in-Capsule service delivers more than just speed. Every capsule filled is weighed in real time, with deviations automatically flagged and corrected. Yields are maximized, and batch records are robust. These quality attributes matter as much in Phase 1 as they do in commercial supply, and our platform ensures that rapid development is achieved while maintaining quality and compliance.

BEYOND THE CLINIC: A GLIMPSE INTO THE FUTURE

These advancements are only the beginning of what AIC technology can deliver. With Fill2Weight now fully scalable and compatible with GMP fill-finish lines, containment isolators, and commercial production settings, AIC is evolving from a clinical enabler into a flexible manufacturing platform. Furthermore, the modular nature of AIC opens doors to a variety of unique applications.

Personalized medicine presents a compelling opportunity. With therapies increasingly tailored to patient subtypes or genetic profiles, batch sizes are shrinking and variability in dose strength is becoming the norm rather than the exception. AIC platforms allow manufacturers to flexibly adjust dose weights without changing hardware or revalidating processes. This

capability supports decentralized manufacturing models and clinical programs where each patient, or small cohort, may require a different dose, drug combination, or release profile.

Oncology and orphan diseases are natural fits for this approach as well. These programs often begin with minimal API, irregular dosing regimens, and highly potent compounds that require strict containment and traceability. Gravimetric AIC systems enable safe, efficient production of such products with minimal material loss and maximum control, while preserving the ability to scale or adapt protocols as the trial evolves.

Dry powder inhalation (DPI) is another area already seeing active exploration. Fill2Weight systems offer the precision and gentle powder handling needed for the fragile, micronized particles used in pulmonary delivery. With increasing interest in inhaled biologics, vaccines, and anti-infectives, the ability to fill small, consistent doses directly into device reservoirs or DPI cartridges could redefine early development for respiratory indications. Trials that once required months of formulation work can now be approached with a plug-and-play powder strategy.

TIMING IS EVERYTHING

The market has changed. Molecules are more complex, timelines are tighter, and investors want speed without sacrificing quality. AIC delivers on that need. Thanks to advances from companies like 3P Innovation, and real-world implementation at sites like AustinPx, this technology is no longer a niche idea; it is a foundational tool for sponsors navigating modern development. Sometimes, the most disruptive ideas simply need time, collaboration, and reinvention to reach their moment. That moment is now for API-in-capsule technology, and at AustinPx, we've made it a platform to turn complex challenges into tailored solutions.