

An integrated approach to enhancing compound management at Merck

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Introduction

In 2018, a collaboration between AstraZeneca, Brooks Life Sciences (now Azenta life sciences), Labcyte (now Beckman Coulter Life Sciences), and Titian Software resulted in the release of the new AcoustiX™ tube (now “acoustic sample tube”) and associated workflow, designed to streamline the compound management process, rapidly prepare library subsets for targeted screening, and achieve higher capacity sample storage and faster sample tube processing.

The adoption of this technology by the pharmaceutical industry continues to gain momentum. Merck Rahway made the strategic decision to augment their workflows with acoustic tubes in 2021, to bring greater efficiency and enable them to support their customers with more rapid request fulfillment and improved compound conservation.

After several months of evaluation, Merck decided to proceed with an integrated solution incorporating SPT Labtech’s comPOUND acoustic stores, Biosero Green Button Go Scheduler, and Titian Mosaic.

This poster outlines the primary technical solutions that have enabled Merck to realize their key strategic objective of introducing acoustic tubes, through robust automation and seamless integration.

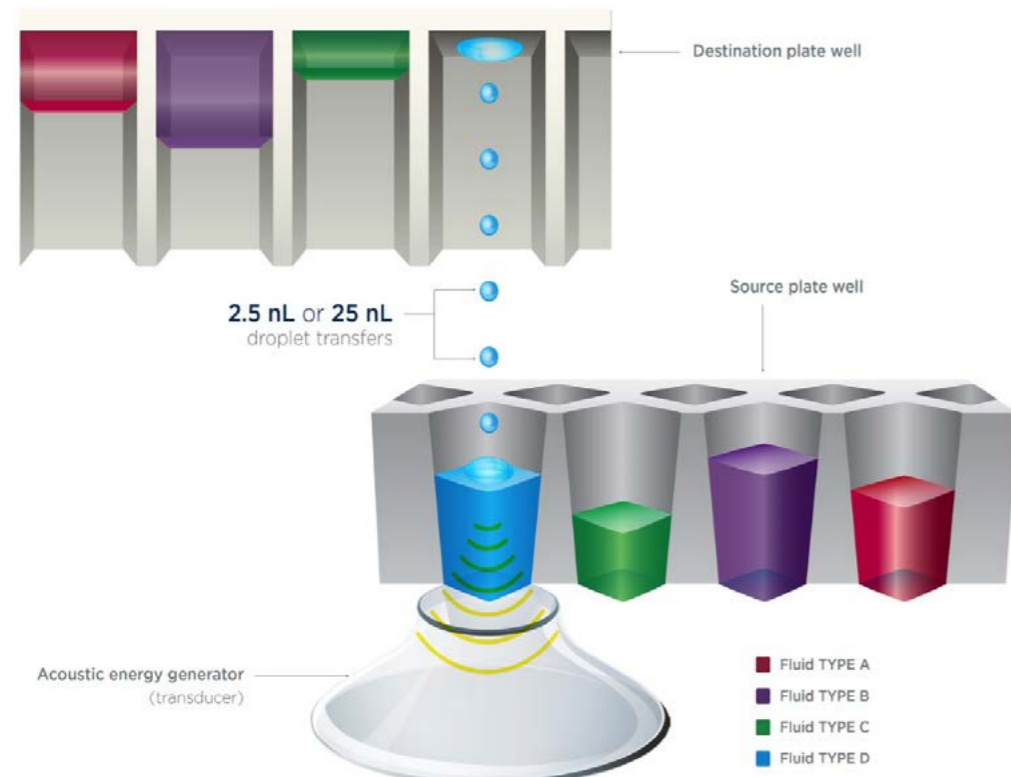
SPT Labtech comPOUND



Challenging features

Barcode

Acoustic dispensing requires the direct coupling of a transducer with the bottom of the tube through a liquid medium.



Acoustic transducer in contact with well/tube

A traditional 2D barcode in the center of the tube bottom would interfere with the integrity of the transducer coupling, so a split barcode is used in the four corners of the tube’s rectangular base.

Base of acoustic tube. Here each 2D barcode is duplicated for reassurance. Any combination of two adjacent 2D barcodes makes one complete barcode.



Rectangular base

The rectangular tubes also present a challenge to most automated pick and place systems. Unlike standard circular 2D barcoded tubes where the tube can enter the rack in any rotational orientation, the acoustic tube can only enter the rack in either 1 of 2 possible orientations 180 degrees apart.

Rectangular base of acoustic tube (left) versus common circular base tubes (right)



An acoustic tube placed into the rack incorrectly sits high in the rack and cannot continue to the downstream process.



Although mechanical pick-and-place robots may be able to rotate tubes and detect their orientation to position them correctly, most do not currently have this functionality. With comPOUND, tubes are picked and placed using a pneumatic system.

Friction fit

The final challenge is a friction fit feature. This is a safety feature to lock the tubes into the rack and tubes naturally stick in the rack when dropped into it.



In order to pick tubes from the rack, they must be released from the locked position.

Solutions

Barcode

Barcode reading in comPOUND has been upgraded, both in terms of imaging and software to interpret the data. This has been tested extensively and shown to be extremely reliable.

Locking rack management

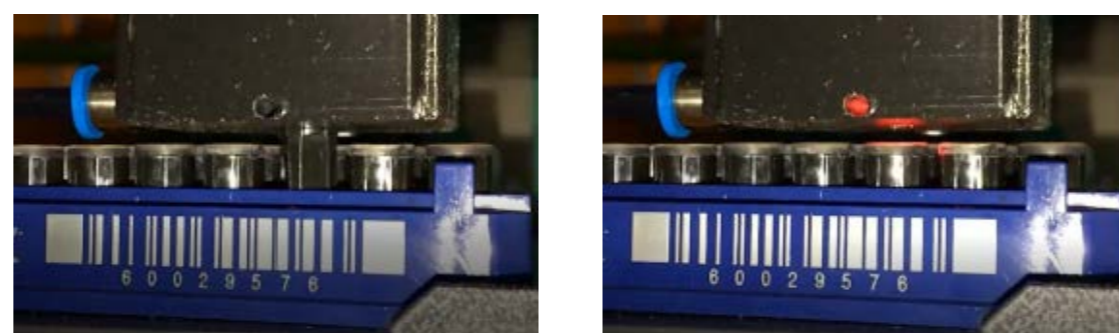
Racks presented to comPOUND for storage have tubes locked in place through the friction fit feature. In the comPOUND acoustic system, a rack release mechanism unlocks the tubes from the rack as the rack is moved into the system. Once released, tubes can be stored using the standard pneumatic system.

Rack release mechanism



Retrieving rectangular tubes

During retrieval, the rectangular base of the tube must be correctly oriented into the slot in the rack. There is a reasonably forgiving lead into the rack, and the pneumatic delivery system is used to induce a spin on the tubes which results in about 1 in 3 tubes entering the rack correctly first time. A sensor detects tubes that are sitting incorrectly and an automatic retry lifts and re-spins the tube. Most re-seat correctly with one retry but occasionally two may be required. This automatic retry runs in parallel with the next tube being picked from the store, so has no impact on overall throughput.



Sensor and automatic retries ensure tubes sit in the rack correctly on retrieval.

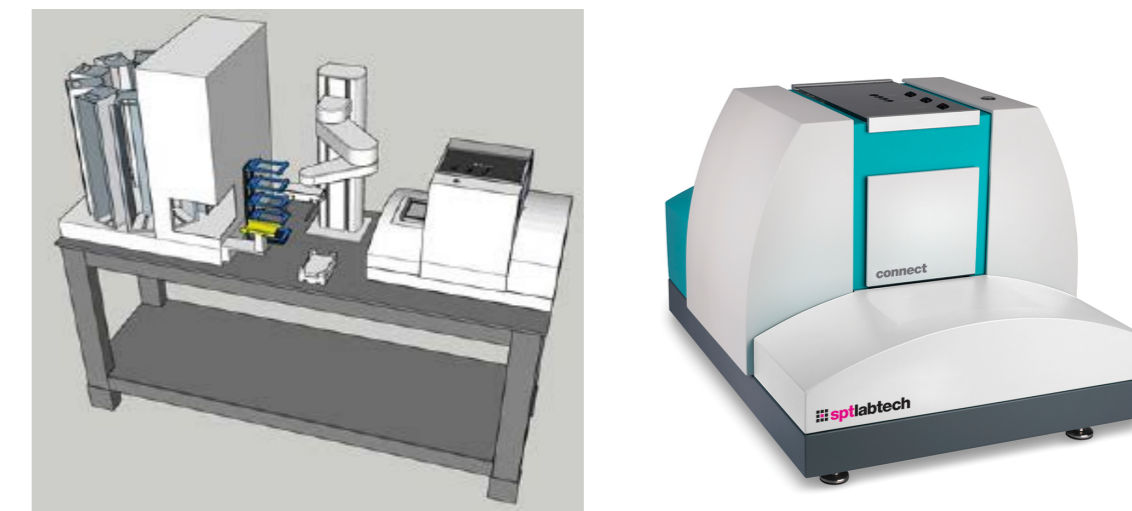
Batch processing can be achieved using the comSTACKER 2 or by integrating into an automated work cell, to provide walk away automation for processing multiple racks of tubes.

comSTACKER 2 enables batch storage and retrieval of up to 15 racks



Fully integrated solution

In order to meet their needs, Merck required a solution capable of working with a collection of acoustic tube libraries with a system capacity of 600K, and the ability to run larger batches for storage and retrieval of 100+ racks per batch. This was achieved by utilizing the “connect” remote input/output device enabling transfer of tubes between the connect and up to 4 comPOUND systems. The connect is an ideal hub to provide direct transfer of tubes between comPOUND stores and an automated work cell.



Biosero work cell (left) and SPT Labtech connect (right)

Merck worked with SPT Labtech and Biosero to develop a fully automated workstation that can manage a library of up to 600,000 acoustic tubes, with the capability to easily expand to 800,000 tubes. The system is able to manage up to 150 racks per batch, either presenting cherry-picked tubes ready for downstream processes or automatic storage. A Cytomat hotel is loaded and unloaded with batches of racks for automatic processing.

User interface

Merck was already using Titian Mosaic to manage their compound management workflows and a key deliverable was the continuity of this key user interface. Working closely with Titian, the integrated system works seamlessly with the existing Mosaic installation.

	Number of comPOUNDs with connect			
Capacity	1	2	3	4
<100,000	~10 mins	<7 mins	<5 mins	<4mins
200,000	~22 mins	<15 mins	<10 mins	<7 mins

The Biosero Green Button Scheduler drives the integrated workstation interfacing with Mosaic to manage work lists and maintain the inventory database.

Capacity and throughput

The solution for Merck provides input and output rates of around 10 minutes per rack of 96 tubes when the store is at full capacity. Higher throughputs can be achieved by running the stores at half capacity, but the throughput at full capacity is a good match for Merck’s needs.

Implementation

Initially, a single comPOUND with a comSTACKER 2 was installed to enable Merck to test the new workflows, with an additional 2 comPOUND systems being brought online along with the Biosero work cell later in 2022, with the system in full production in Spring of 2023.

Conclusion

Having made the strategic decision to include acoustic tubes, Merck took some time to look holistically at their workflows and identify key requirements for a new solution.

Detailed consultations with multiple vendors enabled Merck to develop an approach well-matched to their needs and fostered a collaboration between SPT Labtech, Biosero, and Titian to provide a trusted solution.

In addition to meeting key objectives for improvement of their services, the team at Merck were able to maintain key successful components of their current infrastructure and also develop a system that has the capacity to be expanded in the future.