From plates to tubes: Enabling fully acoustic sample management in drug discovery

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Acoustic liquid handling has become a critical technology in modern drug discovery, enabling precise, contact-free transfer of nanolitre volumes. However, early implementations were constrained by plate-based storage and tip-dependent upstream processes, limiting the full potential of acoustic workflows.

The introduction of acoustic-compatible sample tubes represents a fundamental shift in sample management architecture, enabling fully acoustic, end-to-end workflows. This transition improves assay quality, reduces compound consumption, simplifies operations, and enhances flexibility in compound library design.

This article examines the technical advantages of acoustic tube-based systems and their impact on high-throughput screening and compound management.

What is acoustic technology?

Acoustic technology in sample management uses focused ultrasonic energy to transfer small volumes of liquid without physical contact. Acoustic energy is transmitted from beneath the sample vessel and focused at the liquid surface, inducing controlled droplet ejection into a designated receiving plate.

This contactless transfer minimises contamination risk and preserves sample integrity while enabling highly precise, low-volume dispensing. Tubes designed for acoustic workflows are engineered with geometry optimised for efficient acoustic energy transmission, ensuring consistent droplet ejection. They are compatible with nanolitre-scale dispensing, incorporate integrated identification such as 2D coding for traceability, and are formatted in automation-ready racks to support seamless integration into high-throughput laboratory environments.

Introduction: Beyond partial acoustic workflows

Acoustic liquid handling has long been recognised for its ability to deliver highly precise, contact-free liquid transfer. Yet, in many laboratories, its implementation has been limited to the final stages of assay preparation.

The increasing scale of high-throughput screening - now requiring access to tens of millions of samples annually - has exposed fundamental limitations in traditional sample management approaches. These pressures have driven the need for more scalable, efficient, and integrated solutions capable of supporting next-generation screening strategies [1].

In traditional workflows:

- Compounds are stored in tubes or plates
- Reformatted into acoustic-compatible plates using tip-based systems
- Transferred acoustically into assay plates

While effective, this hybrid approach introduces inefficiencies:

- Intermediate reformatting steps
- Continued reliance on consumables
- Increased risk of contamination and variability

The result is a partially acoustic workflow, where key upstream

processes remain constrained by legacy formats.

This transition underpins the emergence of 'smart screening' approaches, where sample access, assay design, and data generation are tightly integrated for efficiency and scalability [1].

The Architectural Shift: The Tube as the Acoustic Source

Early acoustic implementations were constrained by upstream reliance on tip-based reformatting into plates. The transition to tube-based acoustic sources enables a fully acoustic workflow, eliminating intermediate plates and manual transfer steps [1].

This eliminates the need for intermediate plates and enables:

- Direct transfer from storage to assay
- Removal of tip-based steps
- True random-access compound retrieval

This transition represents a shift from process optimisation to workflow transformation. It enables, for the first time, a truly end-to-end acoustic workflow spanning sample storage, retrieval, and assay preparation.

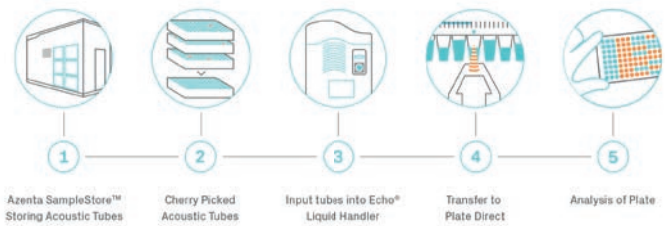

Figure 1: Evolution of sample management workflows.

Limitations of plate-based architectures

Plate-based systems introduce inherent structural constraints that can limit both operational efficiency and data quality across screening workflows. While widely adopted, their format creates challenges in how samples are accessed, handled, and preserved over time.

One of the most significant limitations is how samples are accessed. In plate-based systems, retrieving a single compound typically requires interacting with the entire plate. This broad access model increases unnecessary exposure of samples to environmental conditions, which can compromise integrity.

- Thawing or unsealing an entire plate to access individual wells
- Exposure of all samples to ambient temperature and humidity
- Increased risk of repeated freeze–thaw cycles
- Potential for evaporation, hydration effects, and compound degradation

Another constraint is the reliance on intermediate plates in many workflows, particularly when integrating with acoustic or automated systems. Reformatting steps introduce additional complexity and can impact both speed and consistency.

- Reformatting compounds into compatible plates before use
- Additional liquid handling and transfer steps
- Increased time and labour requirements
- Greater opportunity for handling errors and variability

Plate-based architectures also become inefficient when working with sparsely distributed compounds, which is common in screening and hit validation workflows. Accessing a small subset of compounds often requires interacting with multiple plates, reducing overall efficiency.

- Retrieval of a few compounds may require accessing many plates
- Automation workflows become more complex as plate count increases
- Slower progression through hit validation and downstream studies

The increasing scale of high-throughput screening has exposed fundamental limitations in traditional sample management approaches.

Finally, plate formats can contribute to increased compound consumption. The structural requirements of plates often lead to higher working volumes and unavoidable wastage, which can shorten the usable lifespan of valuable compound libraries.

- Higher minimum working volumes compared to alternative formats
- Increased residual sample within wells
- Greater overall compound usage per experiment
- Higher operational costs and reduced library longevity

The solution

Acoustic tubes: The new sound of sample management

Acoustic tubes address these limitations by enabling direct integration between storage and acoustic transfer.

Design characteristics

- Geometry optimised for acoustic energy transmission
- Compatibility with nanolitre-scale dispensing
- Integrated identification (e.g., 2D coding)
- Automation-ready rack formats

These features allow tubes to function as both storage units and dispensing sources, removing the disconnect between storage and assay.

Figure 2: Anatomy of an Echo Qualified Acoustic Tube

Key advantages of acoustic tube-based workflows

1. True single-compound access

Unlike plates, tubes enable:

• Access to individual compounds without disturbing others

• Elimination of unnecessary exposure

This directly improves:

• Sample integrity

• Stability over time

• Reproducibility of results

• Potential sample wastage

2. Elimination of intermediate workflow steps

Acoustic tubes enable direct transfer from storage to assay:

• No reformatting into plates

• No intermediate liquid handling

This results in:

• Reduced process complexity

• Faster turnaround times

• Lower risk of handling errors

3. Step-change in cherry-picking efficiency

Tube-based systems dramatically improve sparse retrieval workflows:

• Centralised access via tube racks

• Fewer mechanical operations

• Simplified automation

For example, retrieving a single compound from multiple plates requires repeated plate handling, whereas the same operation in a tube-based system can be performed from a single consolidated rack.

4. Significant reduction in compound consumption

Acoustic tube workflows operate at substantially lower volumes:

• Storage volumes on the order of tens of microlitres

• Dispensing volumes in the nanolitre range

This enables:

• Extended compound lifetime

• Increased storage density

• Reduced reagent and compound costs

In large-scale implementations, reductions in sample usage have been shown to approach an order of magnitude, highlighting the impact of miniaturised, acoustic-driven workflows [1]

5. Improved assay quality and data reliability

By eliminating tip-based transfer and reducing handling:

• Cross-contamination is effectively removed

• Mechanical variability is minimised

• Sample integrity is preserved

These factors contribute to more robust assays and more reliable screening outcomes.

6. Flexible and scalable library management

Acoustic tubes enable new approaches to compound library design:

• Storage of multiple concentrations

• Library duplication and distribution

• Parallel workflows for different assay types

This flexibility supports evolving drug discovery strategies and distributed research models.

7. Extended Sample Longevity

Lower consumption rates and reduced handling lead to:

• Longer usable lifetime of compounds

• Reduced need for re-synthesis or replenishment

• Improved sustainability of screening operations

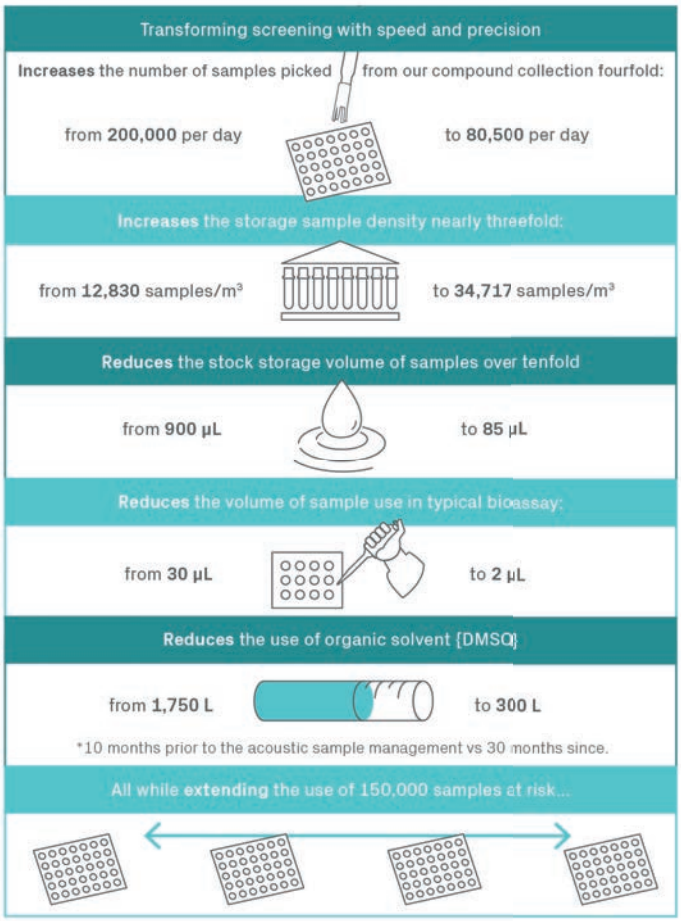

Figure 3: Fully Acoustic Workflow Enabled by Acoustic Tubes.

Industrial validation and scale

The development of acoustic tube-based sample management has been driven by the need to support industrial-scale screening operations. Implementations in large pharmaceutical environments have demonstrated the ability to process millions of compounds annually

while maintaining high data quality and operational efficiency [1].

In addition to enabling scale, acoustic tube-based workflows significantly reduce sample consumption. Reported implementations have demonstrated order-of-magnitude reductions in compound usage, supporting more sustainable screening practices and extending the lifetime of valuable compound libraries [1].

These capabilities position acoustic tube-based systems as a foundational technology for modern, high-throughput drug discovery.

Integration across the drug discovery pipeline

Acoustic tube-based workflows can be integrated across multiple stages of the drug discovery pipeline, including primary and secondary screening, hit validation, dose-response analysis, and assay-ready plate generation. Their successful implementation depends on alignment with low-volume assay design, compatibility with existing automation infrastructure, and well-defined compound handling processes. These factors ensure that acoustic transfer technologies can operate efficiently within established laboratory environments while supporting high-throughput workflows.

Acoustic tube-based workflows are applicable across multiple stages of drug discovery:

- Primary screening
- Secondary screening
- Hit validation
- Dose-response analysis
- Assay-ready plate generation

Successful implementation requires alignment with:

- Low-volume assay design
- Automation infrastructure
- Compound handling processes

Implementation considerations

Transitioning to an acoustic tube-based system typically involves a structured implementation approach. This often includes library migration, where existing compound collections are reformatted or selectively transferred based on compound quality, alongside periods of parallel operation to maintain continuity. Workflow alignment is also critical, requiring validation of compatibility with low-volume processes and seamless integration with existing automation systems. In addition, the appropriate infrastructure must be in place, including acoustic liquid handlers, tube storage and retrieval systems, and automated identification and handling capabilities, to fully realise the benefits of acoustic-enabled sample management.

Transitioning to acoustic tube-based systems typically involves:

Library migration

- Reformatting existing compound collections
- Selective transfer based on compound quality
- Parallel operation during transition phases

Workflow alignment

- Ensuring compatibility with low-volume processes
- Integrating with existing automation systems

Infrastructure

- Acoustic liquid handlers
- Tube storage and retrieval systems
- Automated identification and handling

Reframing the value proposition

The transition from plates to acoustic tubes is not an incremental improvement - it is a fundamental redesign of sample management.

Attribute	Plate-Based Systems	Acoustic Tube-Based Systems
Workflow type	Hybrid (tip + acoustic)	Fully acoustic
Sample access	Bulk	Single-compound
Intermediate steps	Required	Eliminated
Compound usage	High	Minimal
Data quality	Variable	Improved
Operational complexity	High	Reduced

Conclusion

Acoustic liquid handling has already transformed assay preparation. The integration of acoustic-compatible sample tubes extends this transformation across the entire workflow.

By enabling direct, contact-free transfer from storage to assay, acoustic tube-based systems:

- Improve assay quality through enhanced sample integrity
- Reduce compound consumption through miniaturisation
- Simplify workflows by eliminating intermediate steps
- Increase flexibility in compound library management
- Lower operational cost and environmental impact
- Reduction in DMSO and Significant reduction in reagent use (assay miniaturisation can reduce volumes from 20µL to 1µL - a reagent savings of 95%)

These advances align with the broader transition toward more intelligent, scalable screening paradigms, often described as 'smart screening', where efficiency, precision, and data quality are optimised simultaneously [1].

As drug discovery continues to evolve toward higher throughput, greater precision, and increased efficiency, acoustic tube-based sample management provides a scalable, future-ready foundation for next-generation screening.

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