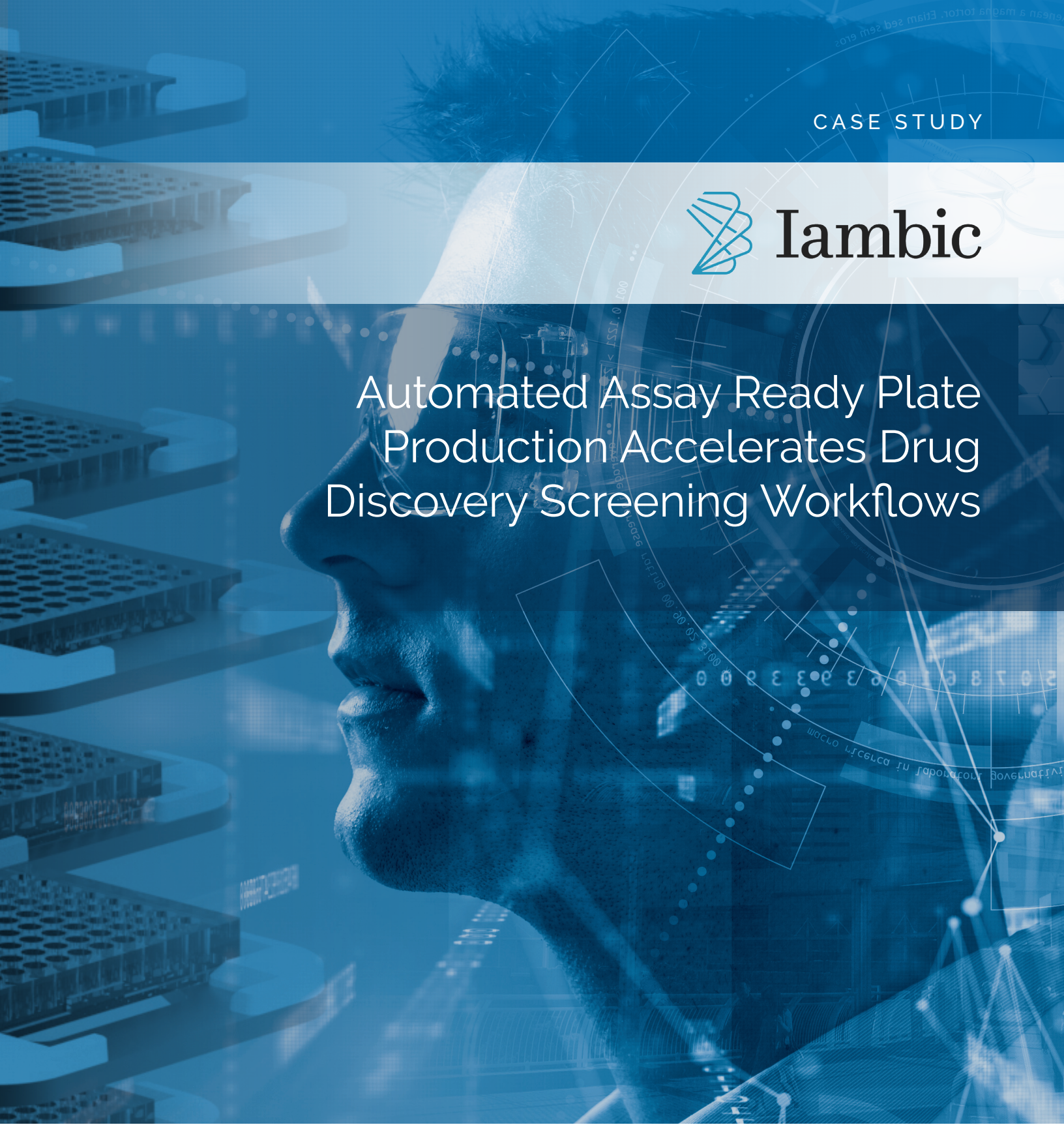
CASE STUDY

Iambic

Automated Assay Ready Plate Production Accelerates Drug Discovery Screening Workflows



HighRes biosolutions

Strategically Placed Transformative Solutions

With its vast potential, artificial intelligence (AI) is poised to change every aspect of daily life. One AI touchpoint with acute value is in the field of drug discovery, where Iambic Therapeutics, based in La Jolla, California, commands the leading edge.

Iambic leverages the predictive capabilities of AI and machine learning to dramatically enhance the speed and precision of chemical exploration. The company seamlessly integrates this cutting-edge model with high-throughput chemistry and biology, resulting in a substantial increase in data generation and a significant reduction in the time it takes to get from candidate development selection to clinical studies.

Iambic is revolutionizing drug discovery by integrating cutting-edge, physics-informed AI to rapidly generate and test new drug candidates. This system enhances drug design with technologies like NeuralPlexer and OrbNet to predict protein-ligand complexes and their interactions with drug molecules, significantly reducing the time and labor traditionally required in drug discovery. The platform accelerates the drug development process by synthesizing compounds quickly and efficiently, supported by high-throughput automated workflows.

Roadblocks to Assay Ready Plate (ARP) Production

Generating assay ready plates (ARPs) is a key element early in discovery workflows at Iambic. ARPs are microplates that contain drug compounds in a standardized layout. The compounds are logarithmically diluted to create a dose-response curve when challenged against target cells within a screening assay.

Initially, ARPs were produced by a manual process that was time-consuming, repetitive and error prone. The manual process of diluting compounds and preparing them, using a digital microplate dispenser alone, required over three hours to complete. Similarly, the manual use of an acoustic liquid handler proved to be equally laborious. One time, a user accidentally dropped a source plate when loading it into the device, resulting in "the loss" of an entire day's worth of productivity for the lab.

Simultaneously, the manual management of a substantially larger picklist posed significant challenges, leaving room for potential errors like misreading barcodes, mismatching compound locations, or selecting the wrong plate labware.

The compound management team at Iambic knew that they needed an automated solution – one that would reduce the risks of error and enhance throughput. "We also wanted to manage time better," remarked Joanna Vo, Senior Associate Scientist at Iambic. "As a smaller company we all have diverse roles and responsibilities. The envisioned automated ARP solution would liberate our team to focus on other critical tasks and facilitate ARP production even outside regular lab hours."

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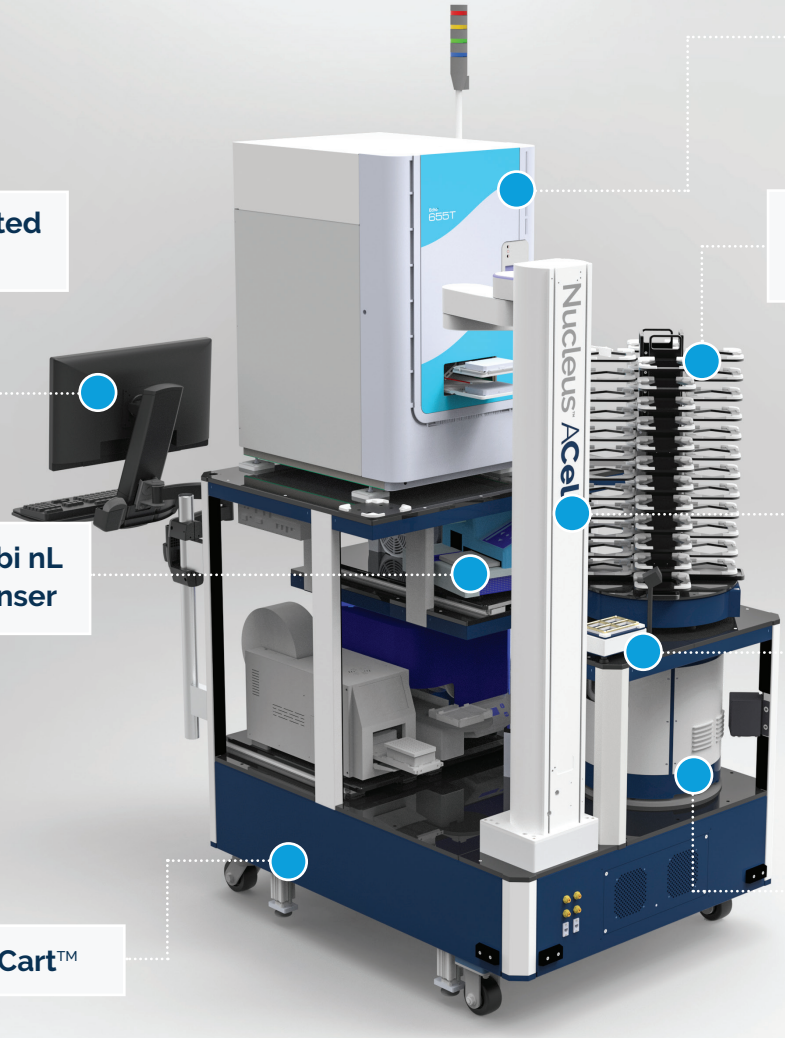
Nucleus® FlexCart™ Assay Ready Plate Workflow Components



Echo 650 Series Liquid Handler

Ergotron mounted Cellario® PC

PicoServe™ Plate Management Device

Nucleus® ACell™ Robotic Arm

Multidrop Combi nL Reagent Dispenser

PlateOrient™ plate orientation device

MicroSpin™ Automated Centrifuge

Nucleus® FlexCart™

Crafting the Nucleus® FlexCart™ ARP Solution

When researching automated solutions, the Iambic team met with experts at HighRes Biosolutions. They hashed out every detail and scenario in context. In addition to Iambic's goals of increasing accuracy, increasing throughput, and being more time efficient, they also expressed a desire for a system that took up minimal floor space and was accessible for users of all skill levels.

"The HighRes team understood our situation and worked with us to accommodate all of our requirements, questions, and concerns in the system design," Joanna added.

A Nucleus automation infrastructure and FlexCart are central to the designed solution. The workflow system is tailor fit with devices and based on the specific goals of the Iambic team. Thoughtful use of vertical space helps conserve precious room in the lab, while modularity means that the system can integrate more or different devices as workflow needs evolve over time.

Cellario® Whole Lab Automation Software controls the Nucleus Work Cell, including all devices. This unified control helps to decrease active user involvement, support consistent performance, and eliminate manually derived errors.

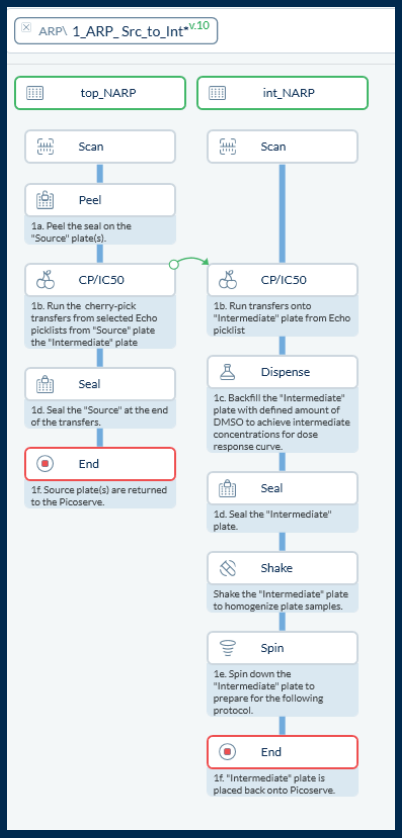
The Automated ARP Workflow in Action

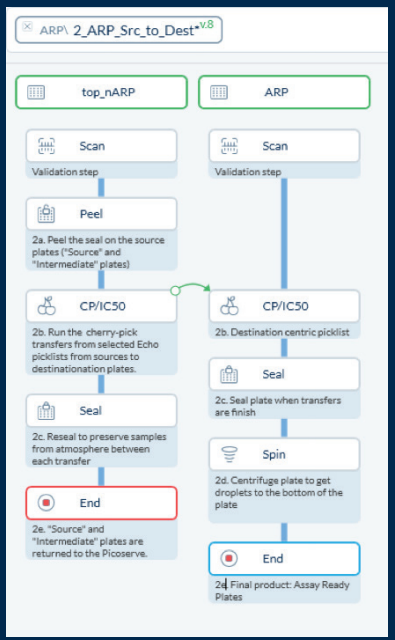
In compound management labs, the majority of which rely on automation-driven processes, users can employ the Cellario system to streamline physical production of ARPs, which can be the bulkiest aspect. This manifests in the form of the sequential execution of two CSV-based protocols, using two picklists that map dispense instructions needed to generate the desired dose-response curve (DRC).

The first picklist used in the first CSV-based protocol generates an intermediate nARP (near Assay Ready Plate) by diluting the required 10 mM compounds in the source plate for the DRC. Once the intermediate nARP is formed, the subsequent picklist is employed in a second CSV-based protocol, which is scheduled to commence immediately after executing the first picklist. This latter protocol utilizes the 10 mM source nARP, along with the intermediate nARP containing diluted compounds as source plates. Scheduling one CSV-based protocol after another, right from the beginning, removes the need for any user input after this point until the completion of both protocols.

As each plate is moved through the system, the plate barcodes are scanned to ensure accuracy in accordance with the picklists. Once the desired protocol is chosen in Cellario, the system autonomously handles all tasks, such as centrifugation, shaking, and sealing/unsealing the plates at the designated times to ensure sample integrity.

The ARPs are subsequently dispatched to Iambic's biology team for testing against target cells. Following the completion of the run, output files are reviewed for quality assurance and then transferred to a Laboratory Information Management System (LIMS) for documentation purposes.





Far-Reaching Automated ARP Workflow Benefits

ARP Production Process Overview Using the Nucleus FlexCart and Cellario Software

With the automated Nucleus FlexCart ARP system in place and validated, Iambic has achieved great strides in time and throughput efficiencies while reducing potentially costly errors.

By eliminating manual compound plating methods, operating the automated system at night and over weekends, and introducing cherry-picked picklists when dispensing across multiple plates, the Iambic compound management team can now support multiple assays and prepare significantly more compounds per week. In fact, using the automated HighRes system, over 1000 compounds can now be tested per week across the different assays supported, including, but not limited to, testing of direct-to-biology high-throughput compound libraries.

The Nucleus FlexCart system also empowers the compound management team to be proactive with plate production rather than reacting to the biology team's requests to create greater efficiencies. With plate production fully controlled by compound management and the automated system, the final ARP is quickly delivered to the biology team as needed, eliminating potential delays and downtime.

In alignment with these time-saving measures, the Nucleus FlexCart-based system eliminates the need for manual intervention and plate handling. Guided by a provided picklist, Cellario seamlessly executes a standardized protocol to orchestrate all the necessary steps for ARP creation. This protocol remains effective regardless of assay layout or dilution curve specifications, eradicating the need for users to manually transfer plates between two liquid handlers for intermediate plate creation and other workflow-related tasks. Additionally, with the capability to schedule multiple protocols through the Cellario interface, user input is only necessary during the initial setup of runs and upon completion for delivery. This newfound efficiency liberates users to concentrate on other responsibilities.

Moreover, the system's capability to operate autonomously outside of standard working hours, without the need for constant user oversight, extends its advantages beyond compound management, allowing biologists to dedicate more time to developing and conducting the necessary assays.

Errors that can occur in manual processes are markedly reduced or eliminated by the automated method. Cellario checks and verifies each plate barcode against the picklist before starting any steps to prevent mistakes in placement, handling, or labeling. In addition to ensuring accuracy across multiple plates, the barcodes help support audit trails and documentation as compounds move through the workflow. Missed dispenses during the workflow are easy to navigate with readily available and well-organized output/audit files from the Cellario system.

Cellario protocol creation is easy to navigate and designed around everyday workflows in the compound management lab. The user interface, and all system devices, are accessible to both new and experienced users alike.

HighRes Service Shines Through

From Joanna's standpoint, the HighRes experience was truly elevated by the exceptional team supporting the automation process. She highlights their consistent availability and support during the compound management's transition to an automated platform and workflow. "The HighRes support team not only met our user-friendly product requirements and aligned with our goals, but also demonstrated patience, expertise, and a sincere commitment to our needs." Additionally, she commends the simplicity of the HighRes customer support portal for accessing further information or requesting assistance.

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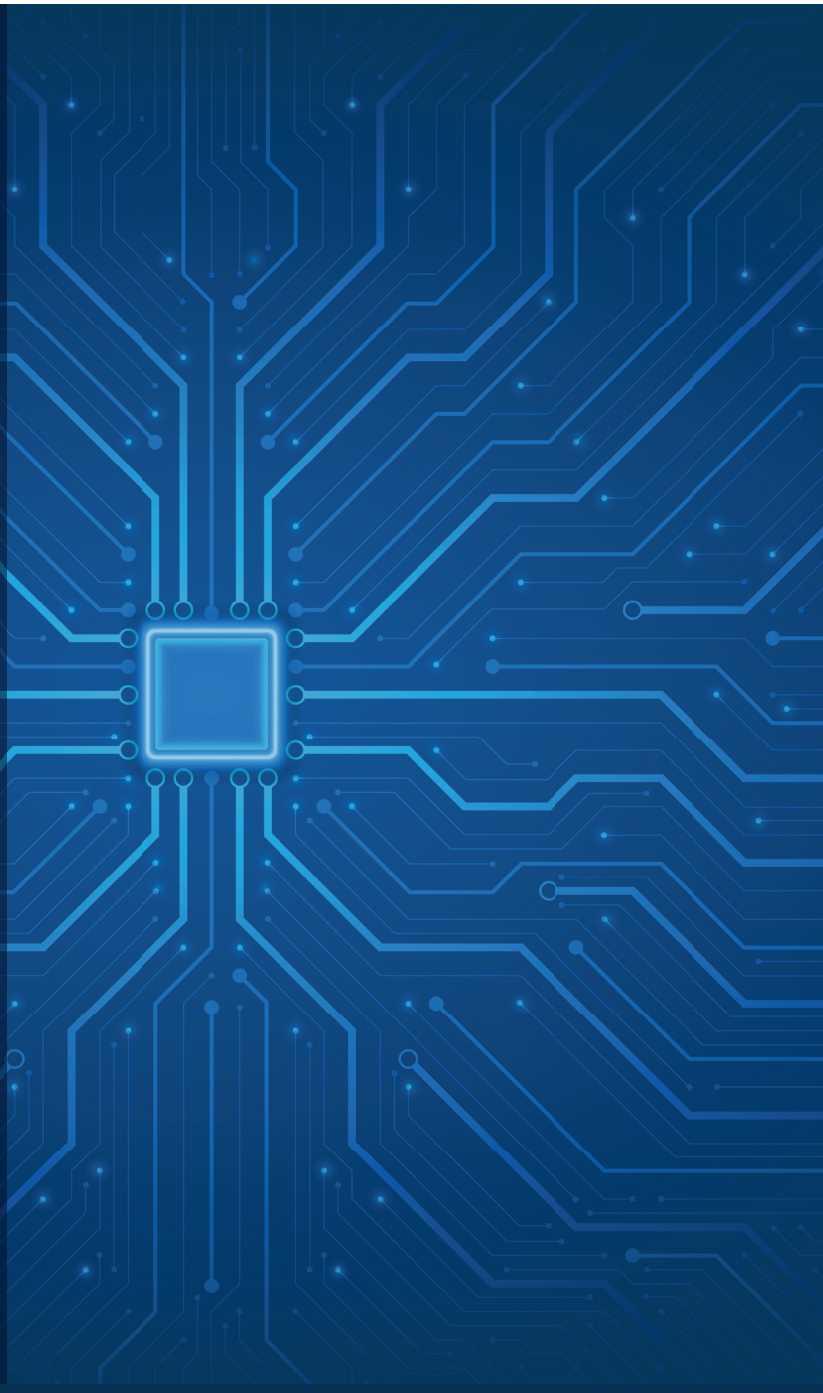
Joanna Vo, Senior Associate Scientist, HTE Operations

Conclusion

The integration of the Nucleus FlexCart has proven to be a significant asset to ARP production and the overall screening operations at Iambic Therapeutics. This automated system effectively circumvents manual resource constraints and reduces errors, resulting in enhanced throughput while allowing users to focus on other tasks. The meticulous and well-documented execution of processes ensures precision, supporting the company's continued growth and focus on building a pipeline of novel therapeutics for patients.



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