CASE STUDY

Aastrom Biosciences

CLIENT
Publicly traded biosciences company based in Ann Arbor, Michigan

CHALLENGE
Find a new partner to manufacture the media reservoir bag (MRB) component of its proprietary bioreactor to eliminate leaks

SOLUTION
- Radio frequency (RF) welding in a Class 7 clean room
- Complete custom tooling redesign
- Improved geometry of weld pattern for proper flow of molten plastic during weld process
- ISO 13485 contract manufacturer with proven quality processes
- Strong project management
- Manufacturing flexibility
- Responsiveness to quality concerns and questions

RESULTS
- Adherence to Aastrom's rigorous testing requirements
- 100% leak-free MRB, currently in clinical trials
- Six-month turnaround from tooling redesign to MRB production, QA and validation
- Long-term, true partnership with a committed supplier

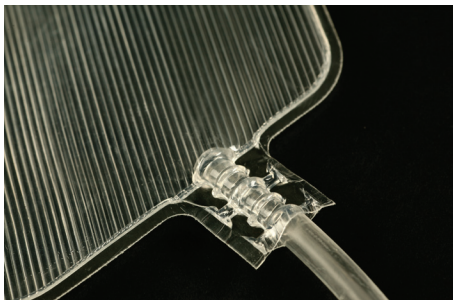
Biosciences company seeks to build exceptional quality into critical component of novel cell processing system

Aastrom Biosciences, Inc. (aastrom.com), is the leading developer of patient-specific expanded multicellular therapies for the treatment of severe chronic cardiovascular diseases (NASDAQ: ASTM).

Aastrom's goal is to help people with severe, chronic cardiovascular and peripheral artery disease realize the promise of cellular therapy. The company's investigational cellular therapy, ixmyelocel-T, is a patient-specific, expanded multicellular therapy produced using Aastrom's proprietary technology which draws on the human body's own natural healing powers. In the ixmyelocel-T production process, Aastrom extracts key beneficial cell types from bone marrow that is taken from a patient's hip in an outpatient procedure.

Using groundbreaking culturing technology, the company expands the population of these naturally occurring cells in a highly automated, aseptic, and fully-closed bioreactor. The resulting cell product is then administered back to the same patient. Ixmyelocel-T is being studied in the treatment of dilated cardiomyopathy (DCM), critical limb ischemia, and other indications.

Aastrom's cell processing system contains hundreds of hardware, software, and disposable components including a custom multi-layer barrier film called the media reservoir bag (MRB) that contains the nutrient mix to feed the cultured cells.



This disposable unit must be completely free of leaks down to a micron level as any compromise can contaminate the entire system and render cells unusable. This would represent a devastating loss for the patient and considerable financial loss for Aastrom.

MRBs produced by a former supplier had significant flaws that increased the risk of scrap, macro- and micro-leaks, and particulate in the production process. To meet the demanding standards of the ixmyelocel-T clinical research program, Aastrom needed to find a new radio frequency (RF) welding partner that could produce a 100% leak-free MRB. The production of all other system components was on track and progress in clinical trials hinged on the MRB issue being solved quickly.

Genesis PLASTICS WELDING

When Aastrom's engineering team identified Genesis Plastics Welding as a potential supplier in 2011 they quickly scheduled a technical audit at Genesis' facility. After the first meeting Aastrom had no doubt that Genesis had the technical skills, facilities, quality processes, and validation procedures to meet its manufacturing standards and aggressive timeline.

During the review process, Genesis identified and confirmed the challenges encountered with the previous MRB and offered a range of innovative and proactive solutions to address problem areas, reduce failure modes, and position Aastrom to move forward.

Genesis reviewed Aastrom's existing tooling and immediately identified weaknesses and made recommendations for tooling and product redesign that could be implemented rapidly.

Because of industry regulations and the complexities of the production process for ixmyelocel-T, Aastrom's requirements for precision and quality control went above and beyond what many of Genesis' other clients typically required.

For example, validation had to include 100% mass flow testing and 100% helium testing to identify leaks as small as five microns. Genesis was able to accommodate all of Aastrom's rigorous testing requirements and develop systems and procedures that adhered to its strict test methodology.

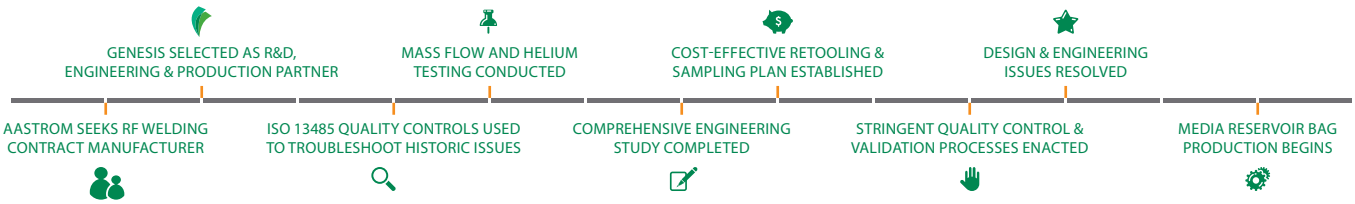
Another important consideration was the ability to achieve the highest standards in sterility and cleanliness in all phases of the manufacturing process. Unlike other RF welders, Genesis is ISO 13485-certified and demonstrates proven quality processes for the manufacturing of RF-welded medical devices and components. Additionally, Genesis' Class 7 Medical Clean Rooms meet FDA requirements for contract manufacturing of Class I, II, and III medical devices.

Along with tooling design, contract manufacturing, quality assurance, and all validation work, Genesis was also able to provide input on factors associated with fixturing, ergonomics, and process improvement. Despite low initial production quantities, Genesis was eager to be a part of this process having immediately recognized the importance of this novel system and its potential market opportunity.

> "For a biotech company, it's a massive undertaking to bring a subcomponent to a new supplier and revalidate it. But Genesis' technical knowledge was top-notch. They didn't just confirm our problems, they presented us with workable solutions. And they helped us meet our very aggressive deadlines."
>
> — Chuck Booth, Director of Engineering
> Aastrom Biosciences

Based on the level of responsiveness and ability to identify workable solutions, Aastrom has found Genesis to be a rare supplier that truly functions as a trusted partner and is dedicated to meeting the highest standards in innovation and excellence.

"Genesis is the perfect supplier," says Chuck Booth, Aastrom Biosciences' director of engineering.



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Genesis Plastics Welding is an ISO 13485:2003 certified contract manufacturer providing radio frequency (RF) welding and heat sealing applications of plastic products for military, medical and other industries. Products include military helmet pad systems, blood pressure cuffs, inflatable bladders, hot and cold therapy devices, compression therapy sleeves, disposable heating blankets and drainage bags. Genesis' proprietary heat sealing technology, ecoGenesis™, allows RF plastics welding of very thin gauge (down to 0.001 inch) polyethylene, polypropylene and low-loss polymers and can facilitate polyvinylchloride (PVC) and polyurethane (PU) replacement with phthalate-free plastics. For more information visit www.genesisplasticswelding.com.

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