

## **ACOUSTIC CELL CONCENTRATION, WASHING & PERFUSION FOR CELLULAR THERAPY MANUFACTURING**

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A major wave of promising cellular therapies is progressing through clinical trials, such that engineers and scientists need to address the challenges of economically ensuring the manufacture of safe and efficacious cell therapy products. These processes often depend on devices and methods that were developed for only related blood cell processing or vaccine manufacturing. Thus, we are in a window of opportunity to tailor innovative technologies to address the emerging specialized needs of cell therapy manufacturing.

Concentrating and washing cells between stages is a repeated bioprocess unit operation, such as to transfer cells from culture medium to cryopreservation medium. Especially for small-scale autologous therapies, cell washing is not well performed by closed-system centrifuges or filters, including due to the loss of potentially lifesaving cells. We previously developed an acoustic cell separation device that has been widely used for 20 years as part of mammalian cell perfusion bioreactors. This non-fouling filter technology uses gentle ultrasonic standing wave forces to separate cells from medium based on density and compressibility differences. We have now adapted this technology to concentrate and then wash cells at high concentrations, so as to reduce the wash volumes by an order of magnitude, thereby reducing the process cost of goods compared to centrifuge washing. The device operation has been optimized to obtain greater than 99.9% washing with 95% washed cell recoveries, such that this acoustic technology could become the method of choice for cell therapy bioprocessing. We also have recently enhanced automated acoustic devices to perfuse over 140 million cell/mL cultures, maintaining >99% cell separation efficiencies. With the simplicity of no physical filter barrier or mechanical moving parts, this tailored technology provides a high performance closed manufacturing device, to perfuse, concentrate and wash cells. The development of robust and economical means of mammalian cell manufacturing is on the critical path to ensuring that promising innovative therapies can become widely available to innumerable patients in dire need.