Microfluidic device for rapid ultra-sensitive antibiotic susceptibility testing of positive blood culture samples

Summary

A leading biotech company in the field of ultra-rapid antibiotic susceptibility testing, asked Gener8 to develop a cartridge for antimicrobial susceptibility testing of positive blood culture samples. The commercial product helps clinicians make more informed treatment decisions on antibiotic selection and dosage for improved sepsis patient outcomes.

Methods Employed

The cartridge was designed using computational fluid dynamics. The data from which was used to calculate the chamber dimensions for consistent and robust diffusion. Material selection was critical and various materials were tested. Optically clear polypropylene were selected due to ease of heat sealing, compatibility with sonic welding, for imaging, and low cost. A thin film of polypropylene was used to seal the channels and wells on the bottom of the cassette. An elastomer (Versaflex) was used as an overmold to create seals and valves. Reagents (antibiotics) were aliquoted into their respective chambers and dried-down. Incorporating a sliding valve allowed the sample-agarose gel mixture to flow in one direction and the reagents in the other. Once the sample-agarose gel mixture set, the valve would open in the opposite direction allowing the reagents to enter. The sliding valve was tested to make sure there was no cross-contamination.

Commercially available cassette with instrument.

At A Glance

Customer

Biotech company

Product

Rapid antibiotic susceptibility testing of positive blood culture samples

Services/ Market

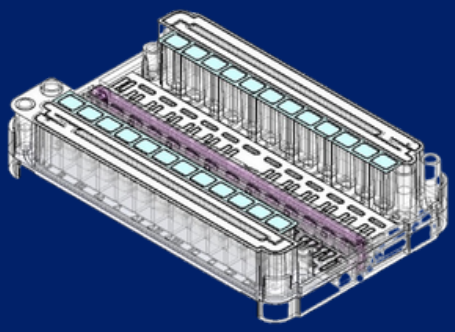
Biotech, Life Sciences

Challenge

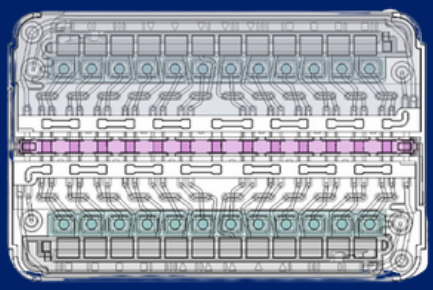
The principal challenge in designing a cassette the size of a microtiter plate that would typically be ran on a large benchtop instrument. All reagents and waste had to be contained within the cassette. The consumable has to accommodate 13 imaging chambers (12 antibiotics and 1 control) with no cross-contamination between the chambers. All reagents including the antibodies had to be preloaded in a stable form for prolonged shelf life. The design of the cassette had to allow an agarose gel and sample mixture to be loaded into the cassette such that no diffusion of antibiotics between chambers occurred. This presented another challenge in handling different viscosities. Another challenge was in designing the dimensions of the chamber into which the gel-sample matrix was injected in order to control the diffusion rate. The cassette was to have no fluid connection with the instrument. The cassette had to be made from an optically transparent material for imaging.

Solution

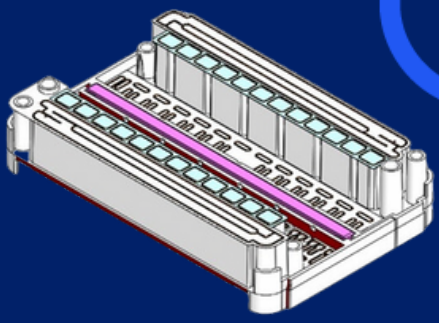
Using our microfluidic expertise, we created an in vitro diagnostic cartridge for rapid susceptibility testing of positive blood culture samples that met the customer's requirements. We designed, prototyped, prototyped injection molding and developed an assembly process to manufacture the cassette. The consolidation of various steps within the cassette, incorporation of complex multichannel microfluidics, flow balancing, sample and reagent delivery, on-cartridge valving, and optical compatibility for imaging, resulted in a 22 hour shorter workflow than traditional culture-based methods.



Transparent isometric view of the cassette.



Solid view of the bottom of the transparent cassette.



Solid isometric view of the cassette.

Expertise Employed

- Microfluidics and Fluid Dynamics
- Mechanical Design and Engineering
- Materials Selection
- Assembly Method Design
- Method for a 'dry' interface of the cartridge consumable with digital microfluidic array (PCB)
- Fluid delivery, droplet control and recovery
- Complex channel sealing using laser welding