Design Viewpoint

Designing Diagnostic Consumables: Custom or Off-the-Shelf?

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Designing point-of-care diagnostic cartridges has always been a custom affair. Specialized designers and engineers use know-how in assay development, microfluidics, and systems engineering to develop a product from top to bottom. The result is a custom design directly and uniquely addressing a market need. However, as the industry matures, novel components, pre-developed subsystems, and even entire white-label systems are increasingly viable options. These off-the-shelf (OTS) options can dramatically reduce the project's cost and risk, but only when ultimately well-suited to the application. Understanding your unique needs and the tradeoffs with each approach is key.

In diagnostic consumables, design tradeoffs are primarily a matter of managing risk. Chief among these is technical risk. Diagnostic cartridges are usually microfluidic systems in which fluids behave non-intuitively, and assays that performed reliably in a wet lab with pipettes and tubes may start to fail. There is a myriad of reasons why. Assay chemistry may be incompatible with material selection. On-cartridge fluid handling may be inconsistent due to bubble formation or poor mixing. Reagent storage and packaging may limit shelf life. Risk can also be operational. Manufacturing and assembly methods may not be scalable. Poor prototyping methodology can lead to untested assumptions and late-stage surprises.

Using modules and components that have been road tested in similar assays can mitigate these risks. Historically, this was nearly impossible because microfluidics was an active research area. But over the last two decades, microfluidics has moved slowly but unmistakably from the research lab to the manufacturing floor, and ultimately into the clinic. As the field matures and methods become more consistent, purpose-built components become better defined.

For example, Microfluidic ChipShop offers an impressive array of pretested, injection-molded modules for unitary operations such as fluid combination, droplet generation, inertial separation and detection using patterned arrays, and electrochemistry. These modules are useful to test component parts of assays—at first independently, then in daisy-chained assemblies. Finally, custom tooling can be developed to combine these modules into a single part, minimizing upfront investment while enabling development of assays using the final manufacturing methods and materials. The primary drawback is each module has a fixed size and shape, with hard interfaces to external plumbing. Sample volumes and fluid control are therefore difficult to customize.

If pre-built modules constrain, specialty components provide the convenience and dependability of OTS designs with greater flexibility. The specialty component approach works well in mixing, a fluid processing requirement common to virtually all diagnostic assays. A dedicated "mixing module" in a cartridge is usually a suboptimal solution, because mixing is desired in the same location as a function like reagent combination, sample incubation, or signal detection.

The temptation to develop an in-house solution is also dangerous because mixing in microfluidic systems is a well-established, deeply challenging problem and the subject of intense academic research. In these cases, adding the right component to an existing module is a helpful solution. Redbud Labs offers a microfluidic mixing chip—MXR—shown to shorten some molecular assays by up to 10 times. Idex Health and Science also offers valves, interfaces, and fittings that pop into a cartridge chassis designed for conventional, low-cost production.

The risk level should be proportional to the development exercise's novelty. The more people that previously solved a problem, the more likely an OTS solution exists. In some cases, entire assays follow well-traveled methodologies; there may already be an entire system available for customization to fulfill technical needs.

These systems are marketed as white-label devices or pre-developed platforms. Contract development firm TTP offers its PuckDx platform, a fully functioning system for PCR-based molecular diagnostic tests. Using a standardized but highly customizable cartridge design, a wide range of sample prep and analysis strategies can be ported to the platform with minimal technical risk. Similarly, Axxin offers pre-built systems for lateral flow and isothermal amplification.

These systems' strength is also their weakness: they are designed to use conventional modalities for sample processing and analysis. This includes relatively large sample and reagent volumes, limited techniques for separation, and fluorescence-based detection. These constraints may make them unfit for development projects with significant innovation in the instrumentation. However, for applications where the innovation is in the chemistry—or in applications with minimal new technology and a novel market strategy—these systems can substantially decrease technical risk and time-to-market.

Despite the number of pre-built tools ultimately used in a development project, diagnostic systems inevitably involve customization and systems integration. Choosing the right team for this work remains critical, and the decision is a function of the project's specific considerations and sensitivities.

Apply close consideration to the specific makeup of the development team. Skilled cartridge engineers have their own bag of tricks, including both tried-and-true components and design motifs. These are deployed to address common processes such as sample collecting, valving, metering, mixing, sealing, filtering, pumping, and storing reagents. An in-house design team's design philosophy is easy enough to study, but be sure to thoroughly review an outsourced design team's portfolio. It is helpful to ask how components were selected, why design strategies were chosen, and how they learn

about new methods and tools.

Design teams can be highly competent, successful, and professional, yet vary substantially in their focus and capabilities. Take three engineering design firms in the southern California area: Symbient Product Development (Vista), Toolbox Medical Innovations (Carlsbad), and ALine (Rancho Dominguez). Each has extensive experience and a set of functional solutions that can be reliably incorporated into disposables. Each can deploy the classic (and highly successful) modular approach to development.

Here, microfluidic functions are broken down into modules, reducing risk and improving functional performance. This allows for a combination of proven fluidic functions with custom-made sensors (i.e., optical or electrical) and then integration with injection molded parts, micro-machined silicon/glass, and more. It typically begins by combining stereolithography, machined parts, and OTS components. Rapid prototyping methods help finalize much of the cartridge. However, in most cases, actual injection molded parts must be developed and assembled using prototype tooling. Fabricating tools and testing prototypes using injection molded parts is sometimes the only way to verify the design and replicate the final manufacturing processes. Consider how this process maps onto these firms' areas of expertise.

ALine has a core competence in engineered laminates and pneumatic control. This can be combined with machining, silicon molding, 3D printing, and injection molding. Later pneumatic controllers are used to test the microfluidic cartridge. ALine retains its capabilities for small-to-medium volume production, smoothing the transfer from development to manufacturing.

Toolbox Medical Innovations believes a blend of custom and OTS solutions usually best serves its customers. This strategy delivers quick and efficient production-ready designs without having to resolve common challenges. Its proprietary "toolbox" consists of tested micro- and meso-fluidic design elements (to store, gate, mix, meter, and shuttle fluids) and fabrication techniques common to high volume disposables (injection molding, thermo-forming, laser welding, and thermal bonding). Without an in-house method and/or OTS solution readily available or feasible, custom solutions are created and become tools for future development.

Symbient Product Development develops microfluidic devices using low-cost injection molding manufacturing methods. It maintains a library of design solutions with customizable methods to meet common microfluidic requirements so product designs can be tailor-made for specific assay protocols while saving development costs. The library includes multiple methods for valving, fluid transfer, metering, mixing sample with reagents, on-chip liquid and dry

reagent storage, volume splitting, channel sealing, and plasma separation. It published papers on low-cost over molded elastomers for valving and plasma separation methods and uses in-house prototyping capabilities like stereolithography, laser cutting, CNC machining, and prototype injection molding to implement solutions from its library and develop new designs.

It is critical designers choose either non-proprietary or readily licensed solutions; the microfluidic cartridge patent landscape is crowded and can be challenging. As a component buyer the main concern should be availability. Ensure selected vendors are not at risk of injunction or other actions disruptive to the supply chain.

Besides your microfluidic application's unique challenges, evaluate technical feasibility, manufacturability, cost-per-unit, and overall performance. Microfluidic design experts should assess tradeoffs needed to commercialize your application, prioritize the features, and recommend alternatives.

Available microfluidic technology can provide a quicker path to market with less development cost, but a complete solution often requires customization. For the business model to work, the revenue model must also work. Often, customization is necessary to reduce the disposable's cost. White-label solutions might work well in research or testing, but can be a force fit for a commercial application. As a point-of-care cartridge becomes too expensive, the available technology loses appeal. Sometimes the technology risks are not obvious—they may manifest as a guaranteed or single source manufacturing contract, freedom to operate concerns, royalty payments, or may not meet ideal product requirements. Understanding the technology's technical and use limitations is important to the decision process. An unencumbered, royalty-free license should be provided with any custom solution. With available OTS solutions, you should retain the right to manufacture where you choose, to control costs. ❖

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