Outsourcing Testing Services
Contract Laboratories Find Need for Speed, Expertise Growing As Companies Large and Small Turn to Testing Providers

Innovation for medical device manufacturers is the cornerstone of their business, so as outsourcing takes hold in the industry, non-core activities such as product testing are increasingly being shuffled to outside labs. This is because contractors offer capacity and expertise their clients lack and do so more cost effectively. And, the use of contract labs is growing across the board, with large and small device makers turning to outside help. Whether they are seeking expert opinion or just need fast turnaround service, many companies view testing providers an integral part of their quality systems.

Another driver in the outsourcing trend is the growing sophistication of medical devices. As products push the envelope, sometimes blurring the boundaries between a device, drug or biologic, applicable testing requirements are also becoming more confusing. That’s when contract labs can provide input—based on their understanding of standards and sometimes participation on standards-setting bodies—that is defensible under scrutiny. Additionally, the use of novel materials in new devices may also require outside experts.

Speed Is Key
As OEMs try to shorten time to market, they’re turning over a number of internal functions to outside vendors who can perform them more quickly, and testing is no exception. Benefiting from economies of scale, labs that perform the same tests for numerous clients can in some instances shave significant time off delivery dates or product submissions to the FDA. While all companies are cost conscious, today’s need to ship...
products as soon as possible trumps just about all other mandates.

Small and medium companies with limited resources have typically looked to contract labs for a host of services, from product testing to problem solving. However, even large medical device manufacturers with centralized labs are turning to outside facilities these days—as safety valves when testing needs have outpaced internal capacity or when a capability just isn’t available internally.

“We see a lot of [large] companies where individual facility managers say, ‘We can’t get the central labs to do it quickly enough,’” said John Bolinder, the marketing and sales manager for Salt Lake City-based Nelson Laboratories.

He pointed out that contracted testing services, even for companies with internal capabilities, seem to have broad appeal. Compared with the cost of holding inventory, outside fees are nominal. “The actual cost of the test will be the least important factor,” he added. Rather than wait for internal testing resources to free up, medical device companies send much of their “overflow” work to outside contractors.

One reason outside labs are able to more quickly conduct testing is that over the years medical OEMs have increasingly changed the focus of lab personnel—nudging them more toward research and development tasks. As a result, many internal testing departments are left short-handed and must recruit the help of contract labs.

“At the end of the day, testing is not their core business,” said Deep Krishnan, director of sales and marketing for TÜV Rheinland in the U.S., an international firm that provides consulting, testing and other services to the medical device industry.

Based in Newtown, CT, Krishnan noted that regulatory testing, especially, is being shifted to outside contractors. Many of these standard tests such as for compliance to EN 60601-1 for electrical safety are routinely mandated in key markets including Europe and the U.S., so labs such as TÜV are familiar with customers’ requirements. That familiarity also enables the labs to perform the tests more quickly and efficiently.

In some instances, OEMs who have in the past conducted their own testing to achieve regulatory compliance are turning over those functions to an outside service provider. In part, it may be more cost effective than staffing its own; additionally, capacity issue is more flexible. Some labs are also partnering to provide comprehensive services that meet just about any needs an OEM might have.

**Specialized Services**

While one-stop contract labs might seem ideal, the fact is many providers specialize their services. Some larger companies offer a wide battery of tests and services, while others focus on a niche area such as material analysis, biocompatibility and the like. Although their offerings are limited compared with their larger counterparts, these “boutique” labs can sometimes provide more in-depth knowledge and expertise in a specific area. They can give insight into the appropriate testing for a new category of devices or the applicable standards to which a new product must conform. In some cases, they have expertise other labs lack.

Monarch Laboratories, for example, specializes in the analysis of leachables/extractables in plastics and glass. It caters to both the pharma and device industries, and sometimes products fall into both categories. Clients ask for materials to be chemically characterized and employ the results in various tasks such as risk assessment.

Chemical characterization may indeed become more important in many markets, said Diane Paskiet, associate director of organic laboratories at Monarch. She said customers in the past were much more concerned with biological test results, but
regulators around the world are becoming increasingly concerned with chemical exposure. For device manufacturers, that means they may have to provide more material analysis information than ever before.

In Japan, for instance, changes in the product review process now require detailed chemical listing of all plastics. This emphasis on materials characterization will require OEMs to either obtain the information from suppliers or perform their own testing, which are not typically routine assays device manufacturers perform. While the makeup of some materials can be found in published databases, the composition of newer compounds might not be listed. Already, some polymer manufacturers have expressed reluctance to offer detailed, proprietary information about their products, so OEMs might have to contact a third party to perform the analysis.

“The chemical tests have become more prevalent,” said Paskiet. “Rather than just biological, [regulators] want to know what kind of exposures would be safe.”

**Adoption of ISO Part 18**

Chemical characterization will likely become an even more important issue in the near future as Part 18 of ISO 10993 (Biological Evaluation of Medical Devices—Chemical Characterization of Materials) moves closer to being approved. This standard, which at press time was out for a vote, is a move away from animal testing toward quantifying materials used in medical devices. This standard will cover a wide variety of issues such as measuring the level of leachables, the screening of new raw materials, assessment of product safety and detection of batch variation.

If widely adopted, the standard would force device manufacturers to provide more data to regulatory bodies. At the same time, there may be differences over which types of tests would satisfy the standards, and contract labs could play an important role in interpreting the requirements, working with regulators to establish guidelines and even developing new protocols.

How much more testing is actually required of OEMs remains to be seen, said Jeff Blair, the president of NAMSA, a Northwood, OH-based testing lab. While new materials will certainly require attention, Blair said
New Assay for Skin Irritation Offers Speedier Results, A More Humane Approach and Quantifiable Data

A test that evaluates a chemical’s potential for inducing allergic contact dermatitis may help medical device manufacturers obtain results more quickly and accurately. Under development for 10 years, some labs may soon begin using the assay instead of a traditional guinea pig test that takes longer and produces more subjective results.

The Murine Local Lymph Node Assay (LLNA) could reduce testing time from 35 days to as little as seven days, a significant time savings, said Tom Herbst, the director of in-life studies and tissue engineering at AppTec Laboratory Services. In addition, the test will produce more quantifiable results than the guinea pig method.

The LLNA determines irritation potential by applying the test chemical, such as extracts of materials used in devices, to mice to induce the production of lymphocytes. By measuring cellular proliferation, this method provides discrete data, compared with the subjective approach of the widely used guinea pig test in which testers determine irritation based on a their visual assessment of the animal’s skin.

Herbst said the new method uses fewer animals but requires a special breed of mice so testing costs may be equivalent to using guinea pigs. However, the shortened testing period is proving to be a significant attraction to a number of companies.

“We’ve had multiple inquiries. That was our primary driving force” for considering adopting the LLNA, he said. Herbst added that the FDA is currently reviewing the test to see if results correlate with the guinea pig assay.

Herbst said it’s unlikely the LLNA will replace the conventional tests because it doesn’t work well with some materials such as metal salts. He said AppTec will likely offer both to clients. Copies of the protocol can be found at [http://iccvam.niehs.nih.gov/methods/llnadc/LLNAProt.pdf](http://iccvam.niehs.nih.gov/methods/llnadc/LLNAProt.pdf)

Educating Customers

For some OEMs, the outsourcing of testing services is as much about seeking expert advice as it is about having products tested. Labs interviewed said some customers come to them unsure about the kinds of tests they need. In some cases, the labs develop their own assays or evaluation methods if the product in question is not easily classified; in other instances, there may be no clear standard. In any case, independent labs must rely on their expertise as well as the input of some outsiders to help choose the right test.

Dean Enrooth, executive vice president of AppTec Laboratory Services, a St. Paul, MN-based company that services the medical device and pharma industries, said he sees customers turning over routine as well as specialized tests to his firm. While some OEMs specify their needs, others are confused about which tests are right for them. He said competent labs can

published information exists for the majority of materials used in medical devices. OEMs can obtain data from vendors or find them on the web.

“There is enough data out there that I don’t see the need to do all this testing,” he said.

Nevertheless, he pointed out, there is a clear movement toward better manage risk through material characterization, adding that regulatory agencies everywhere are concerned with issues such as carcinogenicity. “It’s driving our chemistry business,” he added.

Aside from characterizing materials used in the device, companies are also concerned with the content of packaging and its effect on products. The new ISO standards will likely also drive the scrutiny of packaging materials and how they react to sterilization.

One of the biggest demands for contract testing is to ensure that products meet sterility requirements. Outside labs are often hired by medical OEMs to check batches for sterility, confirm their own results or as advisers to solve quality issues. Many testing labs say sterility testing is a bread-and-butter service they offer to many customers, especially those who outsource their sterilization. In those instances, testing labs often find themselves under time pressure to obtain a batch release or to help customers resolve failed products. As consultants, they can readily identify common failures in packaging and the sterilizing process.

Ensuring package integrity and sterility can often be overlooked by device makers, said Pat Nolan, the chief operating officer for DDL, an Eden Prairie, MN-based contract lab that provides both materials and package testing. Nolan said OEMs under pressure to get products to market may cut corners at times. Some lack the resources internally to examine packaging problems thoroughly. He said he sees many customers outsourcing to get expert advice so they can more efficiently package and deliver sterile products to their customers.

“A lot of these smaller companies can’t afford to employ a packaging expert,” he said. “We’re trying to educate people so [their packaging process] is much more efficient.”
When Outsourcing to Contract Labs, Remember to Ask Key Questions To Determine Qualifications and Competency of Service Providers

Contract laboratories play a vital role in the medical device industry. They are an extension of the manufacturers’ operation and therefore must have the proper quality assurance, costing, staff scientists and service to meet manufacturing requirements. Offerings, which may include a wide range of services in toxicology, microbiology and chemistry, often play a key role in both product development and quality assurance functions.

These labs consult and perform testing that speak to material requirements, required testing regimens, regulatory needs, quality assurance of facilities and product sterilization; they also assist on submissions through reporting and their council. As global standards for safety and compliance change, and manufacturers routinely address the “make versus buy” decision, the use of contract laboratories continues to grow.

Outsourcing Laboratory Trends
Manufacturers’ first decision in considering a contract laboratory is generally time-to-market. Can the laboratory reduce time to market through turnaround of test results, its expertise at compliance issues as evidenced in the report or its ability to more quickly create new and acceptable tests and protocols?

A second significant decision point is control. What sort of confidence can I
place in the laboratory versus doing the testing in-house? The question of trust and experience is often answered over time.

In addition, manufacturers are looking for quality assurance, optimization of costs, a shared accountability for regulatory risk, specific expertise or specialization and, more recently, a reduction or consolidation of vendors that can provide multiple services well.

The determination of which contract laboratory to use can be made by thorough evaluation of the following questions, but a personal visit to the laboratory in the form of an audit to validate an assessment should always be considered.

**Fundamental Qualities**

The areas below are core to any outsourcing relationship, and providers that do not meet these criteria should not be considered for partnership.

- Is their quality system thorough?
- How long have they been in business, and how long have they been providing the service required by the manufacturer? If evaluating a new laboratory, have they been able to gain compliance with all applicable regulations?
- Are they focused on Continuous Improvement?
- Is their technical or scientific experience in the specified product area sufficient? Are credentials and training records readily available?
- What is the breadth of the laboratory offering? Do they perform the testing or subcontract work to another lab?
- Are they committed to Operational Excellence in terms of communications, timeliness, thoroughness and accuracy?

**Financial & Operational Strength**

- Is the contract laboratory financially stable?
- What is the size of the laboratory? Can it handle the scope of the targeted testing needs?
- Is there adequate space, personnel and equipment to handle expanding testing needs?
- Are facilities neat, clean, expandable and organized?
- Does the laboratory have adequate backup to ensure testing is completed on time?
- Does it maintain and follow standard operating procedures specified?
- Are there references from other customers as to the financial and operational strength of the laboratory?
- What is the laboratory’s experience in interactions with the FDA and other agencies?
- Are the fees being charged comparable and optimal? Does the outsource laboratory provide rational pricing that commensurate with turnaround time and value of technical support? Does it help provide the correct testing regimen (no more or no less)?
- Does the laboratory set and meet deadlines.
- Is the laboratory committed to rapid and routine communications on test results, including adverse findings?
- How thorough and effective is the laboratory’s sample traceability system? Is equipment labeled properly? Are reagents labeled and dated properly?
- How effective is the laboratory’s technology and software in assisting control, output and efficiency?

**Quality Systems**

- Is the laboratory’s Quality System compatible with the manufacturers’ system?
- What evidence is there of commitment to continuous improvement?
- Is the laboratory fully accredited to the proper FDA/ISO standards?
- What were the results of the most recent FDA inspections?
- Does the laboratory have the requisite regulatory support to help guide the manufacturer through global approvals?
- How thorough is the documentation system in terms of Standard Operating Procedures (SOPs), special protocols and results reporting?
- Do the SOPs reflect current USP, AAMI and other standards?
- Are archives locked with limited access? What level of confidentiality can the manufacturer anticipate?
- Does the laboratory have active involvement with the standards-setting community?
- Are Good Laboratory Practices (GLP) provided as required? What is the technical competency and experience of the Study Director group that presides over GLP work?

Several of these questions beg additional follow-up (e.g., SOP development, GLP understanding, equipment validation) so a more comprehensive audit checklist for a visit to the laboratory is appropriate. The manufacturer should not only be thorough in referring to the checklist but also use a similar audit for routine repeat visits to the contracted laboratory.

Contract laboratories can provide supplemental core competency to manufacturing partners, which reduces time to market in the development cycle or on the release of sterile, manufactured products. Yet, laboratories must be held to a very high and escalating standard of performance to be trusted partners. The checklist of questions here is only a guideline for manufacturers. Additional questions may arise in different circumstances.

Jeff Blair is President and CEO of Northwood. OH-based North American Science Associates, Inc. (NAMSA). He has 32 years experience in the medical manufacturing, distribution and testing market. NAMSA provides a wide array of testing, products and scientific services to medical device and pharma/biotech manufacturers.
work with customers to determine their needs, choose not only the appropriate but also the right amount of testing and help device makers resolve failures.

In the U.K., the Restriction of Hazardous Substances in Electrical and Electronic Equipment (ROHS) is scheduled to go into effect this August. Medical device and other manufacturers will have to test their electronic products to ensure the concentrations of lead and cadmium do not exceed 0.1%. Although European regulators set maximum concentrations, they did not specify the tests to be used, pointed out Don Shuman, the director of client services at IMR Testing in Ithaca, NY. A firm that specializes in chemical analysis and metallurgical evaluation, IMR has fielded a growing number of questions from clients about complying with the directive. Shuman added that labs are increasingly seeing testing requested for components used in circuit boards, including solder, and can help OEMs map out an appropriate testing strategy.

Outside Expertise

Even when choosing the right test is unclear, labs that participate in standards organizations such as the Association for the Advancement of Medical Instrumentation (AAMI) have external resources and other industry experts to consult with. In some cases, OEMs are advised to consult with their FDA product reviewers to determine the right course of action.

Clearly contract labs no longer provide just testing services; they have become consultant to the uninformed. Having staked out a niche and developed unique expertise, these labs can aid medical OEMs in everyday tasks, take on urgent projects or offer insight their clients lack. While every manufacturer is concerned about costs, the value contract labs return may outweigh their fees. Compared with inventory idling in a warehouse or product development brought to a halt because of incomplete material characterization data, lab fees may prove inconsequential.

“Because cost is an issue with all companies—the cost of holding inventory, cost of time to market—the actual cost of testing will be the least important factor,” stressed Nelson Lab's Bolinder. ☰