



CHALLENGE

To provide clinics, hospitals and reference laboratories with simple, flexible, cost-effective technologies for performing molecular diagnostic services.

SOLUTION

Use JMP® to evaluate product designs, conditions and materials; optimize performance; and identify product manufacturing specifications for molecular diagnostic instrumentation.

RESULTS

eSensor technologies help physicians predict hereditary diseases, determine effective drug dosage levels, identify infectious disease agents and develop plans for patient care.

MORE INFORMATION

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Truly Vital Information

Osmetech® Molecular Diagnostics uses JMP® statistical software to provide potentially lifesaving information

Cystic fibrosis (CF) is a hereditary disease for which there is yet no cure. Approximately one in 30 Caucasians, one in 45 Hispanic-Americans and one in 65 African-Americans are carriers of cystic fibrosis gene mutations. People born with cystic fibrosis are most likely to die in their 20s or 30s.

Today, though, early diagnosis and new treatment methods are facilitating an improved quality of life and a longer life expectancy for those with cystic fibrosis. Genetic testing now allows for the disease to be diagnosed prior to birth, and Osmetech Molecular Diagnostics is helping to make testing for cystic fibrosis more accessible to more people.

JMP statistical discovery software from SAS is assisting in this effort.

Responding to a growing medical need for molecular diagnostic testing, Osmetech Molecular Diagnostics' objective is to "transform molecular diagnostic testing into practical, cost-effective solutions." The idea is to produce simpler, less expensive testing methods so diagnostic testing can be easily processed in smaller laboratories that otherwise would be unable to do the testing.

Osmetech is meeting this objective by providing cutting-edge, cost-effective technologies and tools that offer greater access to molecular diagnostics, including those for life-threatening diseases such as cystic fibrosis.

"Essentially, what we're doing is making genetic testing available in physicians' offices and clinics," says Aviva Jacobs, PhD, who oversees Osmetech's product development. "A person can now go to their doctor to be tested, the doctor will send out the patient's sample to a local lab and the lab can then very quickly and affordably run the tests.



The eSensor® CF Carrier Detection (CFCD) System reports cystic fibrosis carrier results.

OSMETECH
MOLECULAR DIAGNOSTICS

**STATISTICAL
DISCOVERY.™
FROM SAS.**

“Cystic fibrosis research is a good example. We have a test for those who want to know if they have a potential for passing the disease on to their child.

“It’s all about giving people important information they need to make decisions.”

A unique, less expensive approach

Cystic fibrosis is an inherited chronic disease that affects the lungs and digestive system. A defective gene causes the body to produce thick mucus that can both cause life-threatening lung infections and prevent the body from breaking down and absorbing food. Both parents must be carriers for it to be passed on (though even if both are carriers, the chances are only one in four that their child will have the disease).

CF is undetectable prior to birth and there are no known health problems associated with being a carrier. Thus the value of testing is informed knowledge of each parent’s genetic status. Having been tested and alerted that they may be carriers, parents-to-be may then be made aware of what will be involved in caring for a child with CF – medications and respiratory therapy, for example – and healthcare givers can begin planning the treatment for the child from birth.

Osmetech’s eSensor® CF Carrier Detection (CFCD) System is today making more reliable information more

readily available. The eSensor® XT-8 offers highly accurate and reproducible results in about four hours in an easy-to-interpret report, and the eSensor® CFCD System delivers 99 percent accuracy. The report includes a summary “carrier” or “noncarrier” assessment.

At the core of the eSensor® detection technology are DNA fragments attached to electrodes on the surface of a small electronic circuit board. The system performs complex molecular tests that require the simultaneous analysis of multiple pieces of genetic information. Each system cartridge can detect multiple differing DNA targets at once, providing a cost-effective platform for this complex analysis.

Similar diagnostic tools existed prior to the introduction of the eSensor system, but, says Jacobs, “Ours is unique in that our instrument is a lot less expensive. A lot of tests rely on fluorescence, but ours is based on electrochemical detection.”



The Osmetech eSensor® XT-8 System is a complete bench-top instrument for detecting nucleic acids on a microarray.

Jacobs explains that with fluorescence, a laser is required for reading the results, and lasers are quite expensive. In contrast, electrochemical detection only requires simple, inexpensive and highly reliable solid-state electronic components.

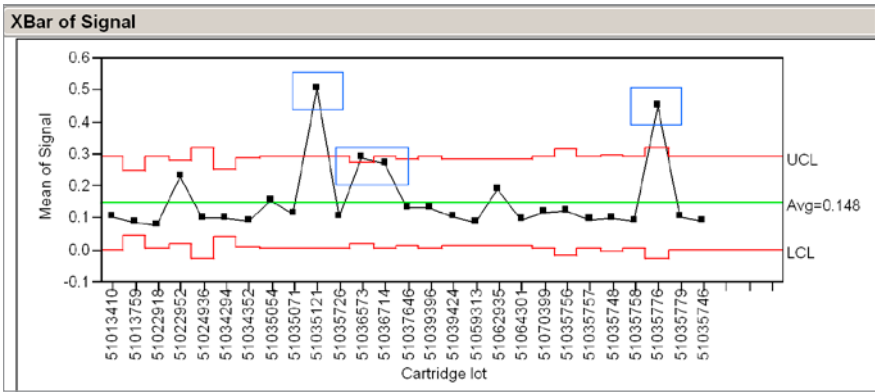
Developing the best eSensor products

JMP statistical discovery software plays a critical role in assuring the reliability of this vital disease-detection device. Osmetech uses JMP to test its product design to make certain the analysis tools built into the eSensor product are accurate and to test the results over time to ensure the product continues to give accurate results.

Each eSensor® cartridge contains 72 electrodes, and studies often involve anywhere from 100 to 1,000 samples, resulting in up to 72,000 data points. Within each study, it’s essential to keep track of samples and experimental conditions associated with each row of data.

JMP is the choice here because of its ability to rapidly process extremely large amounts of data.

“Say, for example, we want to know the shelf life of the product,” says Jacobs. “We’ll do our testing in increments – three months, six months – and we need to make sure that we can compare our results across different conditions.



JMP identifies outliers outside the control limit, flagging data that Osmetech can then explore interactively.

“JMP allows us to condition or append specific information to our data table and then readily draw graphs and look to see if there are any trends. We can then analyze the trends to identify the root cause, which is the key first step in troubleshooting.”

Jacobs and her team frequently use variability plots in the early stages of product development to evaluate different designs, conditions and materials. In addition, once a design is established, the DOE tools in JMP allow the team to optimize even the most complex reagent composition and to determine the limits within which that reagent will give acceptable performance. This latter approach is extremely valuable in setting product manufacturing specifications.

Jacobs’ team is also using JMP for troubleshooting. When developing a new test, Jacobs and her colleagues receive anonymous patient samples from third parties, such as blood-collection sites or clinical laboratories, which they use for the development

and validation of the test. If a potential issue is detected, an experiment is designed. Data is run and variables are evaluated.

If the team chooses to run the data on multiple instruments, it’s easy to interpret with JMP.

“As long as you create a column telling you what instrument you ran it on,” Jacobs explains, “you can say, ‘I want to look at my data by electrode, for example, or by date tested.’ Within the table we have in JMP, we have all relevant information, and the really nice thing about JMP is that it’s interactive.”

Jacobs can draw a graph and look at it and say, for example, “I see a couple of different populations; I need to add a variable to my plot.” She then can very quickly regenerate the plot.

“You just hit the recall button, add a variable and change the order of your variable to look at data a little bit differently.

Warfarin testing to help save \$1 billion

Osmetech has recently received FDA clearance on its new warfarin sensitivity test, using its second-generation product, the eSensor XT-8 System. Warfarin is the most widely prescribed oral anti-coagulant in North America and Europe and is among the 20 most-prescribed drugs in the US. Warfarin is, however, the second-most likely drug, after insulin, to cause adverse effects requiring emergency room visits.

A recent study from the Brookings Institute found that widespread use of warfarin sensitivity testing in the US could avoid 85,000 serious bleeding events and 17,000 strokes a year, saving healthcare costs of approximately \$1.1 billion annually and improving patient care.

Osmetech’s eSensor® Warfarin Sensitivity Test detects the three genetic markers that are known to play a critical role in the metabolism of, and sensitivity to, warfarin. Through detection of these markers, doctors can more accurately and efficiently determine appropriate warfarin dosage levels.

The eSensor XT-8 is designed to support a broad menu of tests and provide accurate results while minimizing technician involvement.

“It’s iterative and interactive,” says Jacobs of JMP. “If you find an outlier, you circle it and subset it, and ask yourself what’s unique about it. It’s that interactive nature of JMP that makes it really easy to quickly generate the graphs and realize, ‘No, that’s not what I want; I’m going to generate something else.’”

JMP software’s role in the successful development of the eSensor products has helped Osmetech reduce analysis errors and troubleshooting time and increase productivity. “Honestly,” Jacobs says, “I don’t know what we’d do without JMP. We use it for almost everything.”

And that could mean absolutely everything to the patient whose test results could lead to early detection and improved quality of life.



SAS Institute Inc. World Headquarters +1 919 677 8000 To contact your local JMP office, please visit www.jmp.com

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