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Expert outlook: Addressing current trends and challenges in clinical research with mass spectrometry

Panelists

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Dr. Michael Vogeser

Keywords

HRAM, LC-MS, immunoassay, Q Exactive, drugs of abuse, novel psychoactive drugs, drug monitoring research

Introduction

The healthcare industry looks toward new solutions to provide better outcomes at lower costs. With more treatment decisions now based on clinical lab results, labs play an important supporting role. Lab tests include screening, detection, and confirmation of various analytes for drugs-of-abuse testing and drug monitoring research. In drugs-of-abuse testing, labs continue to see a rise in novel psychoactive substances (NPS).

Though the testing technologies employed have evolved, the most popular are immunoassay and mass spectrometry (MS)-based tests. The effectiveness of these technologies varies depending on the analysis needed, desired throughput, sample preparation method used, and type of matrix analyzed. Clinical-research-lab use of MS has traditionally provided the greatest value in drugs-of-abuse confirmatory testing in forensic toxicology and in drug monitoring research.

In both fields of work, leading researchers are now advancing new technologies such as high-resolution MS to solve their clinical research challenges.

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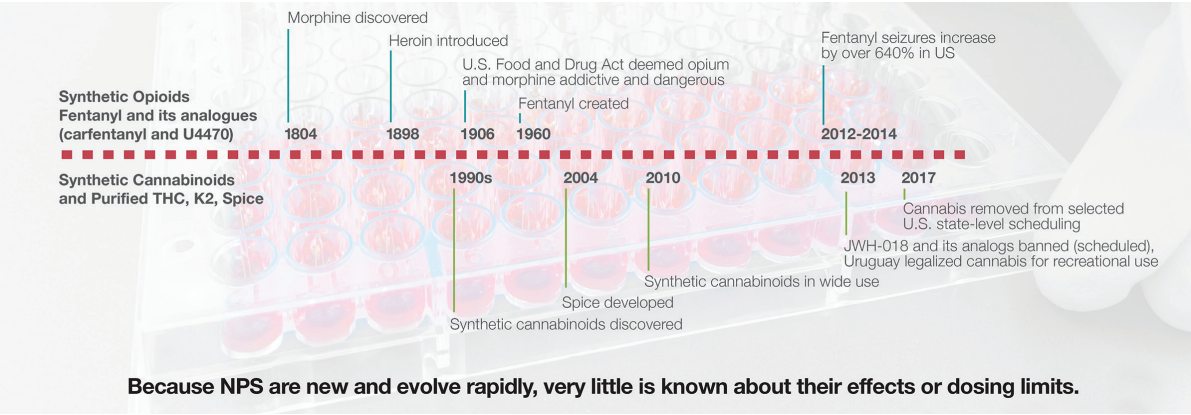
In particular, these leaders are making the switch from nominal-mass to high-resolution, accurate-mass (HRAM) systems such as the Thermo Scientific™ Orbitrap™ mass spectrometer technology. This technology offers labs the flexibility to develop in-house tests for measuring panels of clinically relevant compounds and their metabolites in complex matrices.

In this white paper, **Suparna Mundodi**, Marketing Manager, Clinical Research at Thermo Fisher Scientific, interviews experts **Marilyn Huestis**, recently retired from the National Institute on Drug Abuse, **Michael Vogeser**, specialist in Laboratory Medicine and senior physician at the Hospital of the University of the Ludwig-Maximilians-University Munich, Germany, and **Lawrence Andrade**, Director of Research and Development, Dominion Diagnostics. Their discussion focuses on current trends and challenges in clinical research.

Four themes emerged:

- NPS, the opioid epidemic, and demands for personalized medicine are driving current and future research needs for lab testing.
- Traditional screening methods such as immunoassay aren't keeping pace with testing needs and suffer from insufficient specificity.
- MS-based tests, particularly those relying on HRAM, are enabling labs to screen and quantify a large panel of target compounds in one analysis, with high confidence.
- Unlike immunoassays, MS-based tests are helping researchers identify unknown substances and metabolites.



Because NPS are new and evolve rapidly, very little is known about their effects or dosing limits.

"NPS present the greatest analytical challenge to labs in decades. Unfortunately, it's probably going to continue."

—Dr. Marilyn Huestis, retired, National Institute on Drug Abuse

Dr. Mundodi: Thank you for meeting today. Let's start by discussing the most important trends and concerns in the clinical research community.

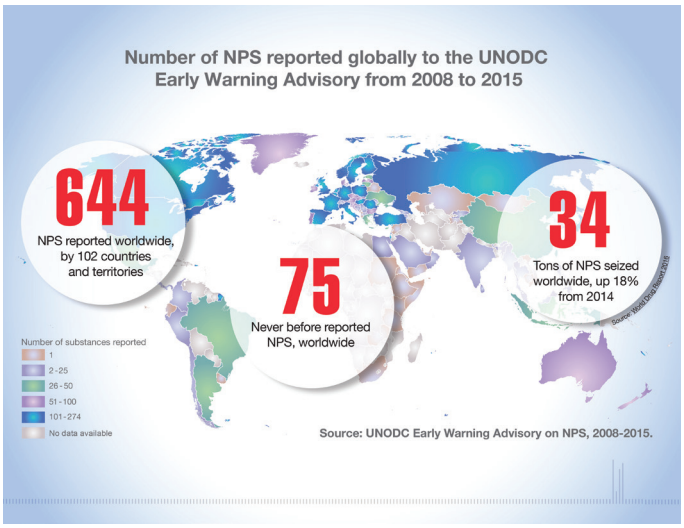
Dr. Huestis: One of the biggest concerns worldwide is the opioid epidemic. It's a major public health and safety problem. Every time there's an overdose or a death, it's not just one individual, but the entire community that's affected. Starting in 2015, there have been more deaths from opioid overdoses than from car crashes. In some areas, opioids are the major cause of drugged-driving cases.

Victims are ending up in emergency departments and hospitals.

Many who began using opioids legitimately became addicted. Though treating pain is critical to well-being, opioid medications have become overprescribed. When individuals become dependent, they need to take more in order to reach the same level of relief. This becomes a vicious cycle as they continue to increase their dosage. At some point, when the cycle extends beyond the prescription, some start "doctor shopping" for more.

Another concern is drugged driving. Since the 1970s, many countries—including the U.S.—have made substantial progress in reducing drunk driving. In 2007, the National Highway Traffic Safety Administration looked at a spectrum of drugs in blood and oral fluid and the results were shocking. They found that 8.5% of weekend nighttime drivers had cannabinoids or cannabis in their bodies. When the survey was redone five years later, there was a 48% increase. As drunk driving decreased, drugged driving increased tremendously. Cannabinoids basically double the risk of a serious motor vehicle crash or fatality. Drugged driving is now a major focus of the office of National Drug Control Policy, and the U.S. is now trying to catch up with E.U. DRUID (Driving Under Influence of Drugs, Alcohol and Medicines) and Australian initiatives, including roadside oral fluid testing.

Lastly, NPS present the greatest challenge to labs in decades, mostly because they represent a wide and growing range of compound classes. Unfortunately, it's probably going to continue because of the high profit margin of NPS and the difficulty in identifying individuals who produce them. In clandestine labs where the compounds are made, there isn't quality control. The result is toxic contaminants, and if there is an overdose or toxicity, we're not sure whether it's the drug itself or some of these other components.



Andrade: Because of the rapid growth in illicit synthetic drugs such as synthetic cathinones, amphetamines, and cannabinoids, traditional screening methods such as immunoassays are falling well short of our needs. Street chemists are moving to *de novo* synthetic techniques now that laws automatically schedule drug analogs along with the drug. Drugs produced in this way are so structurally different that we have to wait for the immunoassay manufacturer to do the research, raise the antibodies, validate it, and make a kit. As a result, we are seeing the clinical research community adopt MS techniques that provide structural information that can identify a new drug—even retrospectively or without a reference standard—and that can screen for many drugs in the same analysis. Orbitrap mass spectrometer technology allows us to easily fill gaps not covered by immunoassay testing.

Dr. Vogeser: Coming from a clinical research lab associated with a university hospital, I have a very different perspective. I'm seeing much closer cooperation between clinical research and the clinic, where the goal is to produce research that will ultimately improve patient care through optimized therapies and personalized treatments.

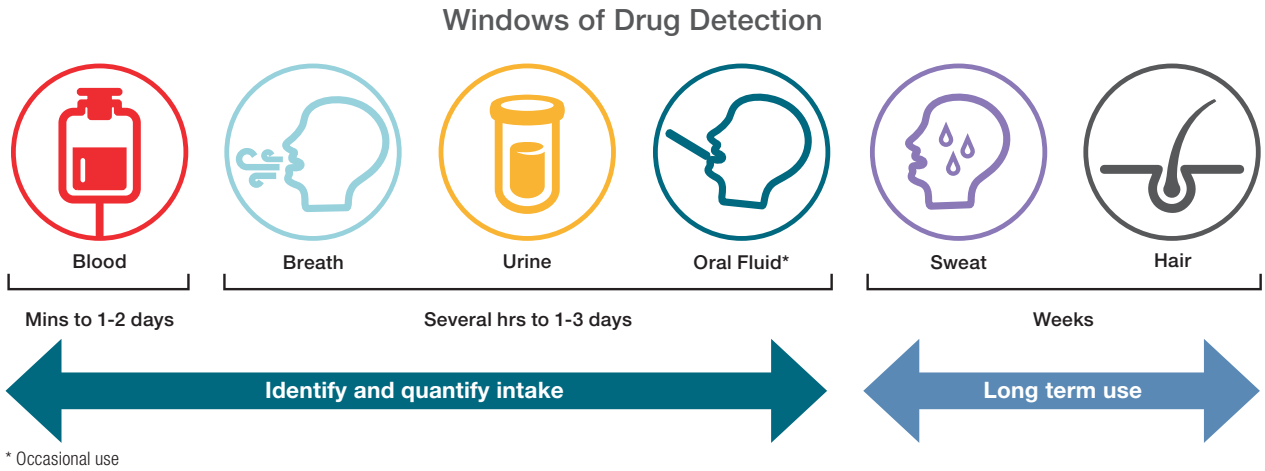
Dr. Huestis: Precision medicine is an important trend. There are a number of different subtypes of opioid receptors that have critical functions in the body. We know some individuals may be more vulnerable to addiction to certain opioids, and the prescribing physician has no way of knowing, because we are not typing receptor expression. We are also just beginning to understand the addictive differences between the opioid drugs themselves.

Dr. Mundodi: What about the impact of legalization of marijuana both for recreational and medicinal purposes?

Dr. Huestis: Beyond concerns for drugged driving, states that have legalized cannabis are seeing substantial growth in many types of edibles. Because edibles are in the shape of gummy bears, lollipops, cookies, and fudge, children are getting into them and ending up in emergency rooms.

"Traditional screening methods such as immunoassays are falling well short of our needs."

—Lawrence Andrade, Director of Research and Development, Dominion Diagnostics



"Each matrix, whether it is breath, urine, blood, hair, or oral fluid, has its advantages and disadvantages and provides a unique view of your results."

—Dr. Marilyn Huestis

Dr. Mundodi: What about trends in the sample matrices you analyze?

Dr. Huestis: The trend is toward analyzing the best sample for the application. Each matrix, whether it is breath, urine, blood, hair, or oral fluid, has its advantages and disadvantages and provides unique view of your results. One important factor is "window of detection," that is how long evidence of drug use can be detected. Hair, depending on its length, can tell you something about use days, weeks, and even months ago.

The distribution of a drug and its metabolites in the body is very different depending on how it is taken. Opioids are not necessarily taken orally—they may be crushed and inhaled, used intravenously, or smoked. If a drug is smoked, there will be very high concentrations in oral fluid. Oral fluid is particularly useful when looking at opioids, because it tells you something about the concentration, as well the route and time the drug was taken.

Today drugged driving is impacting the choice of matrix for analysis. In the U.S, we've tested blood. However, it takes time to get a blood draw—to go to a hospital or to a police station—and many compounds such as Δ-9-tetrahydrocannabinol—THC—the primary psychoactive compound in marijuana—drop like a rock. Our research showed that the THC concentration in blood drops 74% in 30 minutes and 90% in 1.4 hours.

The average time to get blood drawn in the U.S. is between 1.4 and 4 hours. The individual can be highly impaired at the time of the crash or when stopped by law enforcement, but by the time the sample is taken, the blood may test negative.

Since 2004 in Australia, and shortly thereafter in Europe, oral fluid has become the norm because it can be collected at the roadside at the time the individual is judged impaired. If the sample screens positive, a second sample is sent to a lab for confirmation by MS, which has the specificity to ensure an accurate result.

In fact, because it's easy to collect, oral fluid is becoming the matrix of choice in many drug-testing programs. Collection doesn't require same-gender officials, and you don't need highly specialized facilities. Compared to blood, oral fluid is noninvasively collected in small sample volumes, which makes repetitive analysis more practical, and for certain drugs, oral fluid provides better markers. However, analysis of oral fluid requires high-sensitivity detection, and this is where MS can help. Mass spectrometers have become much more sensitive, reducing the volume needed, and multiple assays can be run using that volume.

Everyone is familiar with breath-based alcohol testing, but we aren't looking for opioids in breath yet. Studies have shown that cocaine and cannabinoids can be measured in breath, so in the future breath may become an important matrix.

"In the future, personalization of drug therapy will become much more common. There is simply no alternative to MS as a reliable, versatile, and user-friendly technology toward that future."

—Dr. Michael Vogeser, specialist in Laboratory Medicine and senior physician at the Hospital of the University of the Ludwig-Maximilians-University Munich, Germany

Dr. Mundodi: How is the relationship between labs that are doing the tests, and the clinicians they support, evolving?

Dr. Huestis: If there's a concern about NPS, the lab needs to know because those substances may not be part of a standard screen. NPS cover many different compound classes and thus require much more extensive analysis. It's critically important that communication exists, and that the lab report lists all the analytes tested. For example, tests that used to be done by observing a tissue preparation under a microscope are now done by analyzing biomarkers using an LC-MS/MS system.

Dr. Mundodi: What technologies are generating the most excitement in clinical research today?

Andrade: Thanks to technologies like HRAM MS we are generating a lot of new knowledge in the fields of metabolomics and proteomics, and in new ways to diagnose diseases. Clinical research is very exciting right now, with new assays substituting assays that have been used for 50 years.

Dr. Vogeser: In the future, personalization of drug therapy will become much more common. There is simply no alternative to MS as a reliable, versatile, and user-friendly technology toward that future. At present, the application of MS is far too limited. It should be extended dramatically, because it has the unique ability to address a wide range of analytes and to perform profiling, which better addresses disease complexity.

Dr. Mundodi: Clinical research labs are very comfortable with immunoassay technology. However the FDA recently commented that MS-based analysis overcomes many of the limitations of immunoassay, such as insufficient specificity, inconsistent cross-reactivity, and potentially inadequate detection limits. What is your view?

Andrade: The FDA is correct. It's well understood that the selectivity and specificity of MS are far superior to that of immunoassays. Still, MS and immunoassays do work well together. Mass spectrometers have very low selectivity and specificity for analysis of isomers unless the isomers are separated chromatographically. The enzymes in immunoassays are far more specific for isomers, which helps us to make better decisions than using MS alone. Immunoassays also help us build better MS assays. High-resolution accurate-mass MS in particular has the definite advantage over immunoassays of being able to identify novel psychoactive substances.

The results we generate affect lives. A false positive or negative result for a drug could have very serious consequences for that patient. We want to make sure that we have done all we can to ensure our results are true and accurate.

"It's absolutely key that the proper compound is identified without interferences that could cause false positive results. We know immunoassays can suffer from false positive and negative results."

—Dr. Marilyn Huestis

Dr. Huestis: It's absolutely key that the proper compound is identified without interferences that could cause false positive results. We know immunoassays can suffer from false positive and negative results, whereas MS, done correctly, calibrated, and quality-controlled, can provide robust, highly sensitive results.

Not long ago among the drug-court population in Washington D.C, individuals were all testing negative using immunoassays. When the samples were tested by other methods, 40% of the samples tested positive for synthetic cannabinoids. Today, we have new stimulants, such as synthetic cathionines, many of which will not cross-react with amphetamine immunoassays.

Immunoassays are generally focused on the parent compound. MS offers detection of the parent and the ability to detect its metabolites, which provides additional confidence in a positive result.

Dr. Vogeser: Mass spectrometry is without question superior to immunoassay technology, because unlike immunoassays, MS allows specific quantification of small molecules. For monitoring drugs used in psychiatry research, there is simply no alternative to MS because the immunoassays are not available, and the development of the specific antibodies needed is extremely complex. Mass spectrometry allows for monitoring a wide spectrum of compounds—not only the active compound, but also metabolites. Mass spectrometry also allows us to implement new tests according to our requirements, with a high degree of flexibility and independence from diagnostic providers. Another advantage of MS is sensitivity, which allows us to work with the very small sample volumes we collect by capillary puncture.

Dr. Huestis: There have been a large number of new medications that have been developed, many of which require drug monitoring research, for which there are no immunoassays available. Using MS, the researcher can develop methods that can monitor these new medications.

Andrade: Immunoassays do not provide compound structural information, whereas MS does. This enables researchers to identify new drugs and build these new drugs into their assays without having to wait for an immunoassay manufacturer to do so. And in certain applications, such as pain management, the detection limits are better with MS. MS also enables us to screen for multiple drugs at once, in a single injection, without having to do different pour offs—a huge advantage.

"Mass spectrometry is without question superior to immunoassay technology."

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“Mass spectrometry can address many different classes of drugs together in one analysis.”

—Dr. Marilyn Huestis

Dr. Mundodi: Can you tell me more about the use of immunoassays compared to MS when testing for opiates?

Dr. Huestis: Yes, absolutely. If for instance, you test for opiates with an immunoassay that’s targeted at morphine, it will pick up a few other opiates, but it will not detect the larger universe of opioids—all having the same potential for abuse. Mass spectrometry can target a broad spectrum of opioids, including hydrocodone, hydromorphone, oxycodone, oxymorphone, and tramadol. Currently there are immunoassays for morphine and oxycodone, but there are many others for which immunoassays are not readily available.

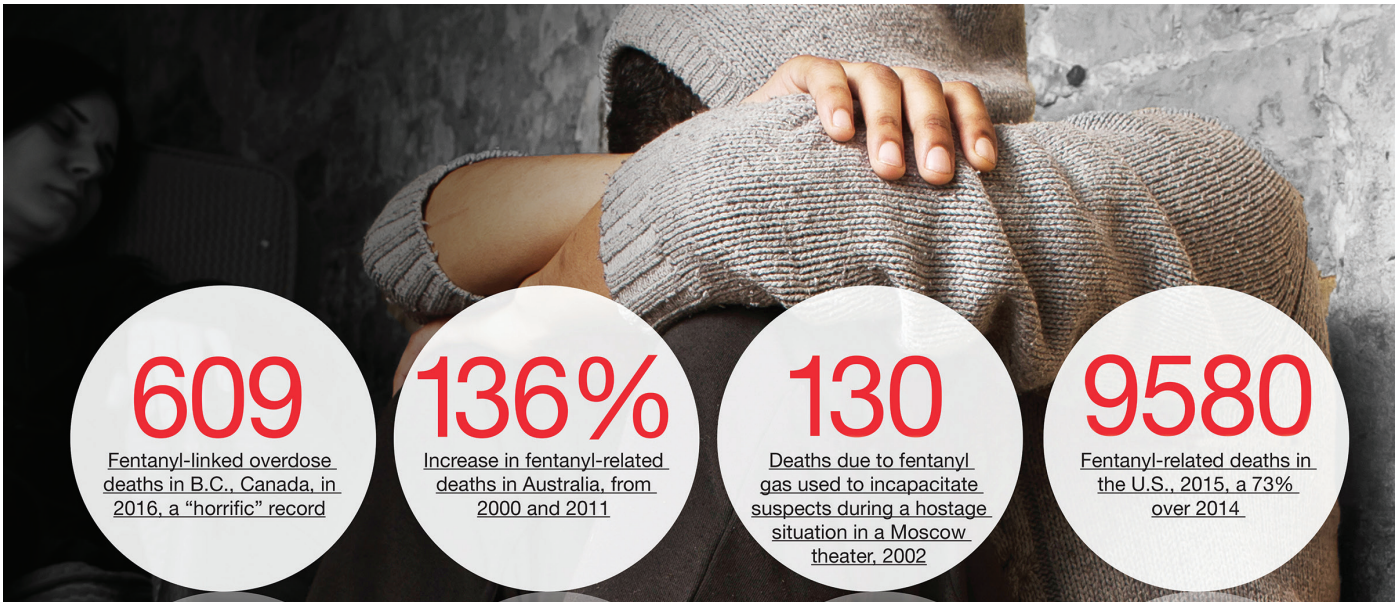
One other concern is that an opioid that interacts with others could be missed. Some of the opioids are very potent—up to 1000-fold as potent as morphine—and are being mixed with, or marketed as, another drug. The unsuspecting individual may think they have taken oxycodone, but the compound needs to be accurately identified to develop an effective response.

Dr. Mundodi: What are the other advantages of MS?

Dr. Huestis: Mass spectrometry can address many different classes of drugs together in one analysis. In drugs of abuse applications, a large number—30 or 40 different important compounds—parents and their metabolites—can be monitored in a single assay, and this can be done with the sensitivity required when analyzing oral fluid. When performing drug monitoring research, you need accurate quantification to ensure that the drug can be detected within the proper range. Mass spectrometry helps by allowing quantification of large numbers of different compounds—anti-psychotics, anti-depressants, and antiretroviral drugs for example—in a single sample analysis.

Of the challenges in the clinical laboratory, cost and throughput are important and MS can address both. Obviously, you have the cost of the equipment itself, but with MS you need many fewer consumables and solvents and, most significantly, immunoassay kits. In addition, as I noted, multiple compounds can be analyzed in a single assay, so you can produce results in very rapid manner, and that can reduce costs.

Thermo Scientific™ Q Exactive™ hybrid quadrupole-Orbitrap MS coupled to a Thermo Scientific™ UltiMate™ 3000 UHPLC with Thermo Scientific™ Transcend™ II system with TurboFlow™ and multichannel technology



"Even the selectivity of triple quadrupole mass spectrometers can be challenged by metabolites of certain drug classes where isobaric and isomeric compounds can give false positives."

—Lawrence Andrade

Dr. Mundodi: So how does MS actually help clinical researchers to identify new drugs?

Dr. Huestis: That's a good question. Often, we don't know how new drugs are metabolized, so looking for unknown metabolites is a challenge. If a lab is lucky enough to have blood or oral fluid, it can look for the parent compound. However, if the lab has a urine sample, the parent compound will rarely be present. In this case, there are two ways that MS can help. Labs can use publications to determine the analytes to look for, and then set up a targeted triple quadrupole analysis. This approach can be difficult however, because new drugs are constantly introduced, and you may not be able to wait until someone else does the research. Alternatively, high-resolution MS allows labs to identify unknown metabolites in-house.

We had wonderful collaboration with the DEA at the National Institute on Drug Abuse. As soon as they began to observe large seizures of a new compound, they provided it to us before it was scheduled. That is important because when a new drug is introduced and is subsequently scheduled, it may take nine months or a year to get that compound on the lab's license.

Even though it's possible to do your own research, it's important for labs around the world to publish their results so others can learn from them. That's what's great about the early warning programs—the EMCDDA program in Europe and the Office of National Drug Control policy in the U.S. The EMCDDA has identified over 600 new drugs since 2008.

Dr. Mundodi: Tell me more about the benefits of high-resolution MS.

Dr. Huestis: High-resolution, accurate-mass MS allows us to screen for a wide spectrum of substances at once, with high selectivity. Accurate mass gives us confidence that we have positively identified the analyte of interest.

Andrade: Even the selectivity of triple quadrupole mass spectrometers can be challenged by metabolites of certain drug classes where isobaric and isomeric compounds can give false positives. High-resolution, accurate-mass technology can resolve some of them and also allows us to obtain structural information that helps to characterize these interferences.

Dr. Vogeser: High mass resolution is of utmost importance for drug monitoring research due to its impact on treatments and disease management.

"MS systems used to require a lot of expertise, talent, and understanding to use them effectively. Now a user can become competent very quickly."

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Dr. Mundodi: How is MS being used in other cutting-edge areas of medicine?

Dr. Huestis: Mass spectrometry is being used to explore the therapeutic potential of cannabinoids. For example, there is a study showing that cannabidiol, a natural cannabinoid, is effective and safe in helping children with a critical seizure disorder. And there are a large number of other seizure disorders for which the anti-epileptic medications available today have not worked. Mass spectrometry is an excellent way for clinical researchers to investigate the diversity of natural cannabinoids that are being considered for therapeutic use, and that will subsequently need to be monitored in clinical studies.

We also use our high-resolution mass spectrometer in experiments with human liver microsomes and hepatocytes to determine drug metabolites. In two or three days we can take a 2500-piece metabolite puzzle and put it together. In addition, when a new drug problem is identified, we can go back to our existing data and determine if and when it became a problem in our jurisdiction. High-resolution MS offers so many opportunities for identifying unusual compounds. It's the best tool we have for addressing a huge problem.

Dr. Mundodi: So, what do you think is the biggest shift you see in MS technology?

Andrade: MS systems used to require a lot of expertise, talent, and understanding to use them effectively. Now a user can become competent very quickly, and the quality of the data is so much better, and you get more information in a shorter period of time.

Overall, we used to think that a tandem quadrupole system was the answer. Now we are graduating to HRAM systems, which I think will become the next gold standard in quantitation. However, it's not one single technology that will give us the best results.

Dr. Mundodi: What are the trends in sample preparation for MS-based assays?

Dr. Huestis: An important sample prep trend is the use of automated online sample preparation. Removing interferences is key to avoiding false negative results. Thermo Scientific™ TurboFlow™ technology has allowed us to remove proteins and other interfering compounds in our matrices efficiently online. Though mass spectrometers have incredible selectivity and sensitivity, in many cases you can't just do a "dilute and shoot," which is a mistake some labs make.

Labs that need high throughput are also adding multichannel LC and discarding the part of the chromatogram that doesn't include the analytes of interest.

"In two or three days we can take a 2500-piece metabolite puzzle and put it together."

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Thermo Scientific™ Q Exactive™ HF-X hybrid quadrupole-Orbitrap MS coupled to a Thermo Scientific™ Vanquish™ UHPLC system

"Mass spectrometry provides substantial cost savings compared to immunoassay. Though MS implementation is expensive, the life of an MS instrument is very long, so, the expense per analysis is minimal."

—Dr. Michael Vogeser

Dr. Mundodi: What is your experience using the Orbitrap-based high-resolution, accurate-mass system in your lab?

Dr. Vogeser: We are testing the Orbitrap mass spectrometer for quantification of small molecules, especially for drug monitoring research. An essential part of precision medicine is the optimization of drug therapy, based on monitoring small-molecule therapeutics, and increasingly, of large-molecule antibodies as well. The Thermo Scientific™ Q Exactive™ system gives us the ability to address the large spectrum of drugs.

The Q Exactive system provides very good analytical performance in terms of reproducibility, linearity, and signal-to-noise, and addresses an extremely wide range of masses. It's also an excellent instrument for both routine and research use in a university hospital lab setting.

Dr. Huestis: Orbitrap technology was attractive to us because it provides excellent sensitivity, and with HRAM, excellent specificity. The system gave us the ability to screen and quantify an entire panel of compounds. We were able to develop a method that looks at 40 different stimulants—amphetamine, methamphetamine, and Ecstasy—but also a large number of new synthetic cathinones. With accurate-mass and isomeric information, there is much more assurance in the identity of the compound detected. The Orbitrap system provided a lot of versatility and could handle almost any problem that we took to it in the course of our work.

Dr. Mundodi: Have you achieved any cost savings using the Orbitrap system?

Andrade: Most of our cost-savings are a result of the system's high resolution. The resolution of the Orbitrap mass spectrometer surpasses even high-end Q-TOF instruments, which we were surprised to find really had a big impact. Biological samples are very complex. We're able to resolve compounds in the mass spectrometer that we might not be able to resolve chromatographically. This helps us reduce sample cleanup and turnaround time, which are the costliest aspects of running a sample.

Dr. Vogeser: Mass spectrometry provides substantial cost savings compared to immunoassay. Though MS implementation is expensive, the life of an MS instrument is very long, so the expense per analysis is minimal. It's a high-efficiency technology because it allows quantification of analytes in a large panel, without additional costs for each added analyte.

Dr. Huestis: Orbitrap technology can get you into high-resolution analysis at a lower cost than other types of high-resolution MS systems available today. We found that it was easy to train people to use.

“Because of its versatility, MS is a tool that you will need to have to help support better health care.”

—Dr. Marilyn Huestis

Dr. Mundodi: If a lab is thinking about adopting MS, what advice can you provide?

Dr. Vogeser: Mass spectrometry is a complex technology, but today’s instruments have a very high level of user-friendliness. Implementing MS is an excellent way to support clinical researchers in their efforts to provide better healthcare in the future.

Dr. Huestis: Because of its versatility, MS is a tool that you will need to have to help support better health care research. Laboratories will need to justify to management the reasons for moving to LC-MS/MS. The most important reason for MS is to be able to offer all the different tests that you want or need to offer. Many times, there aren’t other solutions available. Another reason is the cost effectiveness of MS, and that is determined by the tests that will be performed. What different assays or analytes can you combine into one method? Will it reduce send-outs to reference laboratories? You’re also not going to be using anywhere near as many consumables or kits, and there is tremendous opportunity for automation to reduce cost-per-sample.

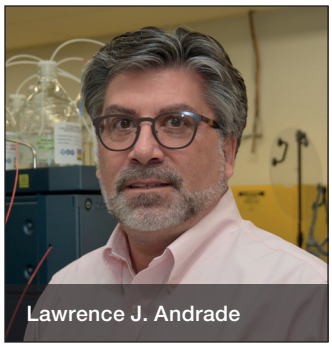
Dr. Mundodi: What does the future hold for clinical research?

Andrade: The field of clinical research has progressed very rapidly. It used to take me eight hours to run a few samples by gel electrophoresis and now one person can push a button and run hundreds of samples per minute. It’s exciting to see.

Overall, instruments are getting faster and more intelligent, smaller, and cheaper. In the future, we will likely use a small mass spectrometer in the field or at the bedside to get an answer faster. Future technologies will require less human input to diagnose diseases or design treatments. We already see this trend occurring in operating rooms and doctors’ offices.

Dr. Huestis: Novel psychoactive substances are not going away, so there will be more need for specialists to determine what the drug is and how it’s contributing to a patient’s state. Eventually, we’re going to use high-resolution MS to solve the difficult life-or-death problem where you have an unconscious person in the emergency room and the clinician needs to know what compounds are present that might be causing toxicity.

The future of clinical research is very bright. Clinical research will be more and more devoted to individualized health care. Labs will have to run more different tests, not fewer, because the spectrum of medications is going to grow. The need for drug monitoring research on an individual basis will become more important to ensure the individual is within the range that provides the best response.



Lawrence J. Andrade

Dr. Michael Vogeser

Lawrence J. Andrade, is currently the Director of Research and Development at Dominion Diagnostics where he oversees research and development projects. The main focus of his team is the development and validation of bioanalytical LC-MS/MS methods for Dominions' definitive urine drug testing platforms. In addition to designing new and optimizing current test panels to continually improve patient care, his team also works to support an in-house program to discover and characterize novel psychoactive substances. They have identified novel opioid interferences that cause false negative and false positive results in UDT opioid testing which was published in the Journal of Analytical Toxicology.

Lawrence is a registered technologist in clinical chemistry and a licensed clinical laboratory scientist and has been with Dominion since 2011. He obtained his bachelor's degree in biotechnology from Northeastern University in Boston, Massachusetts. In a career spanning 30+ years, he has worked for Pfizer, DuPont, Ariad Pharmaceuticals and several contract research, manufacturing and packing organizations operating under GLP and cGMP guidelines.

Dr. Michael Vogeser, is a Specialist in Laboratory Medicine and Senior Physician at the Hospital of the University of the Ludwig-Maximilians-University Munich, Germany (Institute of Laboratory Medicine). As an Associate Professor he teaches Clinical Chemistry and Laboratory Medicine. The main scope of his scientific work is the application of mass spectrometric technologies in routine clinical laboratory testing as translational diagnostics. Besides method development in therapeutic drug monitoring and endocrinology, his work is also focused on quality and risk management in MS, and on clinical testing in general. Michael has published over 150 articles in peer-reviewed medical journals and is secretary of the German Association of Clinical Chemistry and Laboratory Medicine (DGKL) (2016–2019).

Dr. Dr. (h.c.) Marilyn Huestis

Dr. Suparna Mundodi

Dr. Dr. (h.c.) Marilyn Huestis is recently retired from the National Institute on Drug Abuse (NIDA) after 23 years. Dr. Huestis started at NIDA in 1988 as a research fellow while completing her Ph.D. Dr. Huestis' research program sought to discover mechanisms of action of cannabinoid agonists and antagonists, effects of *in utero* drug exposure, and the neurobiology and pharmacokinetics of novel psychoactive substances—the emerging face of drug abuse. Her work has yielded more than 400 manuscripts, most recently with a focus on the effects of marijuana use on driving impairment. As a world-renowned expert on human drug testing, Dr. Huestis serves on the new National Commission on Forensic Science; the Organization of Scientific Area Committee on Toxicology; the World Anti-doping Agency's Prohibited List Committee; the Scientific Working Group on Toxicology; the Transportation Research Board Committee on Alcohol and Other Drugs; and the National Safety Council's Alcohol, Drugs and Impairment Division Executive Board. She has received numerous other awards for her work, including the Distinguished Fellow Award from AAFS in 2015.

Dr. Suparna Mundodi is a Marketing Manager for the Clinical and Forensic Toxicology group at Thermo Fisher Scientific, where she focuses on developing effective go-to-market strategy for Chromatography and Mass Spectrometry solutions for the diagnostics and healthcare markets. She has held various marketing roles in Life Science companies, gaining strong industry domain expertise in genomics and proteomics. During her doctoral work in Biochemistry/Molecular Biology, she authored many publications on the mechanisms of disease resistance. As a Bioinformatics scientist at Carnegie Institution of Stanford University, she focused on the analysis and visualization of large data sets. Her goal is to help scientists around the world to find a cure for genetic diseases.

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