thermo scientific

CAPTURE TRACES OF TOMORROW'S DRUGS TODAY

Identify rapidly evolving novel psychoactive drug substances faster

ThermoFisher SCIENTIFIC

INTRODUCTION

The rise in the manufacturing, trafficking, and use of designer drugs, too easily purchased in head shops or on the Internet, is a serious global concern. Since appearing in Europe in the early 2000s, new psychoactive substances (NPS) have led to many deaths and hospitalizations around the world. Experimenting youth and casual drug users are unaware of the increased potency of many NPS compared to traditional drugs of abuse, and as a result, overdose, experience the bad side of a high, or worse, become rapidly addicted. As many as one new designer drug is introduced a week, resulting in a huge strain on front-line law enforcement, border patrol and drug enforcement agencies, and forensic drug testing labs, globally.

Identification and subsequent legislation to ban NPS cannot keep pace. As soon as one is banned, chemists synthesize a slightly different version, thus producing a falsely considered “legal-high” drug. It takes time and resources to identify these new compounds, and to develop and validate new screening procedures. Fortunately, advances in portable and lab-based technologies are helping to screen NPS, identify unknowns much more efficiently, and may offer the potential to identify location of production.

When results can mean the difference between life and death, and innocence and guilt, accurate results are essential. Thermo Fisher Scientific offers both law enforcement and drug testing labs reliable, cost-effective solutions to help reveal the truth hidden in the growing load of drug-related narcotic and forensic toxicology cases.

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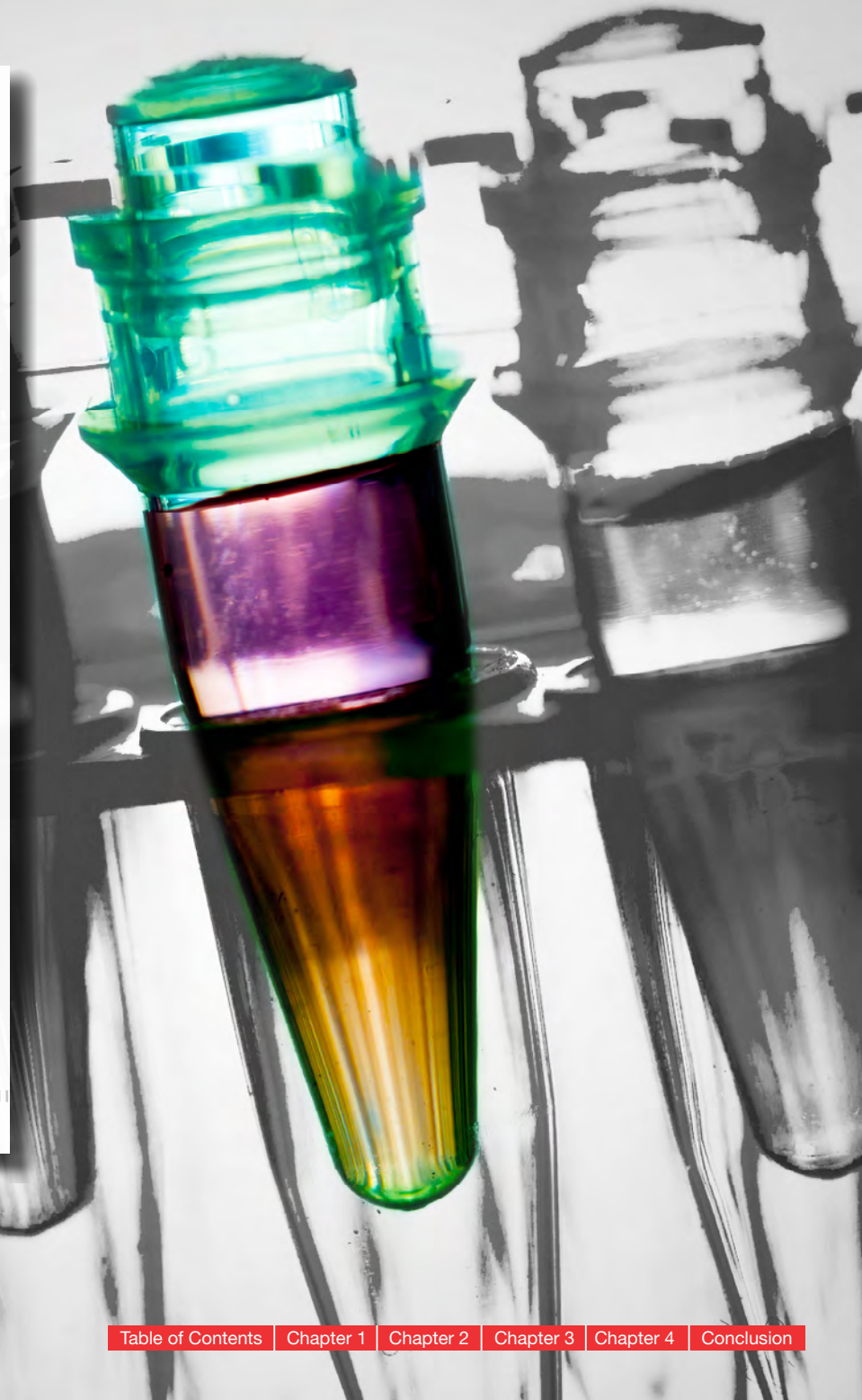
Chapter 1

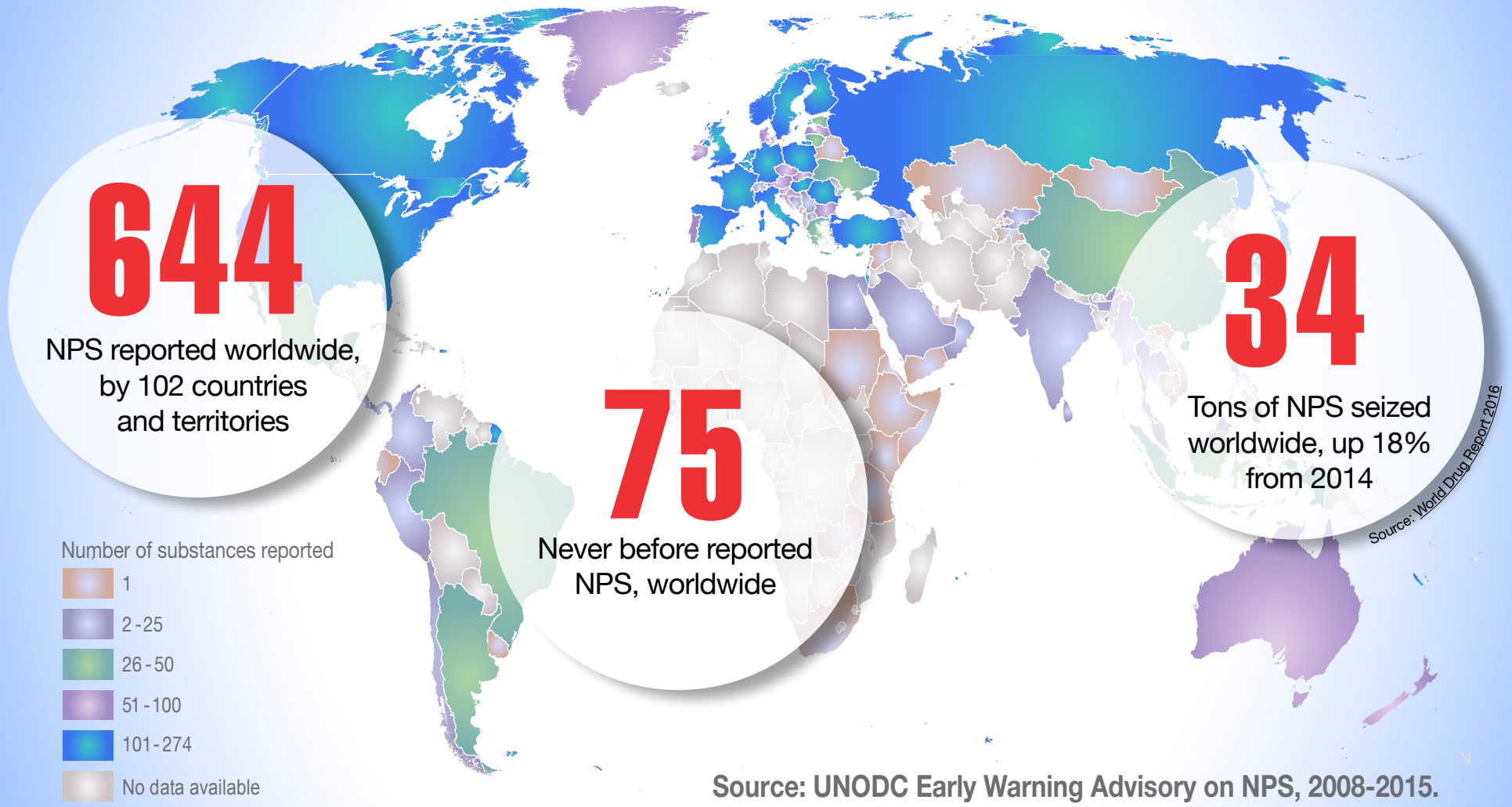
ADDRESS THE GROWING LIST OF NPS; A GLOBAL PROBLEM

Around the world, NPS and their use are rising rapidly, causing a parallel increase in case loads and case backlogs. A recent study by the U.S. Drug Enforcement Administration's (DEA) National Forensic Laboratory Information System found that of 400 U.S. forensic labs surveyed, about 30% reported their drug caseloads increasing year-on-year. Almost 60% of those queried said the influx of newly identified drug compounds was a major contributor to their backlog.

According to the United Nations Office on Drugs and Crime (UNODC), the number of NPS reported worldwide continues to grow, with the largest classes being synthetic cannabinoids, stimulants, and hallucinogens. By 2015, 644 NPS had been reported to the UNODC by 102 countries and territories, with almost an equal number of synthetic cannabinoids and synthetic cathinones reported. Moreover, a wide range of new substances not of the major NPS previously known were reported. World Drug Report 2016



Number of NPS reported globally to the UNODC Early Warning Advisory from 2008 to 2015

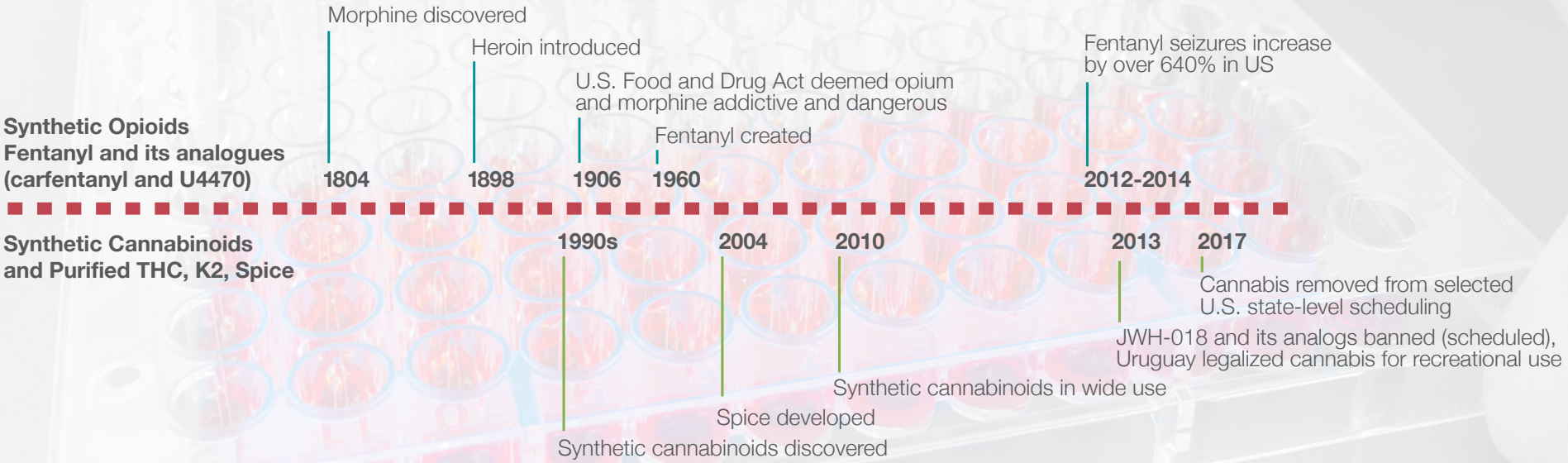


Source: UNODC Early Warning Advisory on NPS, 2008-2015.

History of NPS

Most NPS are drugs modified to mimic the effects of traditionally abused drugs such as marijuana-like (e.g., “K2 spice”) and heroin-like (e.g., “fentanyl analogues”) compounds. Existing drugs and pharmaceuticals that never made it to market are the starting point for many NPS. Illegal drug manufacturers have also used historical plant-based narcotics or stimulants as starting material for their latest NPS.

Many plant-based substances such as Khat (Catha edulis), Ayahuasca (Banisteriopsis caapi), Kratom (Mitragyna speciosa), as well as thousands of other plants, can produce highs. Many are not DEA scheduled, and are becoming popular. (Source: UNODC plant-based substances.)



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

Synthetic Opioids

By the early 1800s, Friedrich Sertürner had discovered and marketed morphine—the active alkaloid in the opium poppy—as a treatment for pain, and for opium and alcohol addiction. Later it was learned that morphine is also very addictive. In 1898, Bayer Co. introduced heroin, and its use spread when addicts discovered that its effects could be amplified by injecting it. Heroin eventually became illegal in 1924.

In 1960, **fentanyl** was created for use as an anesthetic. It is one of the strongest pain relievers, reserved for treating debilitating pain and the terminally ill. **Just a few grains—3 milligrams (mg)—can cause death.** Known as the new heroin epidemic, fentanyl trade has been difficult to control. After laws ban export, import, and sale, new opioid analogs, technically considered legal, quickly appear. Potent in very small amounts, it's easy to transport and elude detection. It's also easier and cheaper to manufacture than heroin, which requires land for growing poppies and labor for harvesting and processing. And, it's very profitable—**two pounds of fentanyl purchased in China for $3,000 to $5,000 turns into $1.5 million on the street.**

Learn more The High Cost of New Opioid Drug Addiction

Synthetic cannabinoids

Compared to cannabis, synthetic cannabinoids are often more potent, with active metabolites that remain in the brain longer. They were discovered in the early 1990s when John Huffman began searching for new analgesics. One of these was JWH-018, which showed a stronger affinity than naturally occurring tetrahydrocannabinol (THC) for key brain receptors.

Clandestine chemists hijacked Huffman's recipes. The popular synthetic cannabinoid, Spice, was developed by a small UK company in 2004. Then inexpensive and legal, and often in the form of plant material laced with active compound, Spice was sold in retail outlets and on the Internet in packaging labeled "Not for Human Consumption" to avoid oversight.

By late 2010, synthetic cannabinoids were widely used. However, it wasn't until 2013 that JWH-018 and its analogs were banned. Garage chemists continue to rapidly synthesize new forms, many of which have been DEA scheduled.

Learn more Sugar & Spice: Synthetic Cannabinoids Aren't So Nice!

Chapter 2
IDENTIFY AND PROHIBIT NPS FASTER

Drug-scheduling legislation is the primary response to combat the spread of NPS, but is often ineffective because field and lab tests haven't identified NPS fast enough to keep pace. As soon as one is banned, a new isomer, derivative, or other variant replaces it. Just a small change in a molecule's structure can cause it to be difficult to detect, if not undetectable, and beyond current regulation. In addition, a seized substance may be comprised of multiple drugs such as heroin laced with fentanyl, or cannabis leaves sprayed with synthetic cannabinoids, necessitating orthogonal methods for detecting untargeted or unknown drugs.

To keep drugs and drug dealers off the streets, and to provide faster treatment for addicts, law enforcement, customs, and other personnel must quickly and safely identify suspected drugs in the field. Certain NPS are very potent such that law enforcement and lab staff must take extreme caution to avoid exposure. Additionally, traditional field chemistry tests of seized substances (a.k.a. narcotics) do not empower these first-responders to make fast and reliable decisions.

In the lab, there is a lack of fast and efficient techniques that provide the structural information needed to identify unknown NPS. Traditional forensic toxicology lab techniques, such as immunoassays, target specific compounds and may not be updated frequently enough to identify the latest NPS. More flexible in scope, orthogonal techniques such as infrared (IR), Nuclear Magnetic Resonance (NMR) and mass spectrometry (MS)-based techniques are now being used in labs to overcome these limitations.

New portable and lab-based solutions that allow identification of NPS with greater speed, safety, and confidence are desperately needed to improve prosecution efficiency and to slow, or stop, the cycle of NPS introduction.

Empowering first responders

At crime scenes, field screening of suspected drugs has typically involved presumptive colorimetric wet chemistry tests where color changes were interpreted to identify a substance. While presumptive tests can be used to establish probable cause and sometimes file charges, confirmatory lab tests are usually performed before a case goes to trial. In some jurisdictions, lab backlogs can exceed six to twelve months, delaying case resolution and potential medical assistance, counseling, and rehabilitation.

Already used by first responders for identification of explosives and hazardous chemicals, small, rugged handheld Raman spectroscopy systems like the Thermo Scientific™ TruNarc™ analyzer are growing in popularity for field-based drug identification. Such systems enable law enforcement to scan a sample for hundreds of drugs and receive clear results in seconds. The on-board software matches the sample against a library of known drugs, precursors and cutting agents, which is regularly updated to include emerging threats. Recent TruNarc software updates have added dibutylone, furanyl fentanyl and U-47700 to its library.

Handheld equipment is now reducing lab backlogs, increasing pre-arraignment adjudication rates, and speeding prosecution, helping authorities stay ahead of emerging drug threats and allowing them to quickly warn communities of new and dangerous substances in circulation. Field tests can also ensure that valuable lab resources can focus on higher-priority cases.

Law enforcement spotlight

QUINCY, MASS. POLICE DEPARTMENT

Quincy, Mass., part of the Metro Boston area, is challenged by the rapid evolution of dangerous illicit drugs. In 2011, the department was making over 315 drug related arrests per year—almost one per day. While traditional drugs of abuse like cocaine and heroin were still prevalent, they were also seeing new psychoactive substances (NPS), like cathinones and new opioid variants.

The Quincy Police Department deployed the TruNarc analyzer to enable officers to more quickly identify a wide range of suspected drugs, and to increase officer safety. In a single test, easily performed through glass and plastic packaging for most substances, TruNarc identifies hundreds of common drugs of abuse and dangerous painkillers, NPS such as furanyl fentanyl, and common cutting agents and precursors. Testing is safer and easier because officers don't have to touch most substances, and the clear results remove the need for subjective evaluation. Rapid results help Quincy get drugs off the street faster, while minimizing their team's exposure to potentially harmful drugs.

Learn how TruNarc is helping law enforcement stay ahead of drug threats.

Watch the video

Improving laboratory testing efficiency

Analyzing samples for known drugs involves a variety of orthogonal techniques to screen for substances, followed by a selective assay to confirm compound identity, and quantify its concentration if requested. Screening and quantification of known substances require reference material and can take two or three days, unless a stat test is requested. If unknown or multiple drugs are involved, more analysis steps are needed because traditional screens can't detect unknowns, leading to further wait times.

Table 1 shows testing techniques used in labs today. Both seized substances (e.g., powder, leaves, pills, and tar) and biological samples (e.g., blood, urine, hair, oral fluid, breath, and vitreous fluid) are analyzed using a combination of gas chromatography (GC), liquid chromatography (LC), and GC-MS, LC-MS and MS/MS hyphenated, techniques. Of these, high-resolution MS (HRMS) including high resolution accurate mass (HRAM) Thermo Scientific™ Orbitrap™-based analysis, is becoming popular for unknown or untargeted drug identification due to its ability to generate richer, more complete information that also allows analysts to re-review data for NPS as they appear, without re-running samples.

Targeted and Untargeted Drug Identification

	Targeted Screening	Confirm	Quantify	Untargeted screening	Retrospective Analysis
Immunoassay	XX				
GC/LC	XXX	X	X		
GC/LC-MS/MS	XXX	XXX	XXX		
HRMS-QTOF	XXX	XX	X	XX	XX
HRMS-Orbitrap	XXX	XXX	XXX	XXX	XXX

Number of Xs represent relative performance.

Publication spotlight

GC-IR REVEALS DRUG STRUCTURES

Investigators working in the criminal justice system are tasked with providing rapid and accurate identification of illegal substances, enabling prosecutors to properly carry out justice. Many crime labs use GC-IR (also known as GC-Fourier Transform IR), a robust hyphenated method, to confirm identification of cannabinoids, bath salts, and other drugs of abuse.

Software libraries used to identify compounds by matching IR spectra can be frequently updated, keeping labs ahead. For example, the lab at the Tennessee Bureau of Investigation (TBI) aggressively seeks out NPS to add to their GC-IR spectral library, often before the NPS become pervasive on the street. Here, Thermo Scientific™ GC-FTIR systems make it possible to confidently identify illegal substances much faster.

Learn more Bath Salts and Cannabinoids Analyzed by GC-IR

Expert spotlight

BETTER APPROACHES TO DRUGS OF ABUSE TESTING

NPS represent an increasing and ever evolving public health threat. Traditional analytical approaches to drugs of abuse testing are unable to respond quickly enough to keep up with the continually changing NPS situation and are therefore unsuitable for this purpose.

With over 30 years' experience in drug testing and a proven track record of introducing new technology to advance lab capabilities, Simon Hudson, Technical Director of the Laboratory and Managed Services (LMS) division of LGC, describes an improved approach to NPS testing. Screening processes can evolve and be refined as new compounds emerge.

Watch the video

"With high resolution accurate mass LC-MS technology it is easy to update your databases and your coverages."

- Simon Hudson, Director, Laboratory and Managed Services

Versatile, fast, and conclusive drug testing

Since their introduction in the 1950s, MS-based techniques have become increasingly popular because the chemical fingerprints—mass spectra—provide the most versatile, fast, accurate, and conclusive results. The versatility of MS expands the scope of samples that can be analyzed and the substances that can be detected, while its speed reduces time to results. The accuracy of MS methods provides confidence in identifying compounds such as NPS.

Popular targeted and untargeted MS workflows screen and confirm known substances by comparing library spectra with experimental mass spectra. Labs traditionally purchase off-the-shelf libraries or build their own, and are beginning to follow select social or cloud based solutions.

High-resolution accurate-mass identification of unknown NPS

High-resolution accurate-mass (HRAM) Thermo Scientific™ Orbitrap™ mass spectrometer technology gives drug testing labs a leg up on the complex NPS problem by significantly streamlining workflows used to routinely screen, confirm and, when needed, identify unknown compounds. HRAM Orbitrap-based systems also allow re-investigation of data for new drugs of interest.

The high-profile overdose of the performer Prince is an example of Orbitrap HRAM MS used to help solve toxicology and cause-of-death investigations. When his body was brought to the Midwest Medical Examiner for autopsy, toxicology screening by Orbitrap-based MS quickly identified fentanyl.

New cloud-based spectral libraries shared across the lab technician community in real time may be essential to identify and regulate new drugs quickly. Orbitrap HRAM libraries like mzCloud™ are easily updated via cloud-based applications, helping labs in one jurisdiction to share with others.

Laboratory spotlights
LIATF

Analyzing more than 7,000 biological samples annually, in a variety of sample matrices including blood, urine and hair, for cases involving driving under the influence, drug-facilitated crimes and post-mortem toxicology, isn't easy. The more than 10,000 seized drug samples, often comprised of heterogeneous mixes, the Laboratorio di Igiene Ambientale e Tossicologia Forense (LIATF) also analyzes, adds to the challenge.

Leading forensics labs like the LIATF are increasingly relying on more advanced MS technology to address analyses of traditional drugs of abuse and NPS, for which certified reference materials and scientific data are not always available. Learn how the LIATF is ahead in solving forensic challenges and reducing backlogs using Orbitrap mass spectrometer technology.

Watch the video

Chapter 3

REDUCE HUMAN AND SOCIETAL COSTS

Drug abuse has serious costs. According to the US DEA, in 2015 over 50,000 people died of drug overdoses. Almost two-thirds of these deaths, more than 33,000, were due to heroin, prescription painkillers, or synthetic opioids. The Aurora Sentinel reported that in 2015, drug overdoses were the leading cause of injury-related death in the U.S.—more than from than guns, car crashes, or suicides.

Up to 100 times more potent than morphine, and many times more potent than heroin, **fentanyl** overdosing is common. **The average lethal amount is just 3 mg compared to 30 mg for heroin.** For this reason, sensitive detection methods such as MS are needed to detect very low levels of fentanyl and its analogs in body tissues and fluids. The difference in strength is due to differences in chemical structure. Both bind to the same brain receptor, but fentanyl is much more potent, binding faster and more tightly.

Users don't know when heroin is laced with fentanyl, so when they inject their usual amount it can be too much. And when dealers add fentanyl, their measuring devices are often not accurate enough to ensure levels below those which lead to an overdose. Finally, since NPS are often homemade with little or no control of quality and potency, their effects are unpredictable.

The abuse of NPS places a huge burden on healthcare, especially on emergency care. According to the Washington Post, **heroin and opiates result in 4105 emergency room visits per day** in the U.S. The symptoms of NPS overdose—panic attacks, psychosis, and hallucinations accompanied by combative or violent behaviors—make treating patients difficult. In addition, because the NPS ingested is usually unknown, it's not possible to prescribe targeted treatment.

Due to the magnitude of the NPS problem, the head of the Jakarta National Narcotics Agency (BNN) has proposed the formation of a national drug labor center. The goal of the center is early detection of emerging NPS and other types of drugs both developed in Indonesia and imported by international drug networks.

609

Fentanyl-linked overdose deaths in B.C., Canada, in 2016, a “horrific” record

136%

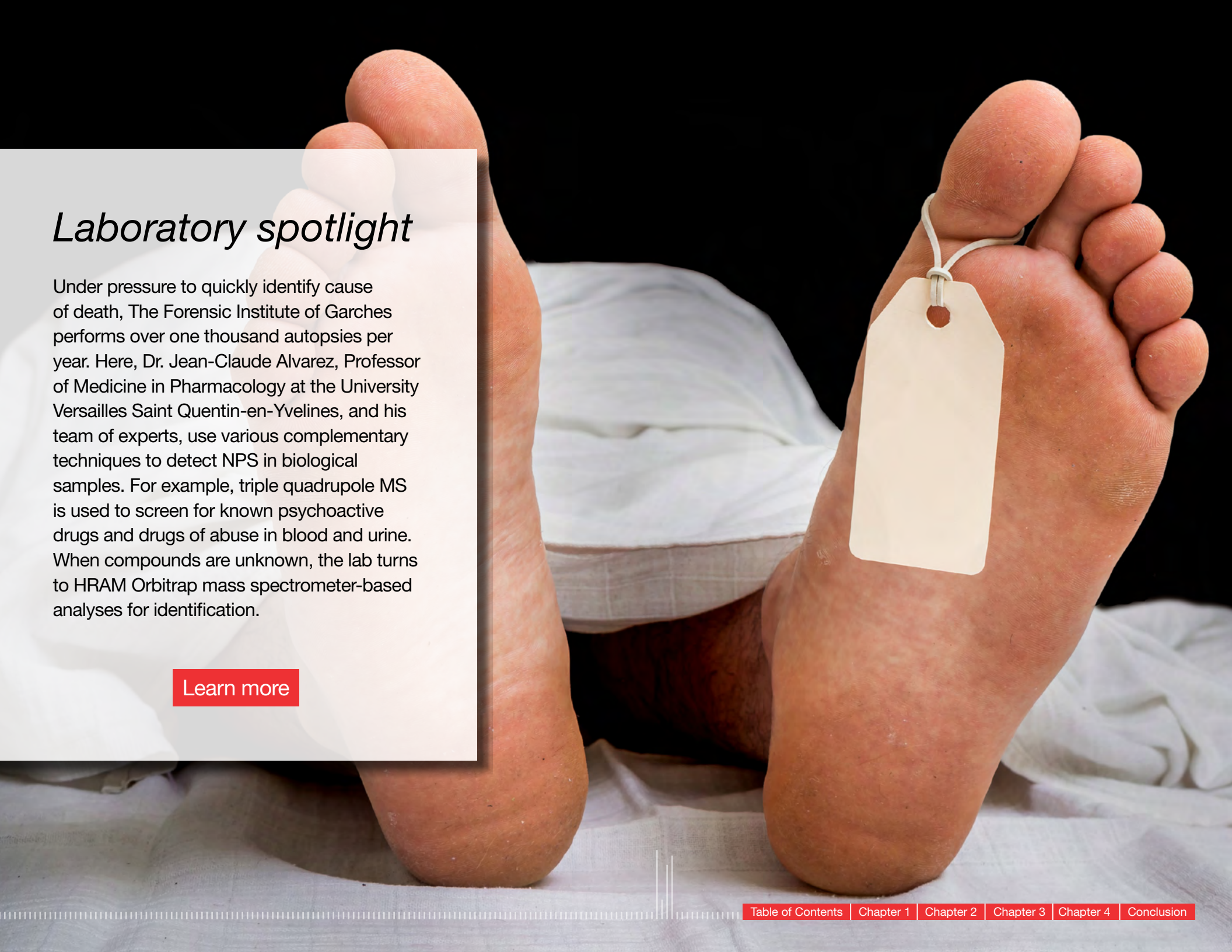
Increase in fentanyl-related deaths in Australia, from 2000 and 2011

130

Deaths due to fentanyl gas used to incapacitate suspects during a hostage situation in a Moscow theater, 2002

9580

Fentanyl-related deaths in the U.S., 2015, a 73% over 2014



Laboratory spotlight

Under pressure to quickly identify cause of death, The Forensic Institute of Garches performs over one thousand autopsies per year. Here, Dr. Jean-Claude Alvarez, Professor of Medicine in Pharmacology at the University Versailles Saint Quentin-en-Yvelines, and his team of experts, use various complementary techniques to detect NPS in biological samples. For example, triple quadrupole MS is used to screen for known psychoactive drugs and drugs of abuse in blood and urine. When compounds are unknown, the lab turns to HRAM Orbitrap mass spectrometer-based analyses for identification.

Learn more

Chapter 4

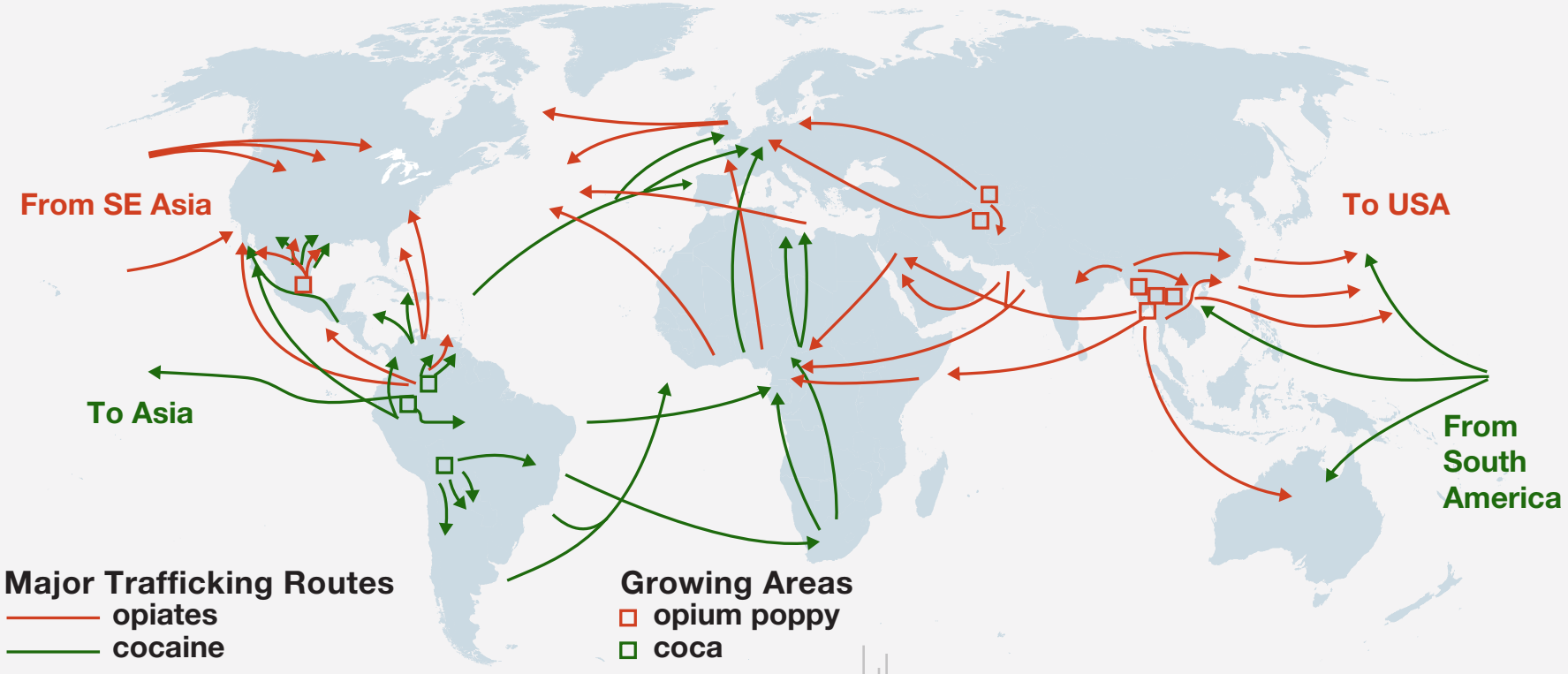
DETERMINE DRUG CIRCULATION NETWORKS MORE RAPIDLY

According to law enforcement agencies, most illicit NPS are manufactured in Asia—mainly in China—with smuggling routes through Mexico to the U.S. and Canada. To control NPS, it is important to not only control and monitor trade, but also to understand the processes used to make them, and their origins—including the "kingpins" who are making them. Still, much is unknown about the supply chain and production of NPS. For example, though syntheses of the common synthetic cannabinoids in Spice are not complicated and can be achieved with inexpensive equipment and chemicals, the details of production, and sources of precursor chemicals and reagents, are unknown.

DETERMINING GEOGRAPHIC ORIGIN AND PRODUCTION METHODS

Unlike other techniques, Isotope Ratio Mass Spectrometry (IRMS) can detect the specific signature — the isotopic signature — of a product that is the result of the geographical origin of its plant-derived material. The technique can also uncover isotopic variations that result from specific production factors such as the raw material used, synthesis method, batch size, and manufacturer.

IRMS can thus reveal important information about a NPS' history, to establish a link between a precursor and a synthetic drug and between two seizures, or to enhance understanding of the NPS market, for example to gauge the impact of a legal measure on drug supply in circulation.



Expert spotlight

DRUG SOURCING USING IRMS

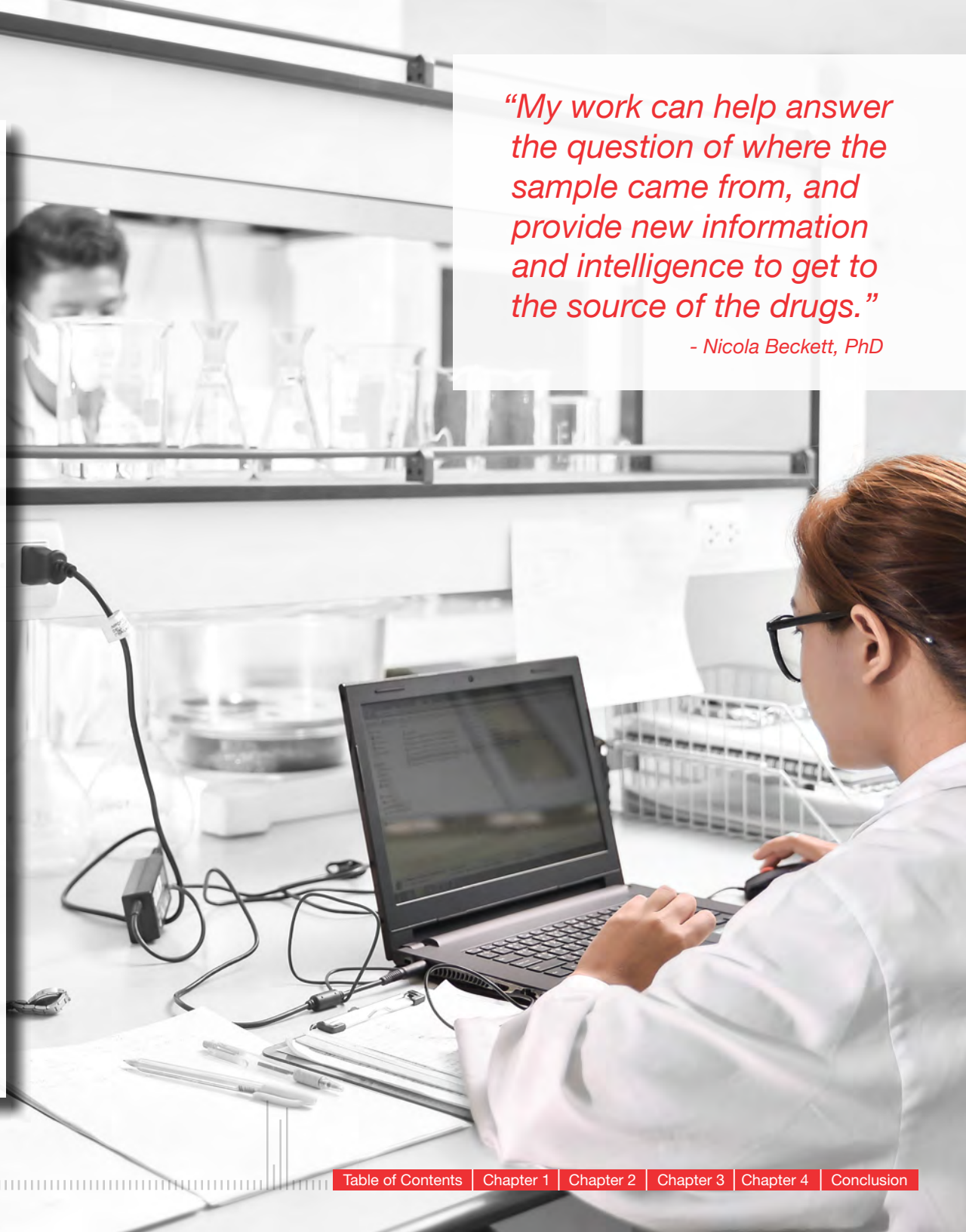
Nicola Beckett, a Ph.D. student from Griffith University in Australia, is using cutting-edge IRMS technology to investigate designer drugs and clandestine labs. Her research uses isotopic profiling to reveal possible links between seized drug samples or to discriminate between drug samples.

Beckett studied samples of two drugs, benzyl-piperazine and trifluoro-methylphenyl-piperazine, that were seized in separate cases in Australia. She determined that one of the drugs might have had a common source, while the other may have had different sources of manufacture.

Learn more Tracking Drug Sources with Isotopes

"My work can help answer the question of where the sample came from, and provide new information and intelligence to get to the source of the drugs."

- Nicola Beckett, PhD



Chapter 5
STAYING AHEAD: CONCLUSION

With so many NPS emerging on the market so rapidly, law enforcement and labs are under pressure to respond faster. Lab investigations can take several months just to identify NPS. Subsequent drug scheduling adds an additional 4-6 months. To stay ahead of drug epidemics will require unlocking clues earlier. New, more effective technology is needed to confront NPS and the challenges they present.

Advances in testing technology

Chemists are on the front line of the war on drugs, teasing out the structures of NPS so they can be named, tracked, and regulated. Though it will always take time and resources to identify new compounds, develop new screening procedures, and revalidate methods, advances in HRAM Orbitrap mass spectrometer technology and cloud-based libraries are helping labs do so more efficiently.

Advances in portable field-testing

Taking off some of the pressure on labs and first responders, new handheld equipment based on lab-proven methodology is reducing backlogs, time to prosecution, and ensuring that valuable lab resources are put to use on the most challenging samples.

Faster spectral library sharing

More spectral library content and cloud-based solutions that allow labs in one jurisdiction to instantaneously share information with others will increase the speed with which NPS are identified and regulated.

Advances in sourcing

To control NPS use and trafficking, it's also vital to trace their origin and map their distribution networks. Techniques such as IRMS are helping to enhance understanding of the NPS market and the effects of law enforcement activities.

ADDITIONAL RESOURCES

The High Cost of New Opioid Drug Addiction	Learn more
Forensic Screening for Drugs in Urine Using High-Resolution MS/MS Spectra and Simplified High-Performance Screening Software	Learn more
Tracking Designer Drugs	Learn more
Simultaneous Determination of 40 Novel Psychoactive Stimulants in Urine by Liquid Chromatography-High Resolution Mass Spectrometry and Library Matching	Learn more
Thermo Scientific Forensic Webinars	Learn more

EVERYTHING LEAVES A TRACE

When results can mean the difference between life and death, and innocence and guilt, accurate results are essential. Thermo Scientific offers both law enforcement and labs reliable, cost-effective solutions for every part of the NPS identification workflow to help reveal the truth hidden in the growing load of forensic toxicology samples. Whether you're focused on meeting today's caseloads or anticipating future emerging NPS, we can help. Because when justice and health are on the line, so is your reputation. Find the truth.

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