

What I find so inspiring about Promega's culture is the commitment to innovation—not just technological—but also in our business practices. We have the freedom and encouragement to align our business practices with what is good for the world.

JESSICA ROSSOL-ALLISON

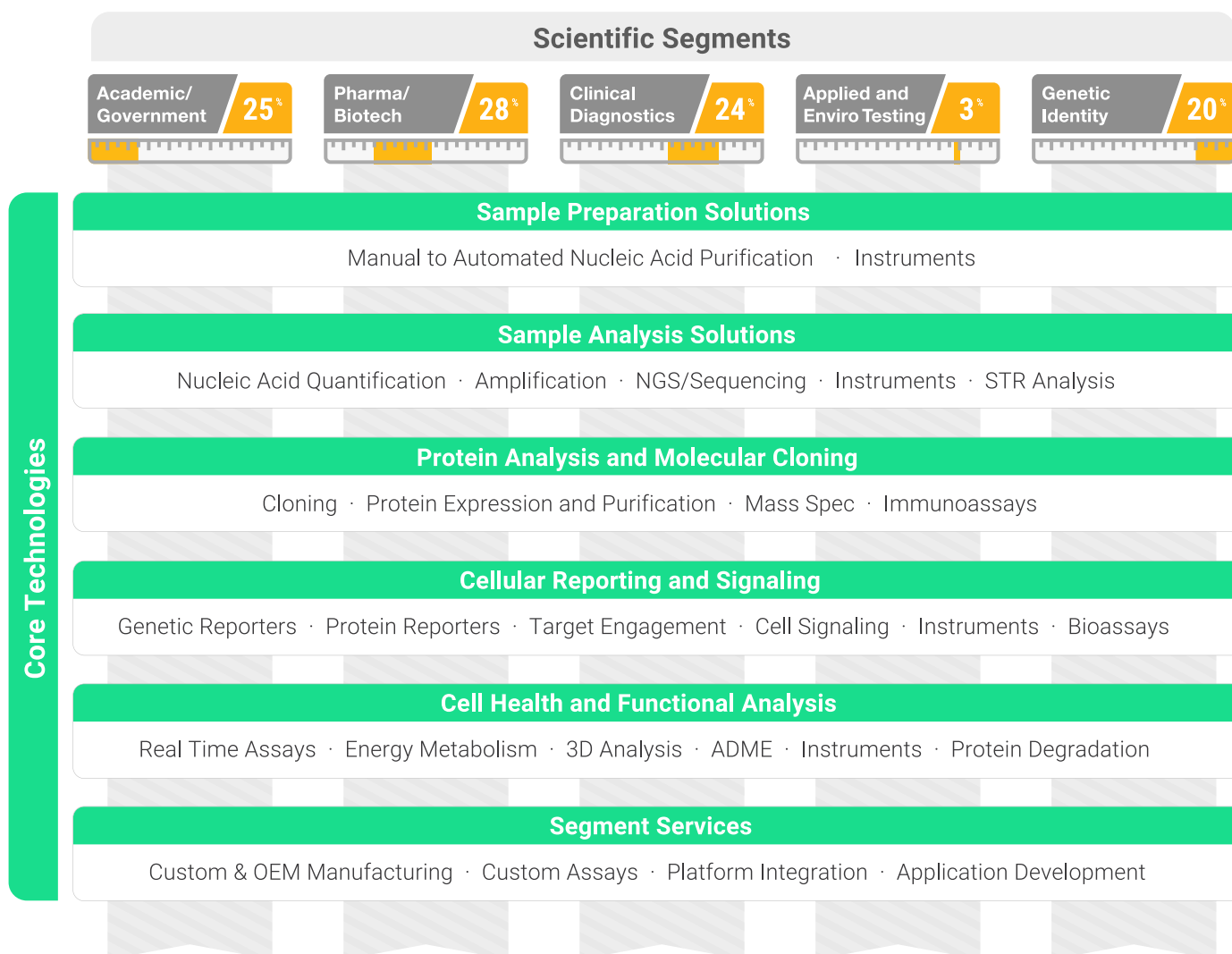
Scientific Client Support Specialist, North American Branch

## PRODUCT REACH

Science is continuously evolving, so the needs of our customers are always changing. Developing the innovative solutions customers need begins with one crucial skill: listening. The solid relationships we build with our customers, taking the time to truly understand their work, allows us to anticipate their needs and problem solve together. Scientists, technicians and analysts use our products and technical expertise every day in laboratory and industrial settings around the world. Our alliance with them, coupled with determined scientific exploration and flexible manufacturing capabilities, enable us to support our customers in their important work to improve the world in profound ways using science.

With high-quality, reliable products at their disposal, basic researchers, applied researchers, clinical practitioners, forensic analysts, quality assurance personnel and others have more freedom to focus on specific

# Breadth of Capabilities



questions at the forefront of scientific discovery, genotyping, quality assurance or clinical practice. The result is better science, healthcare, justice, and product quality, using better tools for faster and more accurate answers.

## CUSTOMER FOCUS

### Forensics and Paternity Laboratories

Forensics and paternity laboratories deal with unrelenting caseloads and tight turnaround times. Dependable results, fast throughput and reliable product supply are critical in this setting. These labs use limited, and often challenging samples, to develop investigative leads from crime scenes. Sexual assault evidence kit backlogs and property crime samples are some of the more challenging samples for labs to process. In addition, forensic labs process large numbers of reference samples to populate local, state and national databases. These reference databases help law enforcement connect arrestees to other crimes for identifying possible repeat offenders. The ongoing testing of the rape kit backlog has identified over 1,000 suspected serial rapists in the United States alone.

In addition to analyzing evidence collected at crime scenes, forensics and paternity labs help bring closure to families whose loved ones are missing or lost in mass disasters, and even help exonerate those who have been wrongly convicted of a crime. Researchers and analysts need to know that they will get optimal and reliable results from the valuable and often irreplaceable samples.

More than ever before, labs will be able to gain more information from challenging sample types, save time with increased sample processing capacity, and experience the flexibility to add samples during runs. All of this will be available with the same high level of service and support that customers have come to expect from Promega.

### GIVING NAMES TO THE MIGRANTS IN A DEADLY SHIPWRECK

More than 1 million migrants and refugees crossed the Mediterranean Sea in 2015 during a massive immigration from the Greater Middle East and Africa to Europe. Deaths at sea rose to record levels in April 2015 when five boats sank with an estimated death toll of 1,200 people. One of the worst disasters was a fishing boat carrying nearly 1,000 people that sank off the coast of Libya. News reports state the accident happened after people saw a merchant ship in the distance and scrambled to attract its attention, overturning the crowded vessel. The Italian coast guard was only able to retrieve 28 survivors. In the months after the deadly shipwreck, only 118 bodies were recovered with hundreds more presumed to be trapped below deck. The Italian government created a task force to recover the boat and identify the victims.

The Forensic Genetics lab at the University of Pavia was brought in to use DNA analysis to identify some of these victims. However, the challenge was extracting DNA from human remains that had been submerged in seawater for 3–14 months. This prolonged exposure to water can damage DNA, making identification difficult. Bone samples from 80 individuals were prepared for DNA extraction and the recovered DNA was then used for STR analysis using the [PowerPlex® ESX and ESI 17 Fast Systems](#). These kits were provided by Promega Italy to help with the effort to give names to the shipwreck victims. Work is ongoing to compare the DNA profiles generated by the STR kits with antemortem records to give closure to those wondering if their loved ones were aboard the sunken fishing boat.



## TRACKING MALARIAL INFECTION

Eradicating malaria is difficult partially because the transmission cycle is complex with multiple different stages that occur inside mosquitoes after consuming a blood meal from humans.

Compounds that could kill the parasite or block transmission in the mosquito during early stages of parasite maturation would be ideal. A recent study describes how our reporter enzyme [NanoLuc®](#) luciferase was combined with a Plasmodium parasite and used to create a model to identify drug compounds that block malarial transmission during the stage where male and female reproductive cells are fertilized.

Expression and activity of the luciferase gene in this mutant strain is controlled by an element that responds only to the sexual states of the parasite. When the parasite was just circulating in the blood, there was little bioluminescence. When the parasite converted into the cells that form a zygote like the stage in a mosquito, the amount of bioluminescence increased, suggesting that [NanoLuc®](#) luciferase was only expressed when these reproductive cells developed.

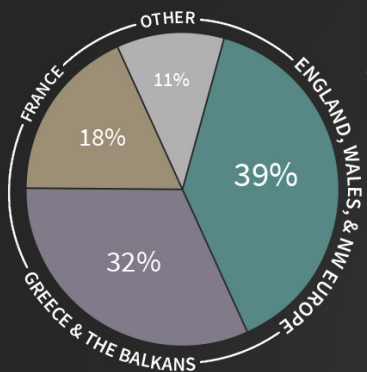
This [NanoLuc®](#) malaria strain called Ookluc was used to test compounds in the Pathogen Box from the Medicines for Malaria Venture. This research kit contains 400 compounds that are active against neglected tropical diseases—125 of the compounds are known to target malaria. Researchers found 31 compounds that blocked over 95% of the reporter parasite conversion into the reproductive cells, preventing the early reproductive stage. These results suggested the [NanoLuc®](#) luciferase-based Ookluc model is ideal for high-throughput screening of compounds that block malaria transmission. Thus, we are one step closer to identifying possible drugs that may eradicate malaria.

We have worked with forensic and paternity laboratories for more than 30 years and support their challenging workflow procedures by providing advanced technologies for efficient DNA extraction through discriminating STR analysis.

## Government and Academic Research Laboratories

Despite increasing pressure and demands, today's academic and government researchers are still at the front line of discovery but require more sensitive research tools to test their hypotheses. They need the newest available tools with enhanced sensitivity and specificity to address more complex biological questions compared to the methods used just a few years ago. From routine applications to more focused ones, Promega continues to develop these improved technologies from next generation nucleic acid isolation and PCR, to advanced assays for cellular biology, metabolism, 3D cellular structures and organoids, to protein manipulation and CRISPR knock-ins for tagging cell lines. To help the modern researcher successfully publish their results, fulfill their research programs and





### ISOLATING DNA FOR ANCESTRY TESTING

For generations the Greek maxim ‘know thyself’ has inspired many to search inwardly and externally about who they are. With modern scientific advances it has become more accessible for humans to discover exactly where their genealogical roots lie as a step on the journey to understand ourselves. With AncestryDNA, this process can be done easily from the comfort of your home. With a saliva sample AncestryDNA can estimate your origins to more than 350 regions around the world enabling you to get inspired by your past, connect with living relatives or complete missing pieces of your family tree.

The magic in that saliva sample that enables AncestryDNA to analyze your past is genetic material called DNA, which must be extracted and analyzed. As a result of AncestryDNA’s strong sales growth, a robust laboratory workflow and reliable partner was required. This critical workflow incorporates the Promega [Maxwell® HT](#) gDNA isolation chemistry, which is used to process every sample. To date, over 7 million people have used Ancestry DNA to better understand the journeys of their ancestors that continues today in each us.

nurture carefully planned careers, Promega is committed to developing the most advanced bioassays, target engagement and protein degradation tools. Promega values people, and we understand that every researcher is an individual with their own stresses and strains.

### Pharmaceutical and Biotechnology Industries

Scientists within the pharmaceutical industry are continuously developing new small molecule drugs that can enter cells easily and affect specific target proteins. Targeted cancer therapies that block the growth and spread of cancer by interfering specifically with the disease cells, but not normal healthy cells are one example where small molecule drugs are used therapeutically. At early phases of drug development, researchers may need to screen more than 100,000 compounds at once to identify leads that can be further optimized and turned into new drugs. The availability of high-throughput compatible, reliable and predictable tools and assays reagents is crucial to the success of these researchers to discover new drugs that would be safe and effective in treating cancer patients.

Over the years, we have developed a broad portfolio of assay reagents that meet the needs of these pharmaceutical researchers and have been used widely during various phases of drug discovery and development. For example, our [NanoBRET™ Target Engagement](#) Assays allow researchers to quantitatively measure the interaction between a molecule and a protein in live cells reliably in a high-throughput manner. This is a significant advancement as these cellular assays can better predict compound performance. In addition to common drug targets like kinases, this NanoBRET™ Target Engagement technology has also been applied to CRISPR-Cas9 gene edited cells to help identify drugs that can lead to oncoprotein degradation.

## Environmental and Food Testing Laboratories

The increasing demands on water and food testing facilities mean there is a need for rapid, reliable solutions to ensure products are safe and authenticate food ingredient claims. Biotechnology offers tools for these testing labs to detect bacterial or other contaminants in food, water or plants. From GMO testing and pathogen detection in food to water quality and contamination analysis, assays need to satisfy the requirements of food and water testing laboratories, including sensitive detection of unwanted microbes and undeclared ingredients.

To screen plants for GMOs or analyze food for pathogen contamination or authenticating ingredients, extracting DNA from these samples is a necessary step. The resulting DNA needs to be pure enough to work in PCR-based analysis, the method most food testing labs use for detection. In Europe, our DNA purification reagents have become a reference standard in authenticity determination of meat products, and European Union Reference Laboratory for Animal Proteins in feeding stuffs (EURL) has developed a Standard Operating Procedure for DNA extraction based on our purification chemistry. In addition, our [Maxwell® RSC PureFood GMO](#) and Authentication Kit was recently selected by the European Reference Laboratory on GMO Food and Feed Testing for developing new SOPs for food DNA extraction, influencing food companies to use our products as part of their routine quality control testing.

Water treatment facilities and desalination plants test the water quality and biofilm formation to reduce energy consumption and improve plant operational efficiency. By partnering with these facilities, we have been able to improve our luminescent bacterial detection assay for specific use with water sampling to help with industrial processes like biocide dosage and timing for water cooling systems. The use of [Water-Glo™](#)



## PROVIDING ALTERNATIVES TO ANIMAL TESTING

Companies that manufacture cosmetics and personal care products need a way to test products they are developing for safety, but there are few alternatives that replace animal skin. Compounds in cosmetics or personal products can potentially cause allergic responses on the skin, known as skin sensitization. This response takes place in the outer layer of the skin, the keratinocytes, and involve inflammatory response in cells and upregulation of antioxidant/electrophile response element (ARE)-dependent pathways that respond to the skin cell inflammation. By developing luciferase reporter cell lines that detect when ARE-dependent pathways are triggered by cosmetics or personal care products, we have created an alternative to animal skin testing. The Organization for Economic Co-operation and Development (OECD) has published Test Guidelines for In Vitro Skin Sensitisation (OECD TG 442D) for two validated cell lines called KeratinoSens™ and LuSens that have been made available globally through acCELLerate (<http://www.accelerate.me>). These cell lines, when used with the [Steady-Glo®](#) or [One-Glo™ Luciferase Assay System](#) luminescent detection assays, are a way to measure skin sensitization.

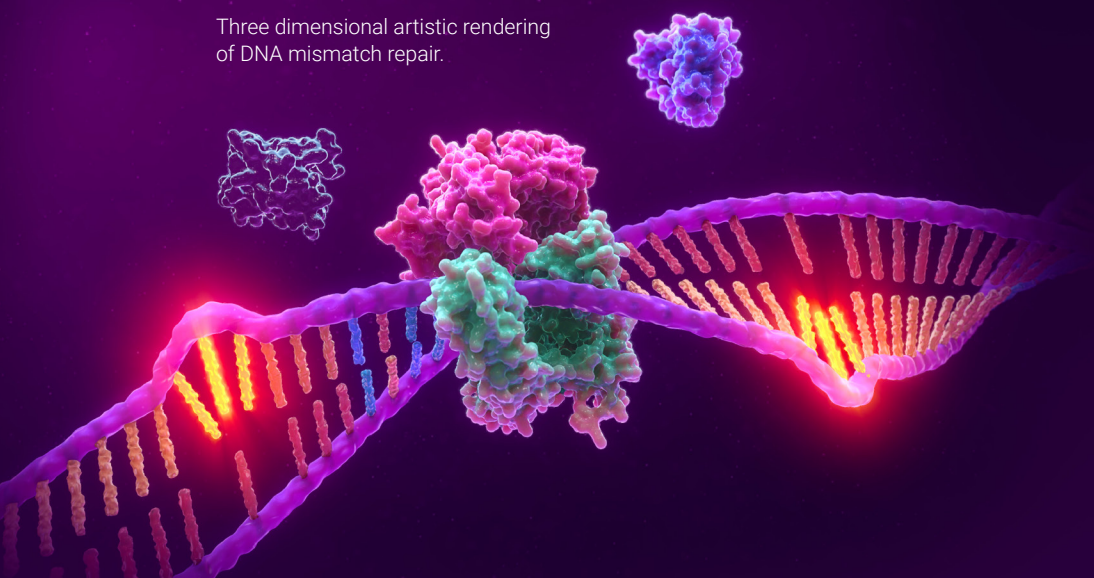


microbial analysis by measuring the amount of ATP in a sample by bioluminescence applies to drinking water, desalination and other areas, and offers a tool by which to improve plant efficiency and is part of ongoing research.

### Clinical and Molecular Diagnostics Laboratories

Clinical laboratories rely on access to high-quality, consistently performing products for their assays. Promega manufactures reagents under a rigorous quality program that contributes to reproducible and reliably performing molecular assays. Products are manufactured to the highest quality standards through maintenance of ISO 9001 and ISO 13485 certification as well as enhanced capabilities for cGMP manufacturing. The [PCR Optimization Kit](#), which launched in 2016, allows customers to rapidly define their own unique PCR master mix for a variety of applications in research or clinical use. This is just one example of how we can provide flexible solutions with product customization options to meet the needs of the clinical laboratory or IVD manufacturer.

Three dimensional artistic rendering of DNA mismatch repair.

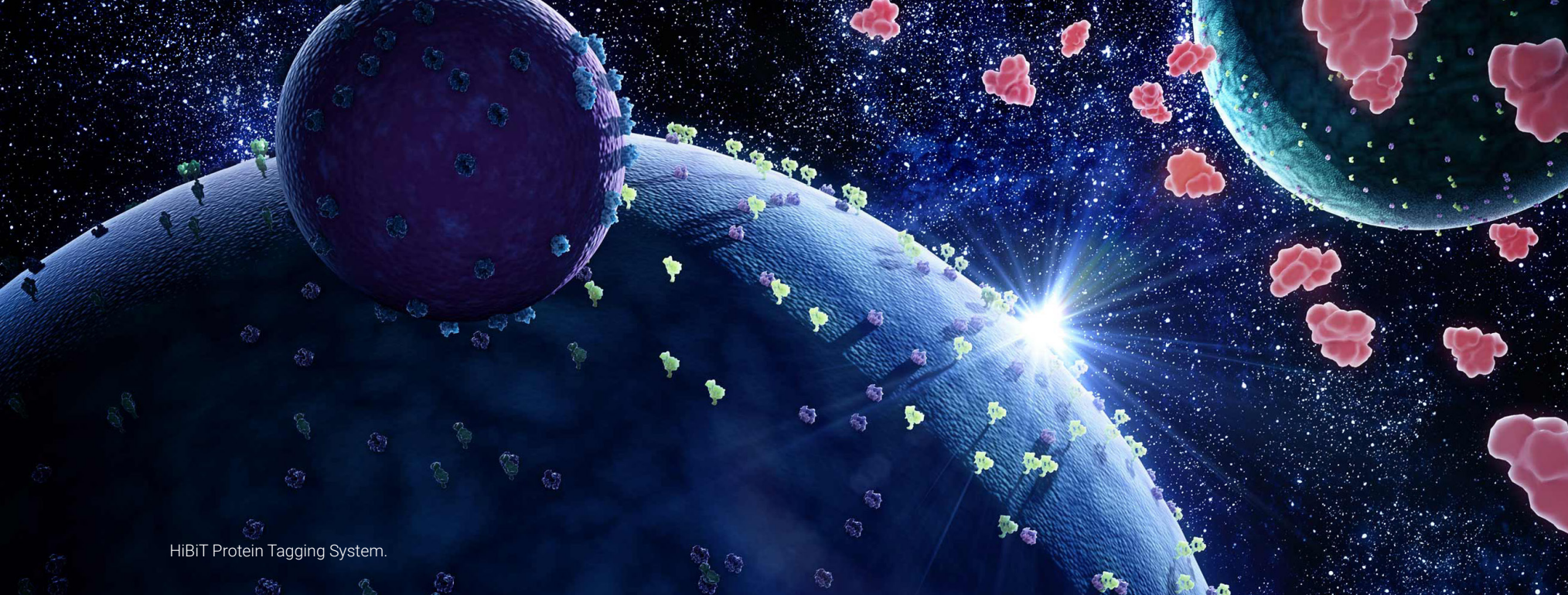


### ESTABLISHED TOOLS FIND NEW MEANING

Promega first developed its [microsatellite instability \(MSI\) Analysis System](#) 15 years ago as a NASA-funded effort for monitoring the effects of radiation on astronauts. The “Research Use Only” technology grew to become the gold standard in nucleic acid-based MSI testing for research labs around the world. With the recent advent of the new cancer immunotherapy treatment Keytruda® (pembrolizumab) based on a common biomarker rather than where in the body a tumor originates, a new application for our MSI technology emerged.

In late 2018, Japan’s Ministry of Health, Labour and Welfare approved a companion diagnostic based on our MSI technology to identify patients suitable for treatment with Keytruda®. The test was developed in collaboration with FALCO biosystems of Kyoto, Japan. The MSI-IVD Kit (FALCO) is a DNA analysis test used to detect high microsatellite instability (MSI-H). MSI-H is a biomarker in tumor tissue indicating that certain sections of DNA, called microsatellites, have become unstable. This instability biomarker shows the major mismatch repair genes that correct errors during DNA replication are not functioning properly. Keytruda® works to boost the ability of one’s immune system to identify and fight these tumor cells, and has been approved for use in patients with the MSI-H biomarker in many countries, including the US and Japan. The MSI-IVD Kit (FALCO) is the first such pan-tumor companion diagnostic test in Japan.

Our latest MSI technology was also recently granted “innovation designation” by the Chinese National Medical Products Administration (NMPA), and we intend to seek US Food and Drug Administration (FDA) clearance for an in vitro diagnostic (IVD) version of our MSI 1.2 platform.



HiBiT Protein Tagging System.

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**“Our Medical Affairs Department allows us to increase our ability to share our knowledge of scientific advances to help physicians and make a difference for families.”**

RANDY DIMOND, Vice President & Chief Scientific Officer

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## Medical Affairs

For over 40 years, Promega Corporation has supported global clinical researchers by providing high-quality, innovative research tools and support. Those researchers evolved their clinical discoveries into today's focus on precise, personalized medicine.

With individualized patient care in mind, we are proud to announce our newest department, Medical Affairs. Our Medical Affairs team, staffed by scientists, will work to provide scientific and clinical expertise to our clients, through medical education.

Promega and our Medical Affairs department are here to provide support to the needs of the clinical customer focused on the concept that every patient has a story, every patient has a family, and the research never stops.



## INVESTMENT IN INNOVATION

To sustain our contributions to scientific exploration and application, we continue to invest in the development and discovery of new technologies. In 2018, 10.8% of total revenue was allocated to research and development. Research is not solely focused on the development of new products as our Advanced Technology Group and a group funded by the Federal Government perform basic research.

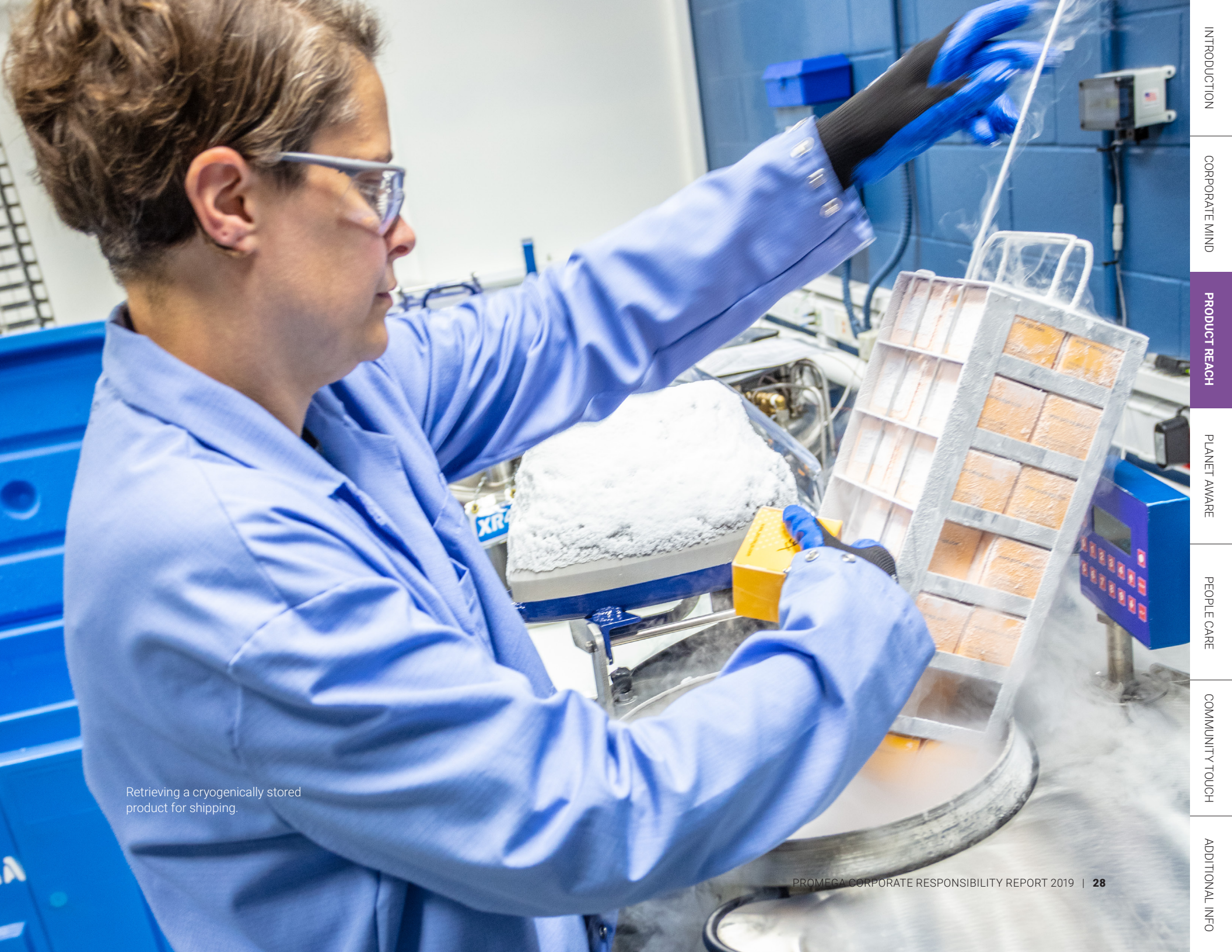
Our growing investment in innovative research resulted in 56 new patent filings in 2018, bringing our intellectual property library to over 380 granted patents and 187 pending patents. Promega research scientists had 20 scientific papers published in 2018. We also work with academic institutions and other entities to license and develop promising technologies.

## Patents

Issued and Pending Applications







Retrieving a cryogenically stored product for shipping.



## QUALITY PROCESS AND PRODUCT

Promega Corporation has a long history of supporting our customers with high-quality products, services and information. Promega headquarters in Madison, WI, USA, was first certified to international standards for quality management systems in 1998, and our commitment continues with our current ISO 13485 and ISO 9001 certifications. The ISO series of quality management system standards are developed and maintained by the International Organization for Standardization. An organization achieving ISO certification has demonstrated to a third party that the organization meets all requirements of the standard and has implemented a quality system capable of developing, manufacturing, testing and delivering high-quality products around the world. ISO certification assures our global customers that Promega is committed to quality and has established reliable and effective processes. The ISO certification exemplifies commitment to our customers, our business, and all those who rely on and benefit from the use of our products. Currently, 16 Promega locations around the world are certified to meet the requirements of ISO 9001, ISO 13485 or both.

In February 2016, ISO 18385:2016 was published as the first international standard specific to the forensic manufacturing community. In 2017, Promega became the first major forensic manufacturer to achieve third-party certification of the published ISO 18385 standard to minimize the risk of human DNA contamination in products used to collect, store and analyze biological material for forensic purposes. Promega products manufactured in alignment with the ISO 18385 standard include a “Forensic Grade” certification logo.

## SCIENTISTS SERVING SCIENTISTS

In 2018, Promega Technical Support scientists handled 15,829 new service requests from Promega customers and more than 30,000 total customer contacts through a variety of channels including phone, email, chat, web-based forms and social media accounts. Technical Support scientists help customers choose the right products, understand how to use them and overcome any issues that may occur.

