Bio/Pharmaceutical NEWS

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Navigate biologics regulatory challenges with a strategic ally to deliver safe, effective biopharmaceuticals to patients

Marian L. McKee, PhD, Vice President, Bio-Pharma Biosafety Testing, Eurofins BioPharma Product Testing

In today's rapidly evolving biopharmaceutical environment, ensuring product safety and meeting increasingly complex regulatory expectations can be challenging. From monoclonal antibodies to cutting-edge gene and cell therapies, all biologics face rigorous biosafety requirements to mitigate the risk of viral contamination. Recent regulatory updates, including the revised International Council for Harmonisation (ICH) Q5A (R2) guidelines and the FDA's movement away from animal-based testing, are reshaping expectations for biosafety strategies.

At Eurofins BioPharma Product Testing (BPT), we understand the pressure our clients face to maintain safety, accelerate timelines, and reduce sample volumes – all while keeping pace with shifting global standards. Our BioSafety Testing team partners closely with our biopharma clients to implement modern, risk-based viral safety programs that combine proven methods with advanced technologies such as next-generation sequencing (NGS). Whether you are navigating regulatory compliance, preparing for IND/BLA submissions, or modernizing your cell bank characterization strategy, Eurofins BPT delivers the expertise and agility to help you mitigate risk and move forward with confidence.

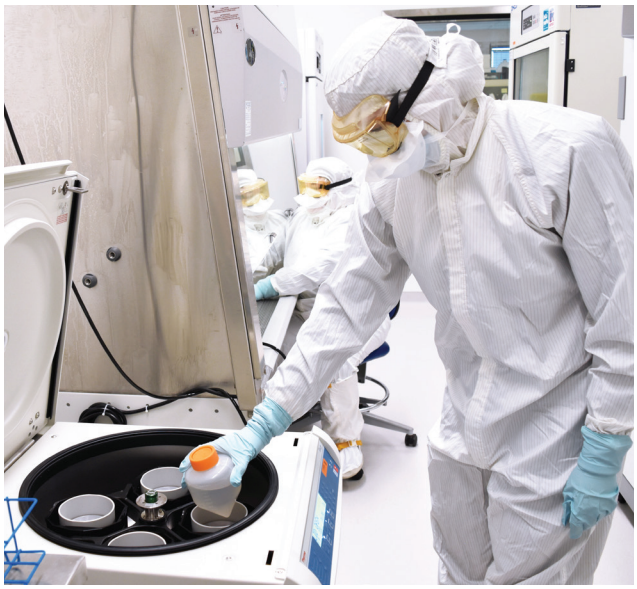
Biosafety testing is required for all biopharmaceuticals, including monoclonal antibodies, antibody drug conjugates (ADCs), vaccines, and the more advanced modalities, including cell therapy, gene therapy, and mRNA products. By their nature, these biologic products are cultivated in environments that can pose diverse risks to product quality and safety. Worldwide regulations outline required testing to mitigate the risk of contamination throughout the manufacturing process. Viral contamination is a particular risk for all biological products. The BioSafety team at Eurofins BPT focuses on assuring the absence of any viral contaminants across the production process from cell banks through manufacturing to product release.

Effective viral risk mitigation is built upon three pillars: Prevent, Detect, Remove. Assuring the integrity and purity of starting materials, including cell banks and media components, are integral to any sourcing strategy to prevent contamination. Validation of downstream processing steps is key to assuring clearance by removal and/or inactivation of any contaminants that may have been introduced during processing. *In vitro* testing remains the primary means of assessing the safety profile of any biologic product. *In vitro* adventitious agent assays (IVAA) are designed to detect contaminating virus and employed throughout manufacturing and prior to product release. IVAA testing, along with sterility, mycoplasma, and targeted PCR methods, is required for every lot of biologic drug manufactured in Unprocessed Bulk (UPB) or Lot Release testing (LRT). Depending on the origin and propagation history of cell banks used for manufacturing, additional *in vivo* virus testing may be required. A successful viral safety plan should be risk-based and designed to include both broad and specific virus detection assays.

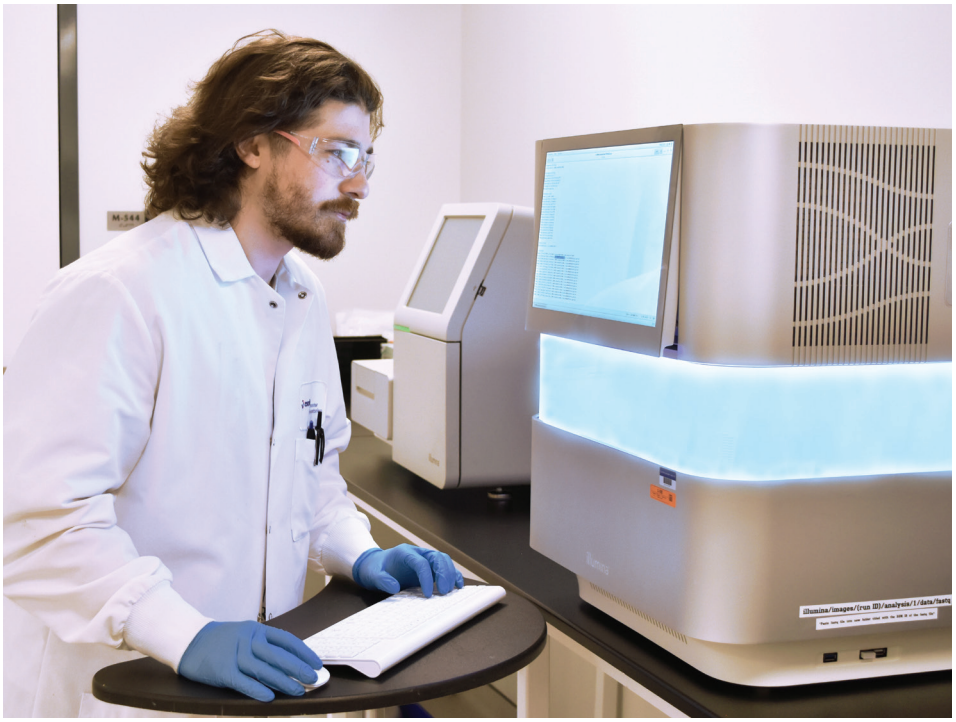
The biopharma industry is undergoing a transformation. Changes in product modalities and manufacturing processes with smaller batches and shorter lot release timelines, an increased desire to move away from animal use, and the advancement in technologies are driving the viral testing field in a new direction. In 2023, the ICH published a long-anticipated update to the guidelines for Viral Safety Evaluation of Biotechnology Products (ICH Q5A (R2)) that was later adopted and published by the FDA in early 2024. The FDA has also announced its plan to phase out animal testing in monoclonal antibody development. The Pharmacopoeia both US and European have chapters embracing the use of alternative methods for safety testing. These and other changes across the regulatory landscape impact the testing we perform to support our clients.

Until recently, NGS was employed as a complementary analysis method in an orthogonal approach to biosafety testing. In the last few years, however, the use of NGS has gained more traction in the biologics and gene therapy marketplace. Both domestic and international regulatory bodies are reviewing more IND/CTA/BLA submissions that contain NGS as part of an alternate testing strategy, especially for replacing *in vivo* tests. With the approval of ICH Q5A (R2), acceptance of NGS in a robust safety testing scheme is gaining momentum. ICH Q5A (R2) states that "NGS can also supplement or replace the *in vitro* cell culture assays for detection of known and unknown or unexpected virus species," and "Non-targeted NGS is encouraged as a replacement for *in vivo* assays."

As the regulatory landscape continues to evolve, Eurofins BPT remains committed to supporting our clients with a proactive, science-driven approach to biosafety. From preventing contamination at the cell banking stage to accelerated lot release with innovative testing strategies like NGS, we deliver tailored solutions to align with your product goals and compliance needs. Whether you are advancing a new therapy or optimizing an existing program, our team is here to help you safeguard quality, keep to your timelines, and meet the highest global standards. With Eurofins BPT as your partner, you gain not only a testing provider but a strategic ally in bringing safe, effective biopharmaceuticals to market.



GMP next generation sequencing identifies contaminants early and optimally delivers rapid, cost-effective results to assure product safety



Victor Muthu, PhD, Group Leader, BioPharma NextGen Sequencing; Marian L. McKee, PhD, Vice President, BioPharma Biosafety Testing, Eurofins BioPharma Product Testing

Next Generation Sequencing (NGS) technology has revolutionized the landscape of molecular biology, enabling high-throughput, accurate, and scalable sequencing for a variety of applications. At the forefront of this innovation, Eurofins BioPharma Product Testing (BPT) offers a comprehensive suite of NGS services, tailored to meet the needs of biopharmaceutical companies at all stages of product development. Our NGS offerings encompass sequence identity testing for plasmids, adeno-associated viruses (AAV), and lentivirus/retrovirus, along with adventitious viral detection services, ensuring quality control and safety in cell therapy, viral vector production, and related fields.

Identity tests are a crucial part of product testing packages submitted to regulatory agencies during the drug development and approval lifecycle. These tests include verifying the identity of plasmids and/or viral vectors that are critical raw materials, drug products (DP) or drug substances (DS) for cell and gene therapy manufacturing. Plasmid identity testing is particularly critical for confirming the presence of the correct insert and ensuring that the plasmid remains free of sequence variants or mutations. AAV and lentivirus/retrovirus sequence identity testing provides an analysis of packaged viral genomes, confirming that they are correctly assembled, free of unintended mutations, and maintain their intended therapeutic functionality. These tests are critical prior to releasing the plasmid or viral vector for downstream processes, including manufacturing.

Non-high throughput methods such as Sanger sequencing can be employed, but these are limited in the sequence coverage and depth that compromises the sensitivity of the assay. NGS is a high-throughput platform enabling rapid, cost-effective, parallel sequencing of DNA and RNA. Unlike Sanger sequencing, which analyzes one fragment at a time, NGS sequences millions of fragments simultaneously. NGS is the method of choice for identity testing as it provides the depth and sensitivity that are needed to identify the presence of any variants in a plasmid and/or viral vector nucleotide sequence. NGS also offers the ability for multiplex sequencing where samples can be batched and sequenced simultaneously, saving both costs and time, which is ideal for start-ups. Validated, GMP methods are ideal for release testing.

Eurofins BPT in Lancaster recently added GMP Sequence Identification Testing (SIT) by NGS to our testing portfolio. The method utilizes short-read sequencing performed on an Illumina® platform. The sequence obtained is compared to a client-provided reference sequence using bioinformatic analysis to identify any mismatches or variants, including insertions or deletions in the plasmid or viral vector sequence. The GMP method for Sequence Identity Testing has been validated in accordance with ICH Q2 (R2) as an identity method with additional attributes challenged to ensure the robustness of the method for detection of variants.

In addition to sequence identity testing, we also offer adventitious viral detection services (AAD). The presence of adventitious viruses in bioprocessing or gene therapy products can pose serious safety concerns and regulatory challenges. Our adventitious viral detection service leverages the sensitivity of NGS to identify a broad range of known and unknown viral contaminants that could potentially compromise product safety. This service is particularly valuable in the production of viral vectors, cell therapy, vaccines, and monoclonal antibody production, ensuring that products are free from contaminating adventitious viruses that could cause harm to patients or invalidate clinical trials. Our NGS-based adventitious viral detection services provide comprehensive evaluation of viral contamination, offering a higher level of detection sensitivity than traditional methods such as PCR or cell culture-based assays.

Our NGS services are powered by robust sequencing platforms, ensuring high throughput and unparalleled accuracy. We offer complete bioinformatics support, providing customers with detailed, actionable insights from the data analyses, including alignment and variant analysis for the SIT services, to contaminating virus identification for the AAD.

Eurofins' NGS capabilities provide high quality, regulatory-accepted results to assure product safety and accelerate getting key materials into manufacturing and medicines to patients. Essential to a complete biosafety program, we enable clients to meet or exceed product milestones and to deliver critical therapies to patients faster than traditional methods.

Sustainability. Efficiency. Consistency.

Tessa Patton, Manager, Bio/Pharmaceutical Microbiology, Eurofins BioPharma Product Testing

When you hear the words sustainability, efficiency, and consistency, do you immediately think of bacterial endotoxin testing? I must admit, it's not the first thing that used to come to my mind when I hear those words. Sometimes Bacterial Endotoxin Testing can feel like anything but sustainable, efficient, or behave consistently, but with new methodology and technology available in the industry, Bacterial Endotoxin Testing is a whole new ballgame.

In the complex world of pharmaceutical quality control, BET plays a critical role in ensuring the safety of drugs, vaccines, and medical devices. Eurofins BioPharma Product Testing's team is excited to onboard new methodology and technology, providing practical solutions to deal with the challenges of Bacterial Endotoxin Testing. Onboarding bioMérieux's Recombinant Factor C (rFC) reagent, as well as the Sievers Eclipse™ Bacterial Endotoxin Testing Platform for Kinetic Chromogenic testing allow Eurofins BPT to demonstrate its commitment to sustainability, improved workflow efficiencies, and ensure consistency within the data we provide.

bioMérieux's rFC is part of their ENDONEXT™ technology and is a nonanimal-derived alternative to the traditional limulus amebocyte lysate (LAL). rFC mimics the natural Factor C that is found in horseshoe crab blood, binds specifically to endotoxin, which triggers a cascade reaction resulting in a measurable signal (either fluorescence or luminescence). The use of a synthetic reagent reduces lot-to-lot variability, which in turn allows for more consistent performance. Eurofins BPT has selected bioMérieux's ENDOZYME® II GOPLATE™ technology to further improve consistency, as well as improve workflow efficiency. The GOPLATE comes pre-filled with required standard curve and positive product controls, which aids in reducing analyst time and eliminating analyst-to-analyst technique variability. This new technology is compliant with USP <86> and EP 2.6.32.

While not completely eliminating the use of traditional LAL, the Sievers Eclipse Bacterial Endotoxin Testing Platform does significantly reduce the use of LAL by up to 90% when compared to the traditional Bacterial Endotoxin methods.

Similar to the bioMérieux's ENDOZYME II GOPLATE, the Eclipse utilizes a microplate that comes pre-loaded with the standard curve and positive product controls, again reducing analyst hands-on time and eliminating variability due to analyst technique. The Eclipse utilizes microfluidics and automation to streamline workflow. The Eclipse does all of this while maintaining compliance to USP <85>, EP 2.6.14, and JP 4.01.

Implementation of ENDONEX and Sievers Eclipse platforms demonstrates Eurofins commitment to innovation, compliance, and sustainability while providing multiple alternatives to our clients for their Bacterial Endotoxin Testing needs. These innovations are not only optimizing workflows but also having a meaningful impact on how the industry continues to advance. While Bacterial Endotoxin Testing is a cornerstone of patient safety, other microbiological tests are as critical to ensuring safety of products, thus creating opportunities to evaluate other advancements in microbiological testing. As the pharmaceutical industry continues to evolve, implementing technologies that lend to efficiency gains, reducing variability, and supporting sustainability is vital.

The Whole Package: Get package testing solutions backed by sterilization and microbiology testing at Eurofins' three San Jose sites

Wesley Harada, Operations Manager, Eurofins Package Testing, San Jose, CA; Luke Miller, General Manager, Eurofins BioPharma Product Testing

Ensuring that a medical device or pharmaceutical product reaches its destination in its original condition is crucial. Package testing should be a part of the Biological Evaluation Plan (BEP), and as a best practice should be done early in the product development process to optimize both cost and time to market. This ensures that the packaging effectively protects the product during distribution; the packaging is compliant with any regulations; and the final packaging is on brand and works for the end user.

Eurofins offers full package testing expertise and guidance to test that product packaging is appropriate for the distribution of the product and ensure that the product arrives to the end user as desired. In our experience, we have seen situations where leaving the design and testing of the packaging to later in the design process has led to costly changes to both the packaging and the product, causing significant delays in launch, particularly when the design of the packaging does not withstand the rigors of transportation.

Another advantage of using Eurofins in San Jose, CA, for your package testing needs is a sterilization facility 15 minutes from the package testing facility, and a full microbiology lab in close proximity to both. We are seeing increased demand for both package testing and sterilization of devices with complex designs, often with embedded electronic components. As a best practice, we complete an R&D evaluation of the impact of testing on a small number of devices in partnership with our clients, before proceeding to validation and full production testing.

Given the expense of implantables, there is a possibility, with client discussion, to use a placebo device with the same volume, dimensions, and weight in lieu of the full device in order to test the device packaging alone, when it is apparent that the rigor of the testing runs will damage the device inside the packaging.

We employ a variety of package testing methodologies in our ISO17025 accredited laboratory to simulate real-world transportation and handling conditions on small envelopes to large pallet sized configurations. These include:

Shock Testing – Evaluates how a package withstands accidental drops or impacts during transportation.

Vibration Testing – Assesses the impact of continuous movement and shaking that occurs in vehicle transit.

Environmental Conditioning – Exposes packaging to extreme temperatures and humidity to determine its resilience.

Sterile Barrier Integrity Testing – Ensures that no microorganisms or contaminants breach the packaging, maintaining the sterile barrier of medical and pharmaceutical products.

We collaborate with clients to design testing programs that align with industry regulations including ASTM, ISTA, and ISO standards. Whether ensuring pharmaceutical packaging stability under extreme temperatures or verifying the tamper resistance of consumer products, we partner with our clients to develop a testing protocol that fits the needs of the product and package under test.

We collaborate with clients to design testing programs that align with industry regulations, including ASTM, ISTA, and ISO standards.

Eurofins Medical Device Services US offers expert guidance and quick turnaround times for small-scale ethylene oxide sterilization needs

John Hodges, Senior Business Development Director, Eurofins BioPharma Product Testing

Regularly audited by the FDA and fully cGMP compliant, Eurofins Medical Device Services' San Jose, CA, Ethylene Oxide (EO) Sterilization site provides high-quality, fast turnaround contract sterilization and validation services for the medical device industry. Specializing in servicing small-scale sterilization projects, and adhering to ISO 11135 and CFR 820, the site operates seven 3M™ Steri-Vac™ GS8X pure EO sterilizers to ensure the elimination of microbial risks for medical devices and their components.

With EO exposure, the preferred modality to sterilize more than 50 percent of medical devices on the market, Eurofins' San Jose site provides the necessary support to meet high market demand. The site's sterilizers have a maximum sterilization capacity of 8 cubic feet to service a unique niche of medical device sterilization needs.

Noted for quick turnaround times, our experts routinely process R&D and production sterilization requests in days and turn around full sterilization validations in weeks.

Eurofins Medical Device Services' experts work with manufacturers to devise robust sterilization plans to address potential concerns with unique and potentially temperature-sensitive devices. This is important as the biggest hurdle to overcome in a typical EO sterilization run is the required use of higher temperatures and humidity. To meet this challenge, we often performs small R&D testing runs on a small number of devices to test the impact of the conditions before moving to runs with larger batches of devices.

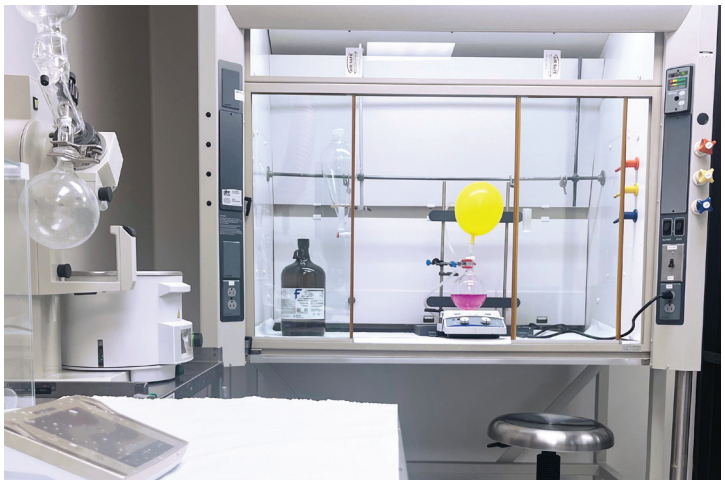
Eurofins' EO sterilization experts work within the new EPA regulations to ensure that more than 99 percent of EO gas used during sterilization is removed from any air passing in and out of the lab.

GMP synthesis of radiolabeled compounds expertise solves safety and efficacy challenges

Craig Schouten, Vice President of Operations, Eurofins BioPharma Product Testing Columbia

Few laboratories have the expertise and systems to perform a GMP synthesis of radiolabeled compounds for human mass balance studies. Eurofins BioPharma Product Testing's radiolabeling and custom synthesis services offer state-of-the-art facilities and an experienced team to support client's synthetic needs.

Our team is equipped to handle a range of projects from custom small-scale synthesis of compounds and reference standards to the manufacture of 14C labeled API for early phase clinical trials in compliance with FDA phase 1 GMP guidance (IQCH Q7a Section 19).



Whether you need radiolabeled compounds for preclinical studies or clinical metabolism studies, our experts can provide guidance on synthetic procedures to meet your specific needs. Our dedicated analytical team can provide assurances on the safety and efficacy of the radiolabeled compounds both on release and stability.

At Eurofins, we have the expertise, facilities, and systems to provide effective, timely, and quality production of radiolabeled compounds.

People are our chemistry

At Eurofins BioPharma Product Testing, our people are the most important element in our chemistry. Their dedication to quality testing, data integrity, and client satisfaction drive our success as an industry leader.

In this regular feature, we introduce you to some of the people who help clients deliver timely therapies to patients and make the world healthier and safer.

Victor Muthu and his family

"When I was about 8 years old, I remember being particularly intrigued by science – and a few years later, more personally important – the genetic aspects of therapies after a family member died of lung cancer," said Victor Muthu, Group Leader, BioPharma NextGen Sequencing at Eurofins' Lancaster, PA, site. "I had a realization that doctors could only do so much with the treatments they had at that time. I was inspired to engage in scientific studies and conversations about the advancement of life-changing molecular, cell, and gene therapies."

Victor brings a world of Next Generation Sequencing expertise to his Eurofins' role from half a world away. After earning a bachelor's degree in Singapore, a PhD in molecular & cell biology in England, Victor came to the University of Pennsylvania School of Medicine for post doc work in genetics and gene therapies. "During a job search, when I saw my current role posted, I was very familiar with Eurofins' stellar reputation, having spent time in Europe, where it is well-known and trusted. This opportunity was clearly a match for my desired next career level. I now come into work every day knowing that I have great team – people I can trust and rely on." Read more about Victor:

What process improvements does your group initiate to serve clients better?

We are always sensitive to the clients' needs and work with them to meet their expectations. This includes expediting delivery timelines to meet their changing needs especially if the client is filing for regulatory approvals. Our team of experts are also available to meet and go the extra mile to assist clients with questions they may have related to our services. We are also expanding our services into other offerings in order to broaden our service portfolio to solve their ever-changing challenges.

Why should clients trust us with their projects?

Clients typically choose a testing partner based on reputation, cost, and expertise. We have extensive experience and deep expertise in NGS and molecular biology in our Next Generation Sequencing Department. We have dedicated dedicated personnel ready to engage in client projects and deliver.

Our NGS projects are well developed for end-to-end offerings. Each method is or will be validated as per ICH Q2 (R2) guidelines to meet regulatory requirements.

Given all of your responsibilities, how would you describe a typical workday?

My typical workday mornings begin on the one-hour train commute from Philadelphia to Lancaster where I work on the train, responding to emails and following up on items that require my immediate attention. Once I arrive on site, I will check in with my team members if they have any project or clients needs on their agenda for the day that they would like to discuss. The rest of my day is mainly spent on driving essential scientific and business activities for the department like attending meetings, writing documents, and planning lab related activities to better serve clients.

How would you characterize your leadership style?

I have an open leadership style where I see everyone in my team as stakeholders in all the work that we do. I encourage strong camaraderie among members in my team and to put the team above self. I also enjoy working alongside them to resolve any issues they may face.

With a growing company, there's always good changes happening. During your tenure at Eurofins is there anything that hasn't changed?

I have been here for close to two years, and the things that haven't changed are the absolute devotion and care to helping clients surpass their testing and regulatory hurdles and the beauty of the campus especially during spring/fall!

How does your group's work impact/ benefit society?

The NGS testing we perform has a direct impact on the safety and efficacy of Advanced Therapy Medicinal Products (ATMPs) especially in cell and gene therapeutics. We test and ensure that the DNA sequence of the raw materials and final product matches the sequence of the intended therapeutic gene and that there are no mutations present.

And when you're not working?

My favorite past time hobbies include fishing and travelling with my wife and two sons. I like travelling to natural sites like State and National Parks especially those with beautiful natural landscape like the Grand Canyon.

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