Lonza

Equip for the Future

The Path to Sustainable and Efficient Product Safety Testing

Industry Insights from the 2023 Global Endotoxin Testing Summit

About the 2023 Global Endotoxin Testing Summit

For several years, our Global Endotoxin Testing Summit has brought together testing experts, researchers, manufacturers, regulators, and conservationists to discuss critical trends and future directions for pyrogen testing in the pharmaceutical industry's quality control (QC) sector.

At our 3-day virtual event, we hosted 17 expert speakers from three world regions – the Americas, Asia, and Europe – and received >1,200 registrants from 67 countries. The focus themes were sustainability and increasing efficiency through automation, digitalization, and smart solutions.

Testing injectables and parenteral pharmaceuticals for pyrogens is critical for their safe market release. Yet the QC sector faces several challenges – from continued test demand growth, and more complex pharmaceutical products, to an ever-increasing pressure to do more with less in addition to new regulatory requirements to improve sustainability.

As pharmaceutical QC teams seek to adapt, two key trends have emerged:

- A move to more sustainable *in vitro* product safety testing methods
- Advance the implementation of digitalization and automation tools to increase testing efficiencies

In this article, we delve into the presentations given by the panel of expert speakers, drawing out the key trends, updates, and insights gleaned from another very successful summit.

Ushering in the Sustainable Future of Pyrogen and Endotoxin Testing

Today, sustainability is a hot topic in a multitude of sectors. And pharmaceutical QC testing is no different. This year, our panel of expert speakers traced the history of pyrogen testing, documenting the significant progress our sector has made on its path to more sustainable test methods – methods that reduce reliance on experimental animals and finite natural resources while offering equivalent or superior performance.

From the RPT to the LAL Test: Early Steps Forward

More than a century ago, Hort and Penfold designed the first test for pyrogenicity – the Rabbit Pyrogen Test (RPT). As described in the presentation of Dr. Xiaoming Wang, Sterility Assurance Subject Matter Expert at Wagner Biotech, the principle of the test is fairly straightforward: 10 mL/kg of product is injected into rabbits, and then the animal is monitored for signs of fever (with fever denoting pyrogenic contamination of the test product).

But despite the longstanding historical position of the RPT as the go-to pyrogen test, several summit speakers drew attention to its considerable disadvantages. For example, Dr. Wang flagged that the RPT suffers from animal-to-animal variation, and also noted that test results are highly influenced by the type of testing sample used. Dr. Ingo Spreitzer, Deputy Head of the Department Microbial Safety at the Paul Ehrlich Institute, added to this list, highlighting that the RPT suffers from a lack of sensitivity, and has no positive controls, standard curves, or endotoxin spiking and recovery.

Perhaps most importantly, though, Dr. Wang, Dr. Spreitzer – and a host of other speakers –commented on the glaring ethical disadvantage of the RPT: that it consumes experimental animals.

Dr. Wang then highlighted the first critical step forward for more ethical and sustainable pyrogen testing: the introduction of the limulus amoebocyte lysate (LAL) test. First discovered in the '60s, the LAL test uses horseshoe crab (HSC) blood, which forms a gel clot in the presence of endotoxins — the most abundant and potent type of pyrogen, and the easiest to introduce into pharmaceutical products. The benefits of the LAL test's introduction are hard to overstate. For one, the LAL test reduced reliance on experimental rabbits, quickly replacing the RPT for bacterial endotoxin testing (BET). What's more, as noted by Dr. Spreitzer, the LAL test has scientific advantages over the RPT: its sensitivity is well known, assay controls are possible, and technicians can create a standard curve thanks to reference standard endotoxin (RSE). The importance of reference standards was later discussed by Dr. Yukari Nakagawa, General Manager at the Pharmaceutical Reference Standards Center, Pharmaceutical and Medical Device Regulatory Science Society of Japan. In her presentation Dr. Nakagawa gave a detailed overview of Japan's endotoxin reference standard strategy, highlighting that high-quality reference standards are critical for globally harmonized BET.

Overall, the takeaway from the discussions was clear — the LAL test has saved countless lives while drastically reducing the number of experimental animals consumed in pharmaceutical safety testing.

A Look at HSC Populations Across the Globe Today

While HSCs have no doubt played a pivotal role in pharmaceutical QC, they are an exhaustible natural resource: a fact that featured heavily in conversations at our summit.

Glenn Gauvry, Founder and President of the Ecological Research & Development Group, provided attendees with a comprehensive overview of the topic, updating us on the global outlook for HSC population stability, as well as discussing the key initiatives helping ensure their protection. Gauvry began with an overview of the many pressures on HSCs, which include marine and terrestrial habitat loss (from extensive coastal urban development and coastline hardening) and harvesting for bait, human food, fertilizer, traditional medicine, and biomedical uses.

But Gauvry had positive news, too. Despite the pressures, **US HSC populations coastwide are stable, thanks to responsible population management and well-established science-backed conservation initiatives**. Such initiatives include, for example, strict harvest exclusion zones, state-by-state harvesting quotas, and a host of other restrictions enforced by the Atlantic States Marine Fisheries Commission (ASMFC) and other bodies (Figure 2). As Gauvry noted, "these far-reaching efforts have helped restore HSC populations to sustainable levels from the decline of the early 1990s. The ASMFC stands as a strong example of science-based management."

Gauvry added, however, that the situation in Asia is much more challenging. Asian HSC populations are still endangered. And it's easy to see why: "The Asian HSC species present complexities far surpassing those of their American counterparts," Gauvry pointed out. "HSC habitats span a multitude of countries, each with unique social, economic, and environmental priorities, and legal protection is limited." Despite the challenges, though, **the committed work of several groups and initiatives is driving promising progress towards more effective HSC population management in Asia.**

The Road to Recombinant Technologies: A Defining Moment

While HSC conservation and pharma industry efforts have played (and continue to play) a critical role in protecting HSC populations the world over, BET demand is only set to grow.

Several speakers highlighted that more needs to be – *and can be* – done, thanks to the power of recombinant alternatives to LAL-based BET methods. Gauvry in particular didn't hesitate when sharing his verdict: "We now face a defining moment with recombinant technology".

The recombinant factor C (rFC) assay, a well-established and sustainable alternative to the LAL test, was first commercialized by Lonza in 2003, and offers a BET method that doesn't rely on experimental animals or finite natural resources such as HSC blood.

Dr. Wang provided a thorough overview of the method, first noting how it works: a recombinant version of factor C, a protein in the enzymatic HSC blood clotting cascade, cleaves a fluorogenic substrate in the presence of endotoxins.

After describing the method's mechanistic principle, Dr. Wang swiftly moved to the myriad benefits of the rFC assay relative to the LAL test:

- **Supply chain security:** rFC can be produced in bioreactors anywhere in the world, enabling vendors to keep pace with growing BET demand
- **Higher specificity:** Unlike with LAL test, the rFC assay does not react with beta-glucans to produce false positives
- **Greater lot-to-lot consistency:** Synthetic production drastically reduces batch-to-batch variability, meaning testing results are more consistent
- **Superior sensitivity:** Fluorescent detection eliminates the need for an amplification cascade while ensuring sensitive quantification of even low endotoxin levels.

Towards the end of her presentation, Dr. Wang made another important observation — that adopting the rFC assay can be simple since the method needs minimal training, and that validation as an alternative method takes as little as one week when using a good protocol.

Clearing Up Confusions Around Atlantic Horseshoe Crab Population Sustainability

Confusion persists among both scientists and non-scientists about the status of the Atlantic horseshoe crab *(Limulus polyphemus)*. So, after the summit, we sat down with Allen L. Burgenson, Global Subject Matter Expert and Associate Director – Testing Solutions at Lonza, as well as a Horseshoe Crab Advisory Panel member to ASMFC, and HSC Working Group member to IUCN (International Union for the Conservation of Nature), to get some further clarity on the matter.

Some in the scientific community are under the impression that the Atlantic horseshoe crab is endangered. Is this true?
There has been a lot of talk, and many presentations, regarding the status of the Atlantic horseshoe crab in the last few years, and much of these discussions revolve around the notion that this species is endangered. This is a misunderstanding of an **IUCN report**, which placed *L. polyphemus* on their "Red List" as "threatened".

Due to this misunderstanding, several groups have circulated erroneous statements regarding the health of the *L. polyphemus* populations along the eastern shores of the United States.

So, what did the IUCN report actually say about Atlantic horseshoe crab populations?
The IUCN report stated that the Atlantic horseshoe crab "is at risk of extirpation in some regions within its range owing to declines in small and vulnerable populations, according to an IUCN Red List assessment."

So, we can immediately see that the threat is to small isolated populations, and is due to a lack of genetic diversity of those populations, not the number of horseshoe crabs in the surrounding areas.

What is the current status of the Atlantic horseshoe crab?
The Benthic Trawl Survey performed by Virginia Tech (and used by ASMFC to determine *L. polyphemus* species abundance) estimates that there are approximately 43 million Atlantic horseshoe crabs in the Delaware Bay alone. What's more, the ASMFC's 2019 peer-reviewed **Stock Assessment** shows that horseshoe crab populations on the US East coast are stable or increasing, except for in one area: the New York Bight.

> "It is estimated that a 30 L bioreactor can produce enough rFC to replace the blood of at least 6,000 horseshoe crabs. So, this is not only saving time and money, but it is also helping protect an increasingly endangered species."
>
> **Dr. Xiaoming Wang,**
> Sterility Assurance Subject Matter Expert,
> Wagner Biotech

Of course, Dr. Wang wasn't the only speaker to weigh in on the benefits of the rFC assay. Professor Yutaka Kikuchi of the Chiba Prefectural University of Health Sciences shared important findings from a large study comparing the rFC and LAL tests. In the study, Professor Kikuchi and his team tested all commercially available rFC products and showed that all are comparable to or better than the LAL test.

The MAT: Closing the NEP Gap

With its long history of established commercial use and wealth of studies demonstrating comparable or superior

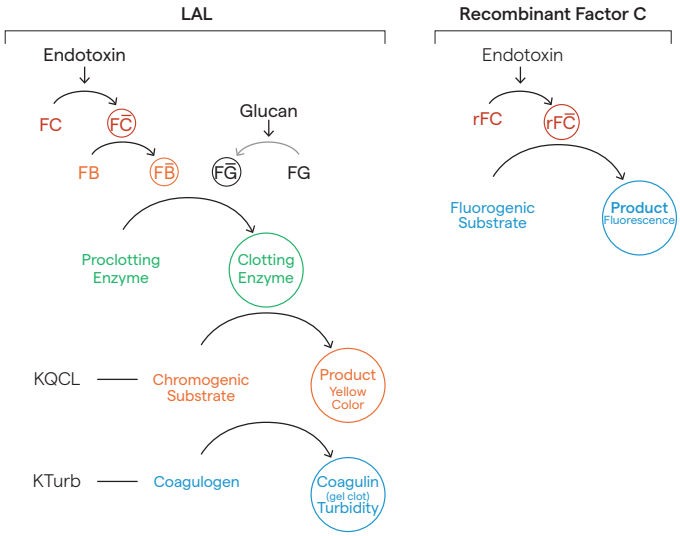

Figure 1.
Comparison of the enzymatic LAL cascade and the rFC reaction. Note that the rFC assay is not susceptible to interference from glucans.

results, the rFC assay represents a substantial step forward on the road to more sustainable product safety testing.

That said, the rFC assay alone is not a sufficient replacement for the RPT. As pointed out by Dr. Djik Maouyo, President of PyroDex, in his talk, **BET – whether using recombinant methods or not – doesn't test for non-endotoxin pyrogens (NEPs)**. While endotoxins are the most potent and pervasive of the pyrogens, NEPs still pose a significant risk to patients' lives. Testing for their presence is therefore critical.

And this is where the monocyte activation test (MAT) comes in – a test that was a point of extensive conversation at our summit.

The MAT is a sustainable *in vitro* test that measures the innate human immune system's response to pyrogens – both endotoxins and NEPs. At the summit, Luca Benedan, Consultant at Eurofins Regulatory & Consultancy Services Italy, and Dr. Marijke Molenaar de-Backer, Senior Scientist of MAT Services at Sanquin Diagnostics B.V., gave a thorough overview of the biological mechanism underpinning the MAT, and explained the simple steps involved in the test: analysts incubate their sample with a source of monocytic cells (typically pooled, cryopreserved peripheral blood mononuclear cells (PBMCs)) for 18 – 24 hours, following which they detect and quantify secreted cytokines (for example, using ELISA), to provide a pyrogenicity readout.

Benedan and Dr. Spreitzer expounded some of the benefits of the MAT, highlighting why it is a superior test to the RPT:

- **Alignment with 3Rs principles:** As an *in vitro* test, the MAT adheres to the principles of the 3Rs, which urge researchers to replace, reduce, and refine tests that use experimental animals. Incomplete sentence

What are the current major threats to Atlantic horseshoe crabs? And what impact does the biomedical sector have?
The IUCN identifies the major threats as overharvest (for bait), habitat loss from coastal development, and climate change effects on sea-level rise and severe weather events. The overharvest threat is mitigated through regulation by the ASMFC, as well as through the Atlantic States through strictly enforced harvest quotas that have significantly reduced the collection of this species for use as bait.

Both the IUCN report and the Stock Assessment state that biomedical uses of *L. polyphemus* do not have detrimental effects on the Atlantic horseshoe crab population. It is through regulation and the conservation efforts of many groups, including LAL manufacturers and the fishery, that this critical population has made such a recovery from the bleak days of the early 1990s.

- **Provides assay controls:** While the RPT lacks assay controls, the MAT enable analysts to determine pyrogen contents against a reference standards (against a reference standard or against reference standards?), allowing a more accurate control of critical limits, and of synergistic effects.
- **Higher sensitivity:** The MAT boasts a limit of detection (LOD) of 0.02 EU/mL, compared to an LOD of just 0.5 EU/mL for the RPT.
- **Greater physiological relevance:** Unlike the RPT, the MAT measures the response of human cells to pyrogenic contaminants, making the test more representative of (and applicable to) humans.

Regulatory Perspectives: Support for the rFC Assay and MAT

The regulatory status and future of the BET assays using recombinant reagents and the MAT is a hot topic. It's therefore hardly surprising that much discussion amongst both speakers and attendees centered around regulations.

Dr. Spreitzer set the scene nicely by summarizing the current regulatory status of the various available endotoxin and pyrogen tests – the RPT, MAT, LAL test, and rFC assay – according to the United States Pharmacopeia (USP), the European Pharmacopeia (Ph. Eur.), and the Japanese Pharmacopoeia (JP) (Table 1).

Dr. Spreitzer then went on to discuss the reasoning behind the European Commission's new pyrogenicity strategy – a strategy which will lead to the full elimination of the RPT from the European Pharmacopeia by 2026.

"Why was there the need for change?" Dr. Spreitzer asked. "The MAT has been an official method of the European Pharmacopeia since 2010. It's superior to the pyrogen test. MAT kits are available. *Yet, RPT users often didn't skip the RPT,* and this clearly contradicts the legal situation in Europe," he added, referring in his latter point to **Directive 2010/63**, which demands manufacturers use an alternative to the RPT.

The need for change when it comes to BET was also clear: given the supply chain risks of relying on a non-native finite natural resource (i.e., HSCs), the new pyrogenicity strategy will ease transitioning to recombinants.

Of course, the change in Europe is a huge step towards more sustainable pyrogen testing. While Dr. Spreitzer was clear about how significant and positive this step is, he was also adamant about what still needs to be done.

"The next big goal is harmonization between the European Pharmacopeia (Ph. Eur.) , the Japanese Pharmacopeia (JP) and the United States Pharmacopeia (USP)," he said, going on to state that, given the dire HSC situation in Asia, it's a shame we can't be faster in our collective efforts to drive greater adoption of the rFC assay.

Methods	Pharmacopoeia Status		
	United States Pharmacopoeia	European Pharmacopeia	Japanese Pharmacopeia
RPT	Compendial	Compendial	Compendial
MAT	Alternative*	Compendial	Alternative
LAL test	Compendial	Compendial	Compendial
rFC assay	Alternative	Compendial	Alternative

* Right at the time of the summit the USP published USP <86> "bacterial endotoxin tests using recombinant reagents

Table 1: Summary of the regulatory status of various endotoxin and pyrogen test methods.

Shortly before the event, with exquisite timing, the USP made a big announcement that takes us closer toward rFC assay harmonization — Chapter <86>, a long-awaited addition to the USP offering guidance on how manufacturers can incorporate recombinant BET methods into their testing. The chapter is now in draft and out for comments.

Implementing the Assays in Your Lab: Tips and Perspectives

As well as offering deep insight into the benefits and regulatory status of sustainable tests, our summit was also the place to be for those seeking how to best implement them in the lab.

It's no secret that many companies are deterred from implementing more sustainable tests owing to the perceived burden of method validation and implementation. However, a key takeaway from the event was that **the process can be remarkably straightforward when planned properly.**

Adopting the MAT

Several speakers across the event shared their experiences of implementing the MAT in their labs, offering detailed and insightful case studies. Luca Benedan, for example, discussed why and how Eurofins implemented the MAT to evaluate pyrogenicity levels across vaccine batches.

In terms of the 'why', Benedan first emphasized the disadvantages of both the RPT and BET methods – the former suffering from false positives and administration route inconsistencies between rabbits and humans, and the latter being unable to detect NEPs. The MAT, with its ability to overcome or sidestep these pitfalls, was noted as the only logical choice.

When it came to the "how", Benedan took viewers through the simple steps of implementation at Eurofins:

1. **Identify fit to the standard curve** (in this case the results indicated that Method C was the most suitable MAT testing method)
2. **Find the geometric dilutions that cover the range of the dose response curve**

3. **Conduct a reference lot comparison test**. Luca found that the MAT passed all relevant tests for assay suitability parameters (non-parallelism, non-linearity, and regression), and found that the potency ratio was within the specified limit.

His conclusion? That the MAT is a sustainable solution for evaluating the pyrogenicity of intrinsically pyrogenic vaccine products.

MAT expert Dr. Marijke Molenaar-de Backer provided attendees with another MAT implementation case study. After echoing Benedan's summary of how the MAT overcomes the pitfalls of the RPT and BET methods, Dr. Molenaar-de Backer showed us how she implemented the MAT for testing the reactogenicity of different outer membrane vesicle (OMV) preparations for a new whooping cough vaccine. In doing so, she shared valuable tips on selecting the right reference product for a Method C test, as well as how to choose the right type of MAT test for the specific test product, exploring the impact of things such as supplemental serum choice.

Like Benedan, **Dr. Molenaar-de Backer concluded that the MAT is a robust, sustainable option** that can be used to determine reactogenicity of different OMV preparations during vaccine development.

Adopting the rFC Assay

Implementation discussions, of course, didn't stop at the MAT. Speakers also shared their reasons for (and experiences of) implementing the rFC assay.

Christy Richey, Manufacturing Supervisor, kicked off discussions by offering a **view into the rFC assay implementation journey at one of Thermo Fisher Scientific's US manufacturing sites** and reasons driving the decision — from greater supply chain security and reduced reliance on finite natural resources to comparable results to the LAL test — all with negligible cost differences. "The Thermo Fisher Scientific mission statement is to make the world healthier, cleaner, and safer. So, what better way to do this than to investigate rFC testing for endotoxins?" she said.

It was also clear that Richey had her sights set on the future of BET when making the decision to move to the rFC assay: "Because it's used in the European Pharmacopeia, it's only a matter of time before the US accepts it as well, so we might as well jump on board with this test method."

Daniel Winter gave more information about the implementation and validation process, this time at the Gesellschaft für Produktionshygiene und Sterilitätssicherung GmbH (GfPS) in Germany, where he is Manager of the BET Department. As with Thermo Fisher Scientific, GfPS implemented the rFC assay primarily for sustainability reasons, coupled with anticipated increased testing demand.

Winter noted that, after comparing different rFC assay suppliers, GfPS chose Lonza's PyroGene® rFC Assay, and validated it according to USP <1225>, comparing the new assay with their existing method – the kinetic turbidimetric LAL test.

For the validation procedure, Winter's team exposed three product samples to low, medium, and high concentrations of endotoxin, and then measured them (in triplicate) with both methods, assessing results against validity criteria (precision, accuracy, specificity, and linearity). And the findings were clear: **the rFC assay was comparable to or better than the LAL test**. As a result, the rFC assay is now part of the company's portfolio and can be ordered as a special test.

Dr. Michael Kracklauer, Manager of Endotoxin Services at Microcoat Biotechnologie GmbH, also discussed product-specific validation, but this time with a focus on just one aspect of the process: low endotoxin recovery (LER) studies. Occasionally, more complex test products can mask endotoxin contamination, whereby analysts fail to recover a known quantity of spiked purified endotoxin from a sample. Dr. Kracklauer provided a valuable and in-depth overview of this phenomenon, as well as describing strategies to test for and overcome it.

Overall, it was apparent from the expert speakers that sustainable method implementation can be swift and straightforward. **While it's true that product specific validation can be more complex (for example, because of test product interference), there are ways to overcome these complexities.**

The Move Towards Automation and Digitalization: Unlocking New Levels of Efficiency in the QC Lab

Whichever way you look, and in whichever sector, automation and digitalization are making their transformational mark. At our summit, we were lucky enough to have a selection of speakers to talk about the transformative potential of automation and digitalization tools for the pharmaceutical QC sector.

The Many Drivers for Automation and Digitalization

Several presenters unpacked some of the most pervasive driving forces pushing more and more organizations to adopt advanced digital technologies in their labs.

Chris Crout, Senior Scientist at Fresenius Kabi, began by listing some of the downsides of non-automated approaches in the QC lab – from smaller sample output to more labor-intensive workflows and a higher risk of human error. He then introduced some of the benefits of using automation tools, focusing on Lonza's PyroTec® PRO Robotic Solution for endotoxin testing as an example.

"The biggest advantage of this system is its capacity for high throughput and efficiency," he said. "For us specifically, we were aiming at becoming a 24/7 facility. This system can prep and analyze 42 samples in one shift."

Additionally, Crout highlighted that such systems enable more accurate and precise measurements as well as helping to drive data integrity. The PyroTec® PRO System in particular, he noted, meets all 21 CFR part 11 requirements.

Dr. Gunnar Zoch, Process Automation and Digitalization Manager at Lonza, added to the list of benefits driving companies towards automation (Figure 2). While not exhaustive, his list touched on several critical benefits, including **greater profits, increased attractiveness to employees, improved data integrity**, and an ability to **better absorb company growth** while **protecting against talent shortages**. Dr. Zoch noted that the latter two benefits are particularly important since companies often grow their manufacturing operations while expecting QC teams to accommodate the expansion with few extra resources and little additional space.

For Lonza's *own* QC automation, Dr. Zoch noted, the main drivers were to support its expansion, enable operational continuity in the face of a potential dearth of skilled labor, and optimize data integrity. He also noted that QC was a good place to start the automation journey as QC operations lend themselves exceptionally well to automation. "[QC testing is] labor intensive and repetitive, with a huge number of samples. And there are well established methods which are customer independent," he stated.

Crout then brought discussion from the present state of automation to the future. To him, the situation is clear: **"The future is automation – and more of it!"**

Indeed, Crout noted that automation vendors are already taking steps to improve today's automation tools further. For example, he highlighted how Lonza is optimizing the PyroTec® PRO Solution by adding sample loading ID functionality and enabling LIMS integration.

The Benefits of Broader Digitalization Initiatives

And discussions weren't just restricted to automation of product safety testing assays; a handful of speakers communicated the benefits of broader digitalization in the QC lab. More specifically, experts shared their insights into the **efficiency and data integrity benefits of eliminating paper-based processes,** and noted how such **digitalization is critical to drive automation readiness across the QC landscape.**

The presentation from Rob Lutskus, Director of Digital Operations Technology at Lonza, was not to be missed. Lutskus shared the benefits of digitalization platforms for water for injection (WFI) testing in particular, highlighting how the comprehensive reporting and analytics features

Figure 2.
The benefits of automation in the QC lab.

of some tools can help companies make more informed decisions.

Yolanda Tang, MODA Implementation Analyst at Lonza Singapore, also took us through a powerful case study of how electronic logs can deliver value for high-volume QC labs, noting **potential savings of 15.25 hours per log, a 98% decrease in total time required, and an 86% reduction in the total actions required**.

Moreover, Lonza's Innovation Program Manager Josiah Hosie discussed data integrity considerations in great depth, concluding that the right digitalization tools can help reduce or eliminate common risks and drive greater overall data integrity.

Insights into a Successful Automation Project: Building a Solid Business Case

Many of this year's speakers had already trodden the path to automation, which meant attendees had an opportunity to hear about some real-world experiences, complete with valuable tips and recommendations.

Rachel Gibson's presentation was a standout session. As a QA/QC Scientist at Ethicon (a Johnson & Johnson medical device company), she offered a fascinating overview of how the company selected and justified investment in an automation system for its QC testing.

Ethicon manufactures surgical sutures and wound closure devices, providing 85% of the world's sutures. As part of its QC processes, Ethicon must test extrusion quench tank process water for endotoxins. However, Gibson noted that the company's testing system was no longer supported by

the manufacturer, meaning Ethicon had to rely on costly outsourced testing. Moreover, Ethicon's suture lines were set to double by 2023/2024, further increasing testing demand. Accordingly, Ethicon began looking for alternative options — namely to bring testing in-house and automate the process.

Gibson discussed the entire exploration and decision process: from looking at the limitations of the current system, defining user requirements, and evaluating good-fit options, to calculating the total costs of ownership of competing systems. Most importantly, **Gibson discussed how she built a comprehensive business case to justify capital expenditure**, noting some of the key variables and expenses that teams should consider. When the costs and benefits were mapped out in such a way, Rachel stated that justifying the investment was easy, especially when taking into account Ethicon's expanded testing requirements.

What's more, Gibson also took us through the implementation process, from the validation procedure and qualification process to the test method development and validation.

Key Lessons Learned

With automation projects under their belts, both Gibson and Dr. Zoch were in a prime position to share some valuable learnings. Amongst Gibson's list of tips were to plan ahead and prepare for the unexpected. She stated that "there will always be challenges when running projects like this," from unforeseen findings during test method validation to equipment issues.

> "Semi-automation is not always a compromise, as it can allow you a quick realization of significant savings, for example, in terms of time and money."
>
> **Dr. Gunnar Zoch,**
> Process Automation and Digitalization Manager at Lonza

Dr. Zoch on the other hand, flagged a different set of key considerations. For example, he noted that **user requirement specifications (URS) can make or break a project** – being an important document not just for GMP purposes but also from a project management perspective, too. "Taking care of your URS and ensuring it is a solid piece of documentation, as well as the foundation of your project, makes a lot of sense," he said.

Dr. Zoch then went on to describe why network architecture – both vertical and horizontal – is also key, as well as highlighting the importance of considering semi-automation, given that it can deliver benefits at a fraction of the capital expenditure of full automation.

The Future of Pyrogen Testing is Sustainable and Efficient

The growing demand for pyrogen testing and increasing complexity of new pharmaceutical products show no signs of changing. Moreover, attention to the QC sector's environmental impact only grows by the day. In this light, **it's clear that the future of product safety testing lies in sustainable testing methods and broader adoption of more efficiency-driving automation and digitalization solutions.**

As demonstrated by the many experts at this year's our 2023 Global Endotoxin Testing Summit, **these solutions are already here** – sustainable *in vitro* tests such as the rFC assay and the MAT are accepted by the compendia, backed by a wealth of studies, and are straightforward to implement, and digitalization and automation platforms are now unlocking unprecedented efficiency for high-throughput testing labs across the globe.

Continuing **the journey toward a more efficient and sustainable future, though, will not be easy**. It will demand continued effort and determination from various stakeholders and will depend on deep collaboration. We hope that our Global Endotoxin Testing Summit – with its expert speakers and engaged attendees – will continue to play a key part in this critical effort.

To that end, we'd like to sincerely thank all of those who made the 2023 Global Endotoxin Testing Summit a success – the attendees for their participation and thoughtful questions and comments, our panel of speakers for their expert insights and perspectives, and everyone behind the scenes that ensured the event's smooth planning and execution.

We hope to see you at the next event.

Speakers from the 2023 Global Endotoxin Testing Summit

- Luca Benedan, Consultant, Eurofins Regulatory & Consultancy Services Italy
- Christopher Crout, Senior Scientist, Fresenius Kabi
- Glenn Gauvry, Founder and President, the Ecological Research & Development Group
- Rachel Gibson, QA/QC Scientist, Ethicon
- Josiah Hosie, Innovation Program Manager, Lonza
- Dr. Michael Kracklauer, Manager of Endotoxin Services, Microcoat Biotechnologie GmbH
- Professor Yutaka Kikuchi, Chiba Prefectural University of Health Sciences
- Robert Lutskus, Director of Digital Operations Technology, Lonza
- Dr. Djikolngar Maouyo, President, PyroDex LLC
- Dr. Marijke Molenaar-de Backer, Senior Scientist of MAT Services, Sanquin Diagnostics B.V.
- Dr. Yukari Nakagawa, General Manager, the Pharmaceutical Reference Standards Center, Pharmaceutical and Medical Device Regulatory Science Society of Japan
- Christy Richey, Manufacturing Supervisor, Thermo Fisher Scientific
- Dr. Ingo Spreitzer, Deputy Head of Department, the Paul-Ehrlich-Institut,
- Yolanda Jun Yin Tang, MODA Implementation Analyst, Lonza
- Dr. Xiaoming Wang, Sterility Assurance Subject Matter Expert, Wagner Biotech
- Daniel Winter, BET Department Manager, Gesellschaft für Produktionshygiene und Sterilitätssicherung GmbH
- Dr. Gunnar Zoch, Process Automation & Digitalization Manager, Lonza

Missed the event or would like to re-watch any of the speaker presentations? All of the 2023 Global Endotoxin Testing Summit presentations are **freely available on-demand**.

For more information on **how Lonza can support a smooth transition to more sustainable and efficient pharmaceutical safety testing**, check out bioscience.lonza.com/endotoxin-testing and bioscience.lonza.com/informatics-paper-less-solutions.

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