

# Day 1

Moderator: Dr. Andrew Teasdale, Principal Consultant Nelson Labs

## 9.00 Introduction

### 9.15 Current landscape relating to N-Nitrosamines

This presentation will examine the origin of the N Nitrosamine issue starting with the contamination of Valsartan and the subsequent lessons learnt. The associated evolution of scientific advancement and the overall understanding related to this subject will be discussed.

Next, we'll delve into the evolution of the issue from small molecule N-Nitrosamines seen in Active Pharmaceutical Ingredients (API) to a much more significant challenge of Nitrosamine Drug Substance Related Impurities (NDSRIs). We'll discuss the challenges this brought and the close to catastrophic impact on drug supply.

Finally, the presentation will explore how this situation was averted, while clearly highlighting the significant challenges that remain for both industry and regulators, as well as the key questions that are still to be addressed.

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[Dr. Andrew Teasdale, Principal Consultant Nelson Labs](#)

### 9.45 How conduct a Nitrosamine risk assessment (NARA) - part 1 - API

This presentation will focus on how the process of N-Nitrosamine risk assessment has evolved, with particular emphasis on the risk of N Nitrosamine formation in the API synthesis.

It will examine how through scientific investigation and understanding a systematic process of risk assessment has evolved based on the concept of a N-Nitrosamine 'fire' triangle. This framework explores the interrelationship between the key vectors of amines / nitrosating agents and conditions.

In addition this presentation, will examine the link between the API risk assessment and the subsequent drug product (DP).

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[Dr. Andrew Teasdale, Principal Consultant Nelson Labs](#)

### 10.15 How conduct a Nitrosamine risk assessment (NARA) - part 1 - DP

The discovery of the potential to form NDSRIs had a major impact on the pharmaceutical industry. This presentation will examine how, despite the complexity, a systematic risk assessment process has developed.

Like API it will look at the critical quality attributes and process parameters that are associated with the risk of NSDRI formation. We will delve firstly into methods to address the theoretical hazard and how to assess this, allied to the principle of ICHQ9 to determine actual risk.

Finally, we'll discuss how identified risks may be mitigated from both a CMC and Pre-clinical perspective including the associated practical and regulatory challenges.

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Dr. Andrew Teasdale, Principal Consultant Nelson Labs

## 10.45 Q&A

## 11.00 BREAK

## 11.15 N-Nitrosamines Assessment and Testing : A Pharmaceutical Company Perspective

N-Nitrosamines remain a key pharmaceutical trace impurity challenge. Case studies will be presented for metformin, bisoprolol and praziquantel to demonstrate how different products require different assessment and control strategies. The control strategy for metformin products involves limiting the NMDA precursor DMA, skip testing of NDMA in the finished product and monitoring of excipient nitrite content. In the case of bisoprolol, the current reliance on skip testing of finished product batches is discussed, alongside a proposed transition toward a higher acceptable intake (AI) limit for nitroso bisoprolol supported by quantitative mutagenicity data. For praziquantel, purge assessments enable exclusion of all but one potential nitrosamine, reducing analytical burden. If time permits, examples of cross company research and advocacy initiatives will be presented that are meant to support sound and science-based regulatory decisions.

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Dr. Joerg Schlingemann, Merck-Serono

## 11.45 N-Nitrosamines in Flexible Packaging Materials – a Challenge for Large Volume Parenterals

Nitrosamine impurities are a significant concern in pharmaceutical quality, particularly regarding APIs. However, recent FDA reports identified small-molecule nitrosamines, such as NDBA, in infusion bags, prompting concerns about their formation or migration from packaging components. With strict intake limits of 26.5 ng per day for the most potent nitrosamines, even trace-level contamination can be problematic, especially given that Large Volume Parenterals (LVPs) may have high application

volumes up to 75 L per day. To address this challenge, a validated SPE-LC-MS/MS method was developed to quantify trace nitrosamines in the ng/L range, focusing on LVP products. Further analysis of several plastic materials revealed nitrosamines and distinct “fingerprints” linked to specific materials. These findings emphasize the necessity of including packaging materials in nitrosamine risk assessments for LVPs.

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[Dr. Lukas Jost, Fresenius Medical Care](#)

## **12.15** The Role of Excipients in Nitrosamine Risk Mitigation: Nitrite Control and Scavengers

- Understanding the role of nitrites in excipients and their contribution to nitrosamine formation
- Explore current regulatory frameworks and their implications for pharmaceutical manufacturing
- Review drug formulation strategies for nitrosamine risk mitigation with excipients acting as scavengers for nitrosating agents or pH modifiers

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[Dr. Ulrich Reichert, Merck](#)

## **12.45** Q&A

## **1.00** LUNCH

## **1.45** Risk assessment of Mutagenic Impurities - areas of concern

This presentation will examine the maturity of the ICH M7 guideline, examining the overall risk assessment process.

It will then look to pinpoint the actual areas of concern, in particular the risk posed by mutagenic degradants and the reason why knowledge of degradative pathways is paramount, examining this through the lens of specific case study.

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[Dr. Andrew Teasdale, Principal Consultant Nelson Labs](#)

## **2.15** Automation and AI-Enabled Strategies for N-Nitrosamine Analytical Workflow Design from Development to Commercial

Discover how automation and artificial intelligence are reshaping analytical workflows for N nitrosamine detection in pharmaceutical products. This presentation focuses on reducing analytical risk, enabling phase appropriate methodologies, and

improving efficiency and data quality from late stage risk assessment through to commercial regulatory control. Practical applications of automation and AI illustrate how modern analytical strategies can deliver robust, scalable, and scientifically defensible outcomes.

Key Takeaways:

- Key sources of risk in N nitrosamine analytical workflows and strategies for their mitigation
- Aligning analytical sensitivity and complexity with development phase requirements
- Practical examples of automated sample preparation to improve reproducibility and laboratory efficiency
- Application of machine learning and AI driven optimization to enhance method performance and accelerate development

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Dr. [Giorgio Blom](#), AstraZeneca and Dr. [Mark Harrison](#), AstraZeneca

## 2.45 BREAK

## 3.00 EU PFAS Restriction Update: Implications for Pharmaceutical Immediate Packaging and Drug -Contact Materials

The presentation will give an overview of the regulatory process leading to the EU PFAS restriction proposed by five Member States in January 2023, its timeline, and key milestones. It will present how more than 5,600 industry comments to ECHA's scientific committees, RAC\* and SEAC\*\*, reshaped the substantially revised proposal published in August 2025, leading to expanded use specific derogations and the inclusion of new sectors such as medical applications, sealing systems, and technical textiles, directly affecting the pharmaceutical industry. The final SEAC consultation closing in May 2026 is the last opportunity for industry to provide input to further adjust the restriction proposal, following the RAC final opinion published in March 2026, and ensure it remains proportionate and feasible.

In the second part, the focus will shift to pharmaceutical primary packaging and materials in contact with the drug product, explaining what time unlimited and time limited derogations mean in practice for pharmaceutical applications. It will outline that continued PFAS use under these derogations is expected to be combined with conditions such as emission minimisation measures, waste management and reporting obligations, and a mandatory, ongoing documented search for sustainable alternatives.

\*RAC : Risk-Assessment Committee

\*\*SEAC : Socio-Economic Analysis Committee

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Dr. [Dali Chouchi](#), PFAS-Expert Consultant

### **3.30 A USP Perspective on Testing, Analysis and other Considerations for PFAS Compounds**

Dr. Ravikiran Kaja, United States Pharmacopoeia (USP)

### **4.00 Pharmaceutical-Grade Elastomers: from controlling extractables to managing PFAS**

The suitability of elastomeric components for pharmaceutical applications is closely tied to their formulation design and the control of extractables. This presentation highlights how key formulation elements (base polymers, fillers, crosslinking chemistries, and processing aids) drive extractables profiles and influence compatibility with today's increasingly sensitive drug products. Strategies to minimize both organic and inorganic extractables, and to ensure robust material performance, will be discussed.

In parallel, growing regulatory pressure on per and polyfluoroalkyl substances (PFAS) has raised concerns among customers about the long term availability of PFAS coated components, widely used for their excellent E&L performance. This session will outline the evolving PFAS regulatory landscape and present how Datwyler is evaluating and managing these developments.

Tine Hardeman, Datwyler

### **4.30 LAB VISIT**

# Day 2

Moderator: Dr. Carsten Worsøe, Novo Nordisk

## **8.30** ICH Q3E Step 2 public consulting and beyond

This presentation will outline the key principles which are the foundation of the ICH Q3E Guideline for Extractables and Leachables and discuss the planned path forward for Step 3, covering the transition from public comments on the Step 2 draft to the final implemented Step 4 guideline and associated training materials. In addition, it will highlight some of the major topics raised during the public consultation phase.

One of the major topics concerns the perceived lack of transparency surrounding the “threshold project,” which underpins the safety and qualification thresholds for extractables and leachables (E&L) compounds in the guideline. Ahead of the publication describing the project and derivation of the non-mutagenic qualification thresholds, the presentation provide a deep dive into the background and approach taken for the threshold project, including the chemical space for E&L compounds, the selection and process used to establish permit-ted daily exposures (PDEs) representative of the E&L compounds, and derivation of the non-mutagenic qualification thresholds.

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Dr. Carsten Worsøe, Novo Nordisk, Dr. Patricia Parris, Pfizer

## **9.30** Q&A

## **9.45** What Health Authorities are looking for in E/L submissions: What can be Learned?

Over the past decade, Nelson Labs has supported numerous pharmaceutical companies in qualifying primary packaging systems and disposable manufacturing equipment for global submissions. While the general requirements of regulatory agencies are well known and understood, the lack of specific guidance may lead to additional queries from authorities like the FDA, EMA, and Health Canada. This presentation discusses how understanding these requests helps to define “best practices” for fine-tuning study designs and analytical depth, using real-world examples reviewed against current regulatory expectations.”

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Ing. Kevin Breesch, Nelson Labs

## **10.15 Non-Targeted Analysis (NTA) in Leachable Studies: What Other Relevant Compounds can be found – at trace levels - in the Drug Product when performing Data Mining?**

Organic impurities are critical quality attributes that directly impact the safety and efficacy of drug substances and products. Traditionally, impurity profiling relies on a targeted approach, focusing on known processes to monitor expected degradants or synthesis impurities. While effective for identified risks, this method may overlook unexpected organic impurities present at low concentrations. These impurities can originate from diverse sources, including the API synthesis route, degradation, upstream manufacturing, packaging interactions, and secondary leachables. Additionally, ingredient contaminants—such as impurities or degradants within excipients—further complicate the profile.

Non-Targeted Analysis (NTA) leachable studies offer a powerful tool to establish a broader impurity profile at trace levels. While these studies are typically comparative, evaluating the drug product as a 'stand-alone' sample enables a truly non-targeted screening. By combining targeted and non-targeted approaches, pharmaceutical scientists can bridge gaps in risk-based profiling and detect impurities that otherwise stay 'under the radar.' This broader perspective provides proactive insights into process-related impurities, ingredient quality, and complex chemical interactions, while also serving as a vital troubleshooting tool for unexpected peaks in routine QC testing.

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[Dr.Ir. Philippe Verlinde, Nelson Labs](#)

## **10.45 Q&A**

## **11.00 BREAK**

## **11.15 Investigation of Nitrosamine impurities in parallel with E&L studies**

The recent regulatory spotlight on leachable nitrosamines in infusion bags was no surprise for Nelson Labs. In this presentation, case studies will be presented where Extractables screening of primary and secondary packaging materials assisted in the risk evaluation /assessment for the presence of nitrosamines in the related Drug Products. In addition, inclusion of nitrosamine confirmatory testing in the Leachable study will be discussed.

Nelson Labs also offers Method Development (MD) for small nitrosamines as well as specific N nitrosamine drug substance–related impurities (NDSRIs), to ensure

correct identification and accurate quantification of these impurities. The successful outcome of a MD study depends on several factors, such as the availability blank matrix, selection of appropriate Internal Standard(s), and the evaluation of matrix-matched calibration. These topics will be discussed, as well as strategies when blank matrix is not available.

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[Dr. Ank Reumer and Dr. Ruth Verplaetse, Nelson Labs](#)

## **11.45 Leachables assessment in biopharmaceutical production: from component level qualification to cumulative leachables profiling**

The increasing use of plastic components and systems in biopharmaceutical manufacturing has driven a growing need for robust and scientifically sound leachables assessments. While component level extractables (and leachables) profiling is well established, translating this information into a comprehensive and cumulative understanding of leachables migrating from an actual manufacturing process remains a key challenge.

This presentation describes an approach to leachables assessment in biopharmaceutical production that bridges component level qualification with cumulative leachables profiling across the manufacturing process. Case studies will be presented illustrating both component level and system level leachables profiling, as well as strategies to challenge theoretical evaluations through analytical leachables testing for process equipment related leachables (PERLs).

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[Dr. Koen Smets, Nelson Labs](#)

## **12.15 Reactive leachables – Insights from leachables studies and how to approach them**

Leachable compounds are routinely evaluated with respect to the toxicological risk they pose to the patient. However, their potential impact on the quality, safety and performance of pharmaceutical drug products, particularly protein drug products, is often underestimated. Certain leachables have the potential to chemically react with the active ingredient or with excipients. In protein drug products, such interactions may induce chemical modifications or conformational changes which can lead to a loss of efficiency, decrease of stability and increased immunogenicity in the patient population at risk. A comprehensive assessment of leachables should therefore go beyond toxicological considerations to include their effects on drug product quality and long-term stability.

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[Dr. Sona Kovackova, Nelson Labs](#)

## 12.45 Q&A

## 1.00 LUNCH

### 2.00 **A strategic Approach to Derisking Unidentified Compounds From being Cohort-of-Concern Compounds**

In Non-Targeted Analysis (NTA) for organic extractables using orthogonal chromatographic methods, unidentified reportable compounds often raise concerns regarding potential high-potency toxicity. To address this, a strategic framework was developed to systematically de-risk these compounds as potential Cohort-of-Concern (CoC) substances.

Initially, 12 relevant CoC compound classes for E/L qualifications were identified. For the most frequent and potent CoC compounds, a suspect screening approach was established by integrating analytical data (RT, MS, RRF) from authentic reference standards into the Nelson database.

Other CoC compounds are addressed through NTA screening against commercial libraries such as NIST and WILEY. A detailed evaluation revealed that these libraries contain over 700 CoC compounds, ensuring their identification through mass spectral matching.

While a 100% guarantee is impossible, this framework provides a robust scientific basis for de-risking unidentified compounds.

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[Dr. Dennis Jenke, Nelson Labs](#)

### 2.30 **Dynamic Headspace-GC/MS: Screening for general Impurities and other Potential Applications**

Static headspace GC is a long established method for analyzing volatile analytes, valued for its simplicity and use in routine analyses, such as residual solvent testing and volatile organic compound (VOC) screening in container closure systems and medical devices. Its dependence on equilibrium partitioning, however, limits sensitivity and can hinder trace level impurity detection. Dynamic headspace GC overcomes these limitations by continuously purging and concentrating volatiles, enabling higher sensitivity and broader applicability across complex matrices. This presentation will compare both techniques and highlight where dynamic headspace offers clear advantages. It will also explore additional opportunities where dynamic headspace can extend beyond traditional workflows to support more robust and sensitive impurity screening.

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[Dr. Jan Baeten](#)

### **3.00** Bridging the gap between unidentified leachables and drug impurities: lessons learned from a decade of structural elucidation projects

Leachables studies are typically performed on drug products that have undergone long-term ageing, often for two years or longer. During this period, ageing may not only promote the migration of leachables from the container closure system but also induce degradation of the active pharmaceutical ingredient (API) or excipients. Consequently, drug product-related impurities observed in long-term leachables samples are often similar to those detected in long-term or accelerated stability studies. This makes aged leachables samples a valuable and often underutilized resource for comprehensive impurity profiling of the drug product matrix.

Beyond primary leachables and drug-related impurities, secondary leachables may form through chemical reactions between container-derived leachables and drug product constituents. The structural elucidation of such secondary leachables presents a particular challenge, as these species are typically unique to a specific combination of container closure system and formulation, with no available reference standards or prior literature data. In this presentation, we provide a guided walkthrough of several case studies from structural elucidation projects that ultimately revealed unexpected crossovers between unknown leachables and drug product impurities, highlighting both analytical challenges and practical learnings.

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[Dr. Ward d'Autry, Nelson Labs](#)

### **3.30** Q&A

### **4.00** END OF OPEN HOUSE