Extractables & Leachables

Including: Important Regulatory Updates – Case Study Section: Selection of Toxikons most interesting Case Studies, presented over the last 10 years!

Overview

When making Parenteral Drug Products, pharmaceutical companies are faced with the need to further investigate the materials that will be in contact with the drug product, either during manufacturing, intermediate storage, storage in its final packaging, or during the delivery of the drug to the patient. While historically, the potential safety issues were the main driver in these kinds of investigations, recently, also quality issues – i.e. for biopharmaceuticals – have become an additional concern.

This workshop will look at “Extractables & Leachables” from many different angles: Definitions, Regulatory, Material & Polymer Science, Analytical E/L Methodologies, Safety Assessments, Study Design for different parenteral primary packaging systems, as well as for injection devices.

In addition, during the workshop, a full session will be dedicated to an in-depth update on regulations, standards and recommendations in this field (PQRI, USP, BPOG…).

Learning Objectives

Upon completion of this workshop, you will be able to:

- Explain in detail the current regulatory requirements for container / closure qualification form an E/L perspective.
- Explain the upcoming changes in regulations, standards and recommendations from PQRI, USP and BPOG and how these changes could impact a future evaluation of a pharmaceutical C/C-system.
- Understand the materials of construction – and their composition – of container closure systems, and how they could impact the safety and quality of a parenteral drug product.
- Put together an evaluation program (review of provided documentation, analytical testing) of different types of parenteral drug product container/closure systems.
- Perform a safety/risk assessment of analytical results, obtained after completion of an E/L study.

Who Should Attend

- Pharmaceutical Packaging and Device Engineers
- Production Engineers, using SU systems
- Regulatory Affairs Officers
- Pharmaceutical R & D Managers
- Analytical Chemists, working on E/L
- Quality Assurance Officers

Faculty

Piet Christiaens, PhD, Scientific Director, Toxikon Europe

Dennis Jenke, PhD, Distinguished Scientist, Baxter Healthcare
WORKSHOP AGENDA

Thursday, 22 Sept 2016  9:00 – 18:00 | Friday, 23 Sept 2016  9:00 – 16:30

Introduction on Extractables & Leachables (E/L)
- What is the importance of a good E/L-qualification?
- Historical cases of leachables, impacting the quality or the safety of a drug product
- Regulatory requirements (FDA, EMA…) for primary packaging

Understanding the Materials, Used in the Manufacture of Pharmaceutical Containers & Closures
- Types of polymers – examples in medical/pharmaceutical use
- Understanding the composition of polymers
- The issues with glass in parenteral applications

Analytical Techniques to Perform Extractables & Leachables Research
- The importance of sample preparation: the corner stone in E/L research
- What are the target compounds for material research
- How does a classification of these compounds assist in finding the right analytical technique
- From basic “screening” methodologies to state-of-the-art equipment

How to Set-up Extractables & Leachables Studies
- Selecting the right conditions for extraction
- How to select the right compounds to monitor in a leachable study
- Designing a leachable study

FULL Session on Updates of E/L- Regulations, Standards and Recommendations
- Pharma Packaging:
  - Preview of the final PQRI Parenteral Drug Product (DPD) & ODP Chemistry group
  - Update on the most recent developments on the USP <661> chapters
- (Bio)Pharmaceutical Manufacturing
  - The BPOG protocol
  - Where is USP with the update on the USP <661.3> Plastic Manufacturing Components standard

How to Perform a Safety Evaluation – Risk Assessment on Extractables & Leachables
- Toxicology 101
- EMA Guideline on Genotoxic Impurities
- ICH M7 (DNA reactive Impurities) and it’s suggested staged approach
- The Threshold Concept of PQRI (OINDP and PDP/ODP)
- Examples

Lead Presenter

Piet Christiaens, PhD, Scientific Director, Toxikon Europe
Piet Christiaens received his Ph.D. from the Analytical Chemistry Department of the University of Leuven (Belgium) in 1991. From 1992 to 1997, he was Lab Manager in two Analytical Contract Laboratories. From 1997 to 2000, he worked as an independent consultant with Shell Chemical Company in Houston, Texas where he conducted research on a new hydrogenation catalyst system for Hydrogenated Triblock Co-Polymers (Kraton Polymers). Since 2001, Piet has been Scientific Director at Toxikon Europe where he develops analytical methods and protocols for both extractables and leachables studies for the Medical and Pharmaceutical Industries. He oversees all laboratory operations at Toxikon Europe and is also supports the European business development team.
E/L Testing for a Small Volume Parenterals

▶ Glass Syringes: the issues with tungsten, glue residues and silicone oil and glass metals leaching
▶ The issue with rubbers: the plunger, the needle shield or the tip cap: different approaches needed?
▶ The impact of Secondary Packaging – option or necessity?
▶ Setting up Extractable & Leachable studies for a pre-filled syringe
▶ Primary Packaging for the lyophilized drug product – modus of interaction with the DP

E/L Testing for a Large Volume Parenterals

▶ The challenge in E/L testing for LVP’s.
▶ Primary Packaging for LVP’s: critical materials and components
▶ Secondary Packaging for LVP: critical points to consider

E/L Testing for Disposable and Single-Use Systems in Bioproduction

▶ How to classify the risk of different Single Use Systems in the bioproduction process?
▶ Understanding BPSA & BPOG recommendations, and how they can be implemented in the Study Design
▶ Performing E/L studies on filters: potential approaches

Case Study Section

▶ Case study examples for Primary Packaging: pre-filled syringes, lyophilized drug product containers, Blow-Fill-Seal applications, large volume Parenterals etc.
▶ Case study examples of the impact on Secondary Packaging: labels, printing inks, carton boxes etc.
▶ Case study examples of Single Use Systems: bags, filters, Tubing.

Dennis Jenke, PhD, Distinguished Scientist, Baxter Healthcare

Dennis Jenke is a Baxter Distinguished Scientist at Baxter Healthcare Corporation where he works with a team whose primary responsibility includes the assessment of material/product compatibility, specifically with respect to establishing the suitability for use of packaging systems, manufacturing systems and administration devices for pharmaceutical products (for example, leachables/extractables and product ingredient binding). He has published extensively in the areas of analytical chemistry, environmental science and material/solution compatibility and serves as an expert reviewer for numerous pharmaceutical and analytical journals. He is the author of the book Compatibility of Pharmaceutical Solutions and Contact Materials; Safety Considerations Associated with Extractables and Leachables and a contributing author to the Leachables and Extractables Handbook. Dennis is a member of industry groups whose charter is to establish best demonstrated practices in the area of material/solution compatibility.