



Workshop Agenda

Tuesday, February 22

8:30 am - 8:45 am

Opening Remarks

Reggie Saraceno, Ph.D.

Boehringer Ingelheim Pharmaceuticals, Inc.

8:45 am – 10:00 am

Session I:

Leachables and Extractables Impact to Pharmaceutical Quality Systems

Moderator

Diane M. Paskiet

West Pharmaceutical Services

It is prudent to assess the critical quality attributes of materials in contact with drug product during pharmaceutical development to enable identification and management of risks associated with patient safety. Packaging and process materials have the potential to compromise drug product quality if substances from these components leach into the drug product. Selection of materials that could have an impact on the drug product quality should be guided by an understanding of the chemistry of materials through properly conducted extractable studies and linking that knowledge to patient safety. This session will provide a background on the scientific principles used for the assessment of leachables and consider the strategic aspects of the PODP leachable and extractable Work Plan. Such a discussion will provide a general overview whose details will be enumerated in the forthcoming sessions.

8:45 am - 9:30 am

Regulatory Perspectives on Extractables and Leachables

Prasad Peri

U.S. Food and Drug Administration

9:30 am - 10:00 am

Overview of PODP Objectives, Testing Strategies, and Milestones

Dennis Jenke, Ph.D.

Baxter HealthCare

10:00 am - 10:15 am

Refreshment Break

10:15 am – 12:15 pm

Session II:

Leachables and Extractables Thresholds and Best Practices Strategies and Rationale

Moderator:

Rajendra (Raj) Uppoor, R.Ph., Ph.D.
U.S. Food and Drug Administration

Leachables are those substances which actually migrate from the components and into the drug product, and are generally regarded to be a sub-set of the extractable profile. There are instances where substances initially identified as extractables are either not present as actual leachables in the drug product or, if present, are at levels so low that they represent a negligible risk for patient safety. In order to facilitate the evaluation of leachables in drug products, scientifically justifiable safety thresholds can be developed and applied to the various categories of drug product. The successful execution of such an approach is, however, dependent upon a requisite degree of analytical support. One of the primary factors that dictate the success of a leachables assessment is the analytical investigation and determination of the critical extractables profile for a given material. The level to which extractables have to be discovered, identified, and quantitated should be driven by the knowledge of the materials along with the configuration, type of drug product, and intended use. This session will discuss the relationship between these two mutually-dependent disciplines as applicable to the evaluation of leachables for POPDs.

10:15 am – 10:45 am

[Threshold Establishment and Rationale](#)

Douglas J. Ball, M.S., DABT
Pfizer, Inc.

10:45 am - 11:15 am

[Integration Toxicology/ Chemistry-AET Concept](#)

Daniel L. Norwood, Ph.D.
Boehringer Ingelheim Pharmaceuticals, Inc.

11:15 am - 12:15 pm

[PODP Approach to Acquire Extractable Profile Data](#)
[The Experimental Protocol](#)

Thomas Egert
Boehringer Ingelheim Pharma GmbH & Co. KG

Summary of Results

Christopher T. Houston, Ph.D.
Bausch & Lomb

Best Practice Recommendations

Alan D. Hendricker, Ph.D.
Catalent Pharma Solutions

12:15 pm - 1:15 pm

Lunch & Poster Exhibit

Typical materials that may be used in container closure and delivery systems were evaluated to support the Working Group's Best Demonstrated Practices. Multiple solvents, extraction, and analytical techniques were employed which resulted in a significant amount of extractables data. Posters will display key data for each type of material in order to provide additional background to support the PODP hypothesis.

- [Acknowledgements](#)
- [Experimental Protocol for Qualitative Controlled Extraction Studies on Material Test Articles Representative of Prefilled Syringe \(PFS\) and Small Volume Parenteral \(SVP\) Container Closure Systems: Extraction Methods and Analytical Testing Procedures:](#) Dennis Jenke, Ph.D., Baxter HealthCare
- [Database of Potential Extractables:](#) James F. Castner, Ph.D., Lantheus Medical Imaging
- [Controlled Extraction Study on Polyvinylchloride \(PVC\):](#) Thomas Egert, Boehringer Ingelheim Pharma GmbH & Co.KG
- [Controlled Extraction Study on Rubber:](#) Diane Paskiet, West
- [Controlled Extraction Study on Cyclic Olefin:](#) Daniel Norwood, M.S.P.H., Ph.D., Boehringer Ingelheim
- [Controlled Extraction Study on Polycarbonate:](#) Christopher T. Houston, Ph.D., Bausch & Lomb
- [Controlled Extraction Study on Low Density Polyethylene:](#) Alan D. Hendricker, Ph.D., Catalent Pharma Solutions
- [Toxicology of Leachables and Extractables:](#) Dennis Jenke, Ph.D., Baxter Healthcare

1:15 pm – 4:45 pm

Session III:

Leachables and Extractables Problem Solving Breakouts

Moderator:

Desmond G. Hunt, Ph.D.
U.S. Pharmacopeia

The extractable profile is a cornerstone for the suitability of a container closure or delivery system. The principles of a controlled extraction study when extrapolated to PODP thresholds must consider parameters such as dose, duration, patient population, and other product/user attributes. The selection and evaluation of product contact material is dependent on the risk to patient safety which has unique challenges for the various dosage forms and routes of administration. This is an interactive session that will highlight how best practices and thresholds can be interpreted using scenarios based on data acquired for particular materials and drug products. Extraordinary challenges exist for certain dosage forms and examples will be given for these cases and special considerations will be discussed.

1:15 pm – 2:45 pm

**Qualification of Drug Product Contact Materials used in Large Volume Parenteral (LVP):
Chemistry and Toxicology Considerations**

Alisa Vespa, Ph.D.
Health Canada

Characteristics and Requirements for Large Volume Parenterals (LVPs)

Gregory A. Sacha, R.Ph., Ph.D.
Baxter Pharmaceutical Solutions

**Challenges Associated with the Safety Assessment of Extractables/Leachables in Large
Volume Parenterals (LVPs) and Potential Chemistry Approaches**

Dennis Jenke, Ph.D.
Baxter HealthCare

The Toxicology of LVPs

Jackie A. Kunzler, M.S., DABT
Baxter Healthcare Corporation

2:45 pm - 3:00 pm

Refreshment Break

3:00 pm - 4:45 pm

**Selection and Qualification of a Product Specific Small Volume Parenterals (SVP):
Chemistry and Toxicology Considerations**

Small Volume Parenterals (SVP): Regulatory, Chemistry, and Toxicology Considerations

Desmond G. Hunt, Ph.D.
U.S. Pharmacopeia

Regulatory Aspects:

Frank Holcombe, Jr., Ph.D.

U.S. Food and Drug Administration

Ingrid Markovic

U.S. Food and Drug Administration

Chemistry Considerations

Edward J. Smith, Ph.D.
Packaging Science Resources

Case Study – Toxicological Impact

William P. Beierschmitt, Ph.D., DABT
Pfizer, Inc

4:45 pm - 5:00 pm

Close Day 1 & Wrap Up

Thomas N. Feinberg, Ph.D.
Catalent Pharma Solutions

6:00 pm – 7:00 pm

Reception & Poster Session

February 23, Wednesday

8:30 am – 12:00 pm

Session IV:

Leachables and Extractables Problem Solving Breakouts

Moderator:

Douglas J. Ball, M.S., DABT
Pfizer, Inc.

Continuing from the preceding session, Session IV will focus on two additional dosage forms each of which has its own unique issues and challenges. The discussion on Pre-Fillable Syringe drug products will include a presentation on the principles of Quality-by-Design (QbD), the envisioned but yet to be fully realized paradigm of the future for pharmaceutical development. The following discussion of ophthalmic drug products will consider the long history of extractables/leachables assessment in these unique dosage forms, as well as introduce the issue of high potency drug products and the possible special considerations associated with these.

8:30 am - 10:00 am

**Selection and Qualification of Product Specific Pre-Fillable Syringe Components:
Chemistry and Toxicology Considerations**

Kumudini Nicholas, B.Sc., M.Sc.
Health Canada

Chemistry Considerations for a Pre-Filled Syringe Case Study

Mike Ruberto, Ph.D.
Material Needs Consulting, LLC

Toxicology Assessment for a Prefilled Syringe: Case Study

Stephen A. Barat, Ph.D.
Forest Research Institute

10:00 am - 10:30 am

Refreshment Break

10:30 am - 12:00 pm

Qualification Challenges for Drug Products Administered via Ophthalmic Route of Administration: Chemistry and Toxicology Considerations

Current Regulatory Recommendations for Leachables in Ophthalmic Products

Linda Ng, Ph.D.
U.S. Food and Drug Administration

Considerations for Ophthalmic Drug Products in Semi-Permeable Packaging

Christopher T. Houston Ph.D.
Bausch & Lomb

Ophthalmic Drug Products: A Regulatory Perspective: Current Industry Challenges and Case Studies

Michael P. Lynch, Ph.D.
Pfizer Global Research and Development

Looking Forward: Potential Application of Toxicological Qualification Thresholds

Mary E. Richardson, Ph.D.
Bausch & Lomb

12:00 pm - 1:00 pm

Lunch

1:00 pm - 3:00 pm

Session V:

Summary of Findings from Case Study Break-Outs/Panel Discussion

Moderator:

James F. Castner, Ph.D.
Lantheus Medical Imaging

1:00 pm - 1:45 pm

Significance of Leachables and Extractables to Pharmaceutical Quality

Gordon E. Hansen
Boehringer Ingelheim Pharmaceuticals

1:45 pm - 3:00 pm

Highlights of Day1 and Day 2

Thomas N. Feinberg, Ph.D.
Catalent Pharma Solutions

James F. Castner, Ph.D.

Lantheus Medical Imaging

3:00 pm - 3:15 pm

Refreshment Break

3:15 pm – 4:30 pm

Session VI:

Future Considerations for Leachables and Extractables

Moderator:

Daniel L. Norwood, Ph.D.
Boehringer Ingelheim Pharmaceuticals, Inc.

3:15 pm - 4:00 pm

[Extractables and the USP: Past and Future](#)

Anthony J. DeStefano, Ph.D.
U. S. Pharmacopeia

4:00 pm - 4:30 pm

[PODP Accomplishments and Next Steps](#)

Diane M. Paskiet
West Pharmaceutical Services