APV symposium on protein reactive leachables

09 - 10 October 2024
Mainz, Germany

Course no.: 7008

Quality Control/Analytic

Target group

This symposium is aimed at pharma professionals and representatives of medical agencies interested in extractables and leachables and wanting to exchange on protein reactive leachables and their possible impact. Apart from an introduction into the topic of protein-reactivity , we want to start a discussion and build a network of professionals working in this field.

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Objectives

The guidelines and best practice guides published to date give a solid understanding of how an extraction study is set up, what analytical techniques are expected and how to handle findings from an extraction study with regard to a follow-up leachable study. The guidelines view on extractables and leachable is very much through the lens of a toxicologist, evaluating substances migrating from single-use and primary packaging materials for their toxicological potential. However, this concept overlooks what these substances may be doing to the drug substance itself. Any compound interacting with a therapeutic protein by covalent or non-covalent means, may cause the protein to directly lose its therapeutic function or cause it to be immunogenic, leading to the formation of antibodies and worst-case to neutralizing antibodies. The last case is particularly devastating when the therapeutic protein is administered as a replacement therapy, like e.g. erythropoietin (EPO). In this specific case a patient would lose it´s capacity to produce erythrocytes becoming dependent on frequent blood transfusions. As it is difficult to predict what structures may be immunogenic and at which concentration, the evaluation of protein-reactivity should be part of the overall extractable and leachable risk assessment strategy.

This symposium will give a brief insight into the regulatory extractable and leachable landscape to build a common ground for participants of all levels. We will discuss the possible risks of protein-reactive extractables and leachables in the context of immunogenicity and the impact on patient safety. Then we will explore different analytical approaches to identify protein-reactive compounds using model substances during extraction studies and how to analyze full-length proteins in product formulation. How in silico and paper-based approaches may be used to assess the risk of protein reactive leachables. Different case studies will be presented to give a real-life insight into possible risks and how they may be mitigated. The presentation session will close with an outlook into the possible future regulatory landscape and how take influence. The symposium will close out with a panel discussion in which all participants are invited to give their view on the current field of protein-reactive extractables and leachables, ask questions and generally build a network of experts.

Course leader

Nick Morley
Element Materials Technology

Nick is a Principal Scientist at Element Materials Technology with over 16 years of experience in the field of extractables and leachables across a range of therapeutic areas and industries. He sits on several British Standards Institute committees as an E&L expert.

Alicja Sobantka
Octapharma

Alicja is currently employed at the Octapharma, where she is responsible for material qualification at corporate level including chemical safety assessment of polymeric processing, packaging, and administration materials and the planning and supervision of extractables and leachables studies.

Steven Watt
A&M STABTEST

In his current position as a business development manager at A&M STABTEST he is involved in customer relations, marketing and the development of new analytical services in the field of pharmaceutical analysis. He is also the project head of the bioassay group, dealing with ELISA and cell-based assays to assess potency and process-related impurities.

Programme

Wednesday, 09. October 2024 14:00 - 18:00 h

Welcome and introduction
Nick Morley, Element Materials Technology; Alicja Sobantka, Octapharma and Steven Watt, A&M STABTEST

Session 1: Introduction to E&L and Protein Reactivity

E&L Essentials: An Introduction to Extractables and Leachables
- Associated Risks: Patient Safety, Product Quality/Efficacy
- Risks Management
- Extractable & Leachable Study Design Considerations
- Regulatory Landscape

Nick Morley, Element Materials Technology

Protein-Reactive Leachables and their potential risk to patient safety
- Definition: Cytotoxicity versus protein reactivity, immunomodulating Evaluation of risks toxicity versus immunogenicity
- Introduction to chemical reactivity incl. theory, potential sources, types of chemical reactions & mechanisms
- High vs. low risk products (Small molecule APIs, Peptides, Oligos, Proteins, Cells/RNA/Gene therapy)
- Effect on drug products incl. historic fail cases / examples (Eprex, Silicone Oil, Tugsten, bDtBPP)
- Regulatory experience (Octapharma regularly experiences questions, particularly from PEI (GER) and EU countries): efficacy (unlikely under physiological conditions) + immunogenicity; no threshold value for immunogenicity! Steven adds info on immune system.

Steven Watt, A&M STABTEST

Sesssion 2: Protein reactive E&L risk management process

Overview & analytical tools
- Routine and release tests commonly used for biopharmaceuticals
- Tests potentially indicative for issues
- Possibilities of extending present tests for monitoring reactive E&L

TBA, A&M STABTEST

In silico assessment of biomolecule reactivity with leachables
- In silico methods can be used to predict the potential interaction of leachables with biomolecules (protein/ DNA based active pharmaceutical ingredients)
- The prevalence of predicted reactive leachables is assessed in a database of E&Ls
- A consensus approach for screening E&L reactivity is shown to be fit for purpose when benchmarked against experimentally determined reactivity values
- A workflow which includes rapid in silico screening followed by an analysis of risk is discussed

Arianna Bassan, Instern

Assessing the risk of leachables interacting with therapeutic proteins
Assessing the risk of leachables interacting with therapeutic proteins
- Despite reactivity alerts, the underlying mechanisms may not necessarily occur in the drug product
- The nature of the protein, its environment and the amount of the reactive leachable need to be considered
- Examples are shown

Alicja Sobantka, Octapharma

Networking dinner

Thursday, 10. October 2024 09:00 - 14:00 h

Session 3: Case studies

Case study I: Artificial exposure of blood coagulation factor IX to form- and acetaldehyde and N-(3-(Dimethylamino)propyl)methacrylamide
- ormaldehyde covalently bound to lysine in two different peptides and the clotting activity dropped by more than half at a formaldehyde concentration of 500 µg/mL
- Acetaldehyde caused a drop in clotting activity starting at a concentration of 50 µg/mL
- (Dimethylamino)propyl)methacrylamide did not impair the activity of the FIX

TBA, Octapharma

Case study II: TBA
TBA, Novo Nordisk

Session 4: Future Outlook & Panel Discussion

Outlook – What can we expect in the protein-reactive leachables landscape in the months to come
- Publication of process
- Regulatory interest: Do health authorities know what they are asking / looking for? Where might regulation go in this field?
- Future methods of identification (how might this be addressed by companies)
- Good time to influence now: Proposal for regulation (ICH Q3E)

Steven Watt, A&M STABTEST and Nick Morley, Element Materials Technology

Panel discussion and Q&A

Closing remarks

Registration by email apv@apv-mainz.de

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Location

InterCity Hotel Mainz
Binger Straße 21
55131 Mainz
Telefon: 0049 6131 58851 0
E-Mail: mainz@intercityhotel.com
WEb : intercityhotel.com

Date

Course no.: 7008
from 09 October 2024 14:00 h
to 10 October 2024 14:00 h

Registration fee

Industry	1490	EUR
Authority/University	745	EUR
Students*	250	EUR

(free of VAT according to § 4,22 UStG)
Coffee breaks, luncheons, dinner and electronic proceedings included.

* Limited places for full time students available; written evidence must be submitted.

Registration

APV-Geschäftsstelle
Kurfürstenstraße 59
55118 Mainz/Germany
Phone: 0049 6131 97 69 0
E-mail: apv@apv-mainz.de
Web: www.apv-mainz.de

You will receive a confirmation of your registration with the invoice.

Hotel reservation

InterCity Hotel Mainz
Binger Straße 21
55131 Mainz
Telefon: 0049 6131 58851 0
E-Mail: mainz@intercityhotel.com
WEb : intercityhotel.com

We have blocked a contingent on the special rate of **104.00 € incl. breakfast and VAT.** The rates are available until 11 September 2024.
Reservation code:
„APV 09.-10.10.2024“

APV symposium on protein reactive leachables, 09-10 October 2024, Mainz, Germany, Course no. 7008

Registration
As soon as you have found a seminar of your interest, it is very easy to register for it via e-mail or online. We will process your registration promptly and certainly are available for any questions that may arise.

Registration confirmation
After your registration was successfully processed, you will receive a confirmation.

Before the event
A few days before the event starts, you will receive important information about the seminar, such as time, date, addresses etc.

After the event
You will receive a certificate confirming your participation. Furthermore, we would like to ask you to fill-in our evaluation sheet to make sure we get better every time.

Follow-up
After the event, we are open to receive any suggestions and critique that might arise during the seminar and will certainly help you with further questions you may have.

Declaration of consent in respect of data protection

☐ By registering for this seminar, I agree that the APV uses my data for the purpose of processing the order and provides me with all relevant information.

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