ECA Academy
Your GMP/GDP Information Source

GMP Certification Programme
Certified Quality Control Manager

Speakers

Dr Raphael Bar
BR Consulting, formerly with Teva, Israel

Dr Helmut Buschmann
AiCuris, Germany and RD&C, Vienna

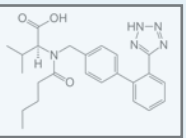
Dr Norbert Handler
RD&C, Vienna

Stability by Design

- Stability testing in product design and method development
- Focus mainly on small-molecule APIs and drug products

28/29 April 2021 | Vienna, Austria

Including Nitrosamine Impurities



Highlights

- Forced degradation studies in the pharmaceutical industry
- Overview and regulatory view
- Common degradation reactions
- How to perform your own forced degradation study
- Thermal Stress studies to support shipping/distribution
- Reactions and forced degradations in solid state – innovative approach
- How to perform a successful and compliant nitrosamine risk assessment (including API, excipients, drug product, packaging, transport, etc.)

Includes workshop and case studies on interaction and incompatibilities, forced degradations and photostability.

Forced Degradations for development of stability-indicating methods and Stress Testing for prediction of stability of formulations and shipped finished pharmaceuticals

Objective

Forced degradations are the basis for development of analytical methods, for drug formulation development, for understanding the degradation mechanisms and for predicting the stability behavior of active ingredient and drug product. Stress testing is the basis for predicting the stability behavior during storage, shipping and distribution of active ingredient and marketed drug product. Both forced degradation and stress testing are regulatory requirements.

Background

After an overview of the basic chemistry of the common degradation reactions, this course will teach you how they are practiced in the pharmaceutical industry, and how you can carry them out on your own, while ensuring that all degradation products are chromatographically detected and subjected to a mass balance.

Among the topics to be discussed will be:

- An overview of the basic chemistry of the degradation reactions
- Common practices of forced degradations in the pharmaceutical industry
- Practical aspects in carrying out forced degradation studies
- Photodegradation of active substance and drug product
- How to ensure that all degradation products are detected
- Peak purity by LC-UV
- Set up a mass balance in degraded samples with guided exercises (A hand-held calculator is required!)
- Comparing degradation rates to estimate impact of a process change on the drug quality
- Performing stability studies to support shipping/distribution of medicines
- Investigating an excursion from a label storage conditions
- Requirements, guidelines and risk assessment related to nitrosamine contamination

Target Audience

Personnel from the following departments will highly benefit from this course:

- Stability Personnel
- Analytical R&D
- Quality Control Formulation Development
- Quality Assurance and RA
- CROs offering analytical services
- Qualified Persons (QP)

Moderator

Dr Raphael Bar

Programme

What is Stress Testing and what are Forced Degradations – Regulatory View

- Regulations (ICH, EU and USFDA)
- Chemical stress of drug substance and product
- Physical stress of excipients and active pharmaceutical ingredient
- Is a forced degradation study a GMP study?
- Purposes of stress testing:
  a. development of stability-indicating methods
  b. optimization of a formulation (API-Excipients compatibility study)
  c. Prediction of stability behavior (accelerated testing of pharmaceuticals)
  d. Evaluation of temperature excursions during shipment/distribution

Common Degradation Reactions of APIs and Excipients

- Reactivity of common chemical functional groups
- Major mechanisms of chemical degradation
- Hydrolysis (alkaline, acidic)
- Oxidation (Autoxidation, peroxide and metal-mediated)
- Photolysis
- Case studies for APIs and excipients

Impurities and Degradation Products resulting from reactive APIs, Excipients and their Impurities

- Reactivity of common chemical functional groups
- Major mechanisms of chemical degradation
- Hydrolysis (alkaline, acidic)
- Oxidation (Autoxidation, peroxide and metal-mediated)
- Photolysis
- Case studies for excipients

Reactions and Forced Degradations in Solid State – Innovative Approach

- Differences liquid phase – solid state
- Reactions and degradation in solid state
- Kinetics
- Alternative approach to mimic and predict solid state degradation

Forced Degradation Studies in the Pharmaceutical Industry

- Common practices of forced degradations
- Examples of forced degradations studies
- Is there a general methodology for chemical stress?

How to Perform your own Forced Degradation Study with:

- Heat (with and w/o humidity)
- Acid and base
- Oxidation
- Mechanical stress factors (e.g. grinding, milling ...)

Photodegradation

- Essential terms of light irradiation
- Light chambers: Options 1 and 2 according to ICH
- Irradiation of drug substance and drug product samples
- Sequential versus simultaneous irradiation of UV and visible light

Mass Balance in Degraded Samples of Pharmaceuticals

- Definition and equations for mass balance
- Determination from chromatographic analysis of degraded samples
- Correction of mass balance for response factor
- Correction of mass balance for molecular weights
- Exercises of mass balance calculations

How to Ensure Chromatographic Detection of all Degradation Products

- Ensuring chromatographic elution of all degradation products (Gradient mode, varying mobile phase solvents; various modes of chromatography)
- Detecting all degradation products (LC-PDA, LC-MS, universal detector)
- Techniques to confirm undetected degradation products (Flow injection analysis, UV spectrophotometric analysis)
- Determining peak purity by LC-PDA (spectral and matching homogeneity)

Comparative Accelerated Degradation Rates

- A quality control tool of pharmaceutical products - monitoring process changes
- A development tool for optimizing drug formulations- Excipients - API compatibility studies

World Climatic Zones for Drug Stability Storage

- Mean Kinetic Temperature (MKT) and relative humidity
- Interpretation of MKT
- Temperature profile of a shipment of medicines
- Global climatic zones by ICH and WHO

Thermal Stress Studies to Support Shipping/ Distribution

- Studies at elevated extreme temperatures
- Studies at low extreme conditions
- When, how and what?
- Cyclic studies to support shipping/distribution

Excursions from storage label conditions

- Excursions and Time-out-of-Storage during shipping/ distribution
- Understanding the evaluation of the impact of temperature excursion on shelf-life
- What stability data are required to investigate temperature excursions
- Estimation of a maximal “Time-out-of-Storage” of a pharmaceutical

Nitrosamines

- Latest requirements and guidelines from EDQM and EMA
- Scientific and chemical background
- How to perform a successful and compliant nitrosamine risk assessment (including API, excipients, drug product, packaging, transport, etc.)
- Case Studies

WORKSHOPS

- Photostability of a drug product under manufacturing conditions
- Workshop on Forced Degradations
- Workshop with case studies for interaction and incompatibilities

Note: In order to fully benefit from the workshops, attendees should preferably bring a hand-held calculator.

Speakers

Dr Raphael Bar, BR Consulting, Israel

Dr Bar headed the Analytical R&D Laboratories at Teva Pharmaceuticals and the analytical QC laboratory at Pharmos. He served in the Scientific Advisory Board of global PDA (USA) and is presently a board member of Israel PDA Chapter as well as a member of the organizing committee of the Israel Society for Analytical Chemistry. For the lasts ten years, Raphael Bar has been a pharmaceutical consultant for the Pharma and bio-Pharma industries.

Dr Helmut Buschmann, AiCuris, Germany and RD&C, Austria

Dr Buschmann is a senior management executive with over 20 years of international experience in drug discovery research and drug development in the Pharmaceutical/Biotechnology sector. Currently, he is “Head of Chemistry, Pharmaceutical Development and Patent Affairs” at AiCuris in Germany. Together with Norbert Handler he founded RD&C Research, Development & Consulting GmbH in Vienna in 2014, where he is involved in several projects.

Dr Norbert Handler, RD&C, Austria

Together with Helmut Buschmann he founded RD&C Research, Development & Consulting GmbH in Vienna in 2014, where he currently holds the position of a managing partner. He is involved in several projects ranging from drug discovery and development, regulatory affairs, IP management to impurity profiling. He is acknowledged as consulting engineer in Austria and appointed as general authorized and certified expert for pharmaceutical chemistry at the trade court in Vienna.

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GERMANY

Reservation Form (Please complete in full)

Stability by Design, 28/29 April 2021, Vienna, Austria

Title, first name, surname

Department | Company

Important: Please indicate your company's VAT ID Number | Purchase Order Number, if applicable

City | ZIP Code | Country

Phone / Fax

E-Mail (Please fill in)

General terms and conditions
If you cannot attend the conference you have two options:
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- Cancellation until 1 weeks prior to the conference 50 %
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Date
Wednesday, 28 April 2021, 9.00 h - approx. 18.00 h
(Registration and coffee 8.30 h - 9.00 h)
Thursday, 29 April 2021, 8.30 h - 16.00 h

Venue
Radisson Blu Park Royal Palace Hotel, Vienna
Schlossallee 8
1140 Vienna, Austria
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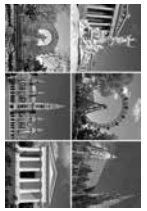
Fees (per delegate, plus VAT)
ECA Members € 1,590
APIC Members € 1,690
Non-ECA Members € 1,790
EU GMP Inspectorates € 895
The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on the first day, lunch on both days and all refreshments. VAT is reclaimable.

Accommodation
CONCEPT HEIDELBERG has reserved a limited number of rooms in the conference hotel. You will receive a room reservation form/POG when you have registered for the course. Reservation should be made directly with the hotel. Early reservation is recommended.

Registration
Via the attached reservation form, by e-mail or by fax message. Or you register online at www.gmp-compliance.org.

Social Event

In the evening of the first course day, you are cordially invited to a social event. This is an excellent opportunity to share your experiences with colleagues from other companies in a relaxed atmosphere.

Conference language
The official conference language will be English.

Organisation and Contact
ECA has entrusted Concept Heidelberg with the organisation of this event.
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