ECA Academy
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GMP Certification Programme
Certified Validation Manager

Speakers

Dr Raphael Bar
BR Consulting, Israel

Dr Raluca Ilinca Schmitt
Bayer, Germany

Understanding Design of Experiments (DoE) in the Pharmaceutical Industry

12/13 October 2021 | Heidelberg, Germany

Development and robustness of a pharmaceutical process and analytical procedure

Highlights

- DoE by Hand Calculations: Effects and Interactions
- Acquaintance with Minitab
- Basic Statistical tools for Interpretation of DoE Output
- Are the Factors Significant?
- Full Factorial DoE Experiments with Minitab
- Screening Design Experiments with Minitab
- Optimisation with Response Surface Methodology
- Case Study DoE: Development of a Medicinal Product
- Strategy of DoE in Drug Development Process

Inclusive practicing calculations with Minitab

Objective

This course will explain the basics of DoE with practicing with factorial and fractional DoE as well as DoE by RSM If you have no or little previous knowledge with DoE, you will learn how to set up an experimental design and how to explore the effect of factors that influence either a development/production process or an analytical procedure while taking into account interactions between the factors.

To better understand and assimilate the DoE principles, you will learn first to calculate the main effects and factors interactions by simple manual calculations (with Excel). Then, you will learn how to use Minitab software program to create a variety of DoE designs, analyze and interpret them. Multiple exercises and examples from pharmaceutical development and laboratory analysis such as robustness studies will be solved by the participants. The participants will learn how to interpret the output of a DoE programme.

Background

With FDA´s Process Validation Guidance for Industry from 2011 and the Annex 15 Revision 2015 process validation has changed to a life cycle. And the life cycle starts with the development which delivers process knowledge and the critical process parameters. To get there the FDA mentions „Design of Experiments" (DoE). Therefore, DoE is a tool for implementing the process validation life cycle.

Also, ICH Guidelines Q8 (Pharmaceutical Development) and ICH Q9 (Quality Risk Management) speak about DoE as a tool, also in relation to Quality by Design (QbD= approaches).

Meanwhile, DoE is also common practice in other pharmaceutical areas, i.e. in the analytical development or as a CAPA measure for process optimisation.

Target Audience

The addressees of the event are employees from the development, quality control lab and quality assurance departments who are using DoE or wanted to use DoE in the future. We address also GMP auditors and inspectors and validation personnel also involved in DoE.

Moderator

Dr Raphael Bar, BR Consulting, Israel

Each participant should bring a laptop with Excel and a previously downloaded 30 day free-trial Minitab 19 program from http://www.minitab.com. This program should be downloaded on a laptop a few days before the beginning date of the course and verified that it works on the laptop.

Programme

Introduction

- DoE and Quality by Design
- Regulations (EU and FDA)
- A factorial experiment
- DoE vs one-at-a-time experiment
- Where is DoE applied in development and validation of analytical methods
- Where is DoE applied in manufacturing process development and validation

DoE by Hand Calculations: Effects and Interactions

- Factorial experiments (categorical and numeric factors)
- Two and three factorial designs
- Manual calculation of main effects
- Manual calculation of interactions
- What is an orthogonal DoE
- **Exercises with Excel**

Acquaintance with Minitab

- Basic structure of Minitab software
- Input of data
- Running a DoE
- Plotting output results
- **Practicing with Minitab**

Basic Statistical tools for Interpretation of DoE Output

- F-Test
- t-Test
- p-value
- ANOVA
- Diagnostics for goodness of fit to model
- **Exercises with Excel**

Are the Factors Significant?

- Deviations from normality plot
- Making replicate experiments
- Adding experiments at centre points
- Using known variability
- **Exercises with Excel**

Full Factorial DoE Experiments with Minitab

- Two factor full DoE experiments
- Interactions between two factors
- Plotting Main effects and Interactions
- Interpretation of DoE Minitab output
- Does the linear fit the model?
- Significance with p values
- General full factorial DoE
- **Exercises with Excel**
- **Exercises in interpretation of Minitab outputs**

Screening Design Experiments with Minitab

- Two and three factor experiments with Minitab
- Aliasing in DoE experiments
- Resolution of DoE experiments
- 4-7 fractional factorial DoE
- Blackett-Burmann designs
- Definitive screening design
- **Exercises with Minitab:**
  - **Robustness of HPLC method with fractional DoE**
  - **Optimisation of a process with fractional DoE**

Optimisation with Response Surface Methodology

- 22 factorial experiments with RSM
- Contour plot
- Surface plot
- Concept of Design Space
- **Exercises: optimization of drug solubility with RSM design**
- **Effect of process parameters on dissolution assay and variability**

Case Study DoE: Development of a Medicinal Product

- Why we use DoE in the pharmaceutical development?
- Example: DoE for formulation selection / optimization
- Example: DoE for manufacturing process optimization
- DoE vs "traditional" approach – when to use which?

Strategy of DoE in Drug Development Process

- Screening experiments
- Fractional experiments
- Full factorial experiments
- Optimisation experiments: Surface Response Methodology
- Design Space versus Proven Operating Range (PAR)
- Normal Operating Range (NOR)
- Robustness of experiments of a process/method

Speakers

Dr Raphael Bar
BR Consulting, Israel

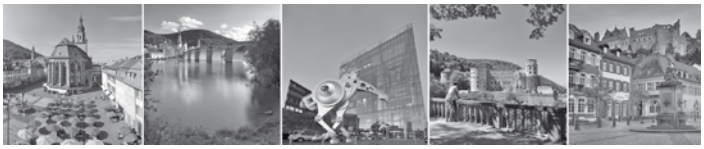
Dr Bar headed the Analytical R&D Laboratories at Teva Pharmaceuticals and subsequently the analytical QC Laboratory at Pharmos. For the last twelve years, Raphael Bar has been a pharmaceutical consultant for the Pharma and Bio-Pharma industries. His interests encompass also statistical evaluation of laboratory data.

Dr Raluca Ilinca Schmitt
Bayer, Germany
Senior Expert Statistician

Raluca Ilinca Schmitt earned a Degree in Mathematics and in Statistics and received a doctoral degree in Statistics. She worked as a lead biostatistician at Genzyme and Bayer. Since 2014 she is an expert statistician for the chemical and pharmaceutical development within the department Process Understanding and Intensification. The daily business focus lies on DOE in the QbD frame and multivariate statistical analysis.

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.



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Reservation Form (Please complete in full)

Understanding Design of Experiments (DoE) in the Pharmaceutical Industry
12/13 October 2021, Heidelberg, Germany

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

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Date
Tuesday, 12 October 2021, 09.00 – 17.45 h
(Registration and coffee, 08.30 – 09.00 h)
Wednesday, 13 October 2021, 08.30 – 17.00 h

Venue
Qube Hotel Bahnstadt
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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.

Conference language
The official conference language will be English.

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