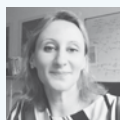


Speakers



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

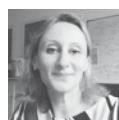
- Screening experiments
- Fractional experiments
- Full factorial experiments
- Optimisation experiments: Surface Response Methodology
- Design Space versus Proven Operating Range (PAR)
- Normal Operating Range (NOR)
- Robustness of experiments of a process/method

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.

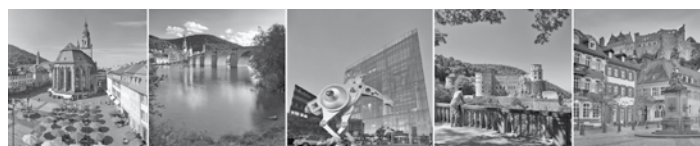


Dr Raluca Ilinca Schmitt
Bayer, Germany
Senior Expert Statistician

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.



Heidelberg – Optimal Accessibility via Frankfurt

As one of the most beautiful cities in Europe, Heidelberg is at first sight an interesting venue – but is it also easily accessible? The answer is: Yes! The connection to Frankfurt Airport is convenient and fast. Next to London, Frankfurt Airport offers the most frequent air connections in Europe. It takes only about 45 minutes to get from Frankfurt to Heidelberg.

TLS:

<https://www.tls-heidelberg.de/en/>

Lufthansa Airport Shuttle:

<https://frankfurt-airport-shuttles.palasis.com/?locale=en>

HLS:

<http://www.hls-online.com/PCS-Flughafentransfer.html>

Train: You can also take a train to get from/to the airport, which takes less than one hour.

<https://www.bahn.com/en/view/index.shtml>

If the bill-to-address deviates from the specifications on the right, please fill out here:

Reservation Form (Please complete in full)

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

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

Phone / Fax

E-Mail (Please fill in)

CONCEPT HEIDELBERG

P.O. Box 101764

Fax +49 (0) 62 21/84 44 34

D-69007 Heidelberg

GERMANY

General terms and conditions

If you cannot attend the conference you have two options:

1. We are happy to welcome a substitute colleague at any time.

2. If you have to cancel entirely we must charge the following processing fees:

- Cancellation until 2 weeks prior to the conference 10%.

- Cancellation until 1 week prior to the conference 50%.

- Cancellation within 1 week prior to the conference 100%.

CONCEPT HEIDELBERG reserves the right to change the materials, instructors,

or speakers without notice or to cancel an event.

If the event must be cancelled, registrants will be notified as soon as possible

and will receive a full refund of fees paid. CONCEPT HEIDELBERG will not be re-

sponsible for discount airfare penalties or other costs incurred due to a cancel-

lation.

Terms of payment: Payable without deductions within 10 days after receipt of

invoice.

Important: This is a binding registration and above fees are due in case of can-

cellation or non-appearance. If you cannot take part, you have to inform us in

writing. The cancellation fee will then be calculated according to the point of

time at which we receive your message.

In case you do not appear at the event without having informed us, you will have

to pay the full registration fee, even if you have not made the payment yet. Only

after we have received your payment, you are entitled to participate in the con-

ference (receipt of payment will not be confirmed!) (As of January 2012).

German law shall apply. Court of jurisdiction is Heidelberg.

Privacy Policy: By registering for this event, I accept the processing of my Personal Data. Concept Heidelberg will use my data for the processing of this order, for which I hereby declare to agree that my personal data is stored and processed. Concept Heidelberg will only send me information in relation with this order or similar ones. My personal data will not be disclosed to third parties (see also the privacy policy at http://www.gmp-compliance.org/eca_privacy.html). I note that I can ask for the modification, correction or deletion of my data at any time via the contact form on this website.

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

Grüne Meile 21

69115 Heidelberg, Germany

Phone +49(0) 6221 / 18 799-0

Email bahnstadt@qube-heidelberg.de

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.

GMP/GDP Certification Scheme

Building on your education the ECA GMP/GDP certification programmes provide you with the appropriate supplement to acquire this qualification. Simply choose any three courses within the programme according to your professional interest. Your certificate is then valid for two years. To renew it, you can pick any training from the ECA courses and conferences list within that two-years period – allowing you to broaden your knowledge in GMP and GDP compliance.

Organisation and Contact

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

CONCEPT HEIDELBERG

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pommeranz@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation, etc. please contact:

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schopka@concept-heidelberg.de.