ECA Academy
Your GMP/GDP Information Source

GMP Certification Programme
Certified Quality Control Manager

## Speakers

Dr Raphael Bar
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# EU GMP-/FDA-compliant Sampling

## Live Online Training on 07/08 May 2024

*EU GMP-/FDA-compliant Sampling Plans with Efficient Procedures and Reduced Sampling*

## Highlights

- Regulatory and compendial requirements
- Statistical sampling
- Sampling plans
- Classification of nonconformities and allocating AQL to classes
- Risks in sampling
- Sampling and inspection of packaging materials
- Sampling of powders (APIs and excipients)
- Tools for sampling
- Sampling according to the WHO
- √N rule: its uses and misuses
- Reduced sampling and reduced testing, Skip-Lot testing
- Reference/retention samples
- Charting and trending nonconformities and nonconforming items
- Practical examples/exercises
- Video demonstration of sampling activities
- Q&A sessions

## Objective

The aim of this Live Online Training is to discuss the process of the statistical sampling of

- finished drug products
- packaging materials (primary and secondary)
- medical devices
- starting materials (APIs and excipients)

and to define the prerequisites for implementing a system for reduced sampling and reduced testing for these products.
This course is also intended to give a practical training on the use of the most common sampling standards: ISO 2859-1:1999 and ANSI/ASQ Z1.4. Starting with regulatory and compendial requirements around sampling, this course will also address

- charting and trending nonconformities and nonconforming items
- good quality practice around sampling plans
- reference and retention samples

Participants will learn how to read and to use the standards for selecting a sampling plan with an understanding of the associated producer and consumer risks.
Practical examples and exercises (including polling questions) and Q&A sessions on both days ensure interaction and that all questions are answered.

## Background

Sampling of materials is one of the most important processes in pharmaceutical companies. Accordingly, its importance in international guidelines is also high.

Sampling by attributes is a process of inspecting a representative sample of identical product units of product for presence or absence of nonconforming units or nonconformities before accepting or rejecting the whole lot of product. Regulatory agencies require a sampling plan that utilizes basic elements of statistical analysis or provide a scientific rationale for taking a representative sample according to the lot size. In the light of these regulatory requirements, one may wonder whether the √N rule is a statistically valid sampling plan.

According to chapter 6 of the EU GMP Guidelines, the sampling plan used should be appropriately justified and based on a risk management approach.
Representative samples should be taken and recorded in accordance with approved written procedures.

FDA requires as well in the Code of Federal Regulations (21 CFR Part 211.84), that sampling should be done upon statistical criteria.

In the past the Military Standard 105 D was commonly used in the pharmaceutical industry, but this standard has been withdrawn and is now obsolete. Today either the ISO Standard 2859:1-1999 or the ANSI Z1.4 are applied. These standards are widely employed in various types of industries which are required by regulatory authorities to follow a statistically sound sampling plan.

## Target Audience

This GMP Education Course is directed at all those employees from quality control units and production units in the pharmaceutical industry who are competent or responsible for sampling, testing and release of starting materials (APIs and excipients), packaging materials (primary and secondary) as well as finished pharmaceutical products. This course is also of interest to personnel from quality assurance and to those employees from API, excipient or packaging material suppliers who want to inform themselves about the requirements of the pharmaceutical industry on the testing of these materials.

The course does not require prior knowledge in sampling and statistics.

## Programme

### Regulatory and Compendial Requirements around Sampling

- Principles of sampling plans
- Regulations: US GMPs, EU GMPs, WHO
- What types of sampling plans are used for products/ materials?

### Statistical Sampling and Withdrawing a Sample

- Sampling Attributes vs. sampling by variables
- Nonconforming items and nonconformities
- 100% Inspection vs. Acceptance Sampling
- Statistical Sampling error
- Withdrawing a sample
- Random and stratified sampling
- Generating a random number with Excel

### Acceptance Sampling Plans in ISO-2859-1/ANSI Z1.4

- How is the standard structured?
- How to use the single and double sampling plan + explanation of examples
- Switching rules between Normal-Tightened-Reduced inspections Structure of the Standards

### Classification of Nonconformities and allocating AQL to Classes

- Classification schemes
- Classification of nonconforming items (Class A, B, C...)
- Classification of nonconformities (Class A, B, C...)
- Examples of nonconformities in pharmaceutical preparations (Ooptional)
- Allocating AQL to various classes

## Practical Examples/Exercises: Step-by-step Use of ISO-2859-1/ANSI Z1.4

- Practical examples for a single- and double-sampling plan (exercises)
- Practical examples for use of the switching rules
- Exercise in using tables of sampling of ISO-2859-1

## Producer and Consumer Risks in Sampling with ISO-2859-1

- Ideal OC curve
- Risk of rejecting a good lot (alpha risk)
- Risk of accepting a bad lot (beta risk)
- Determining sampling risks in ISO 2859-1

## Exercises with Producer and Consumer Risks in Sampling with ISO-2859-1

- Acquaintance with risk tables of ISO 2859-1
- Guided exercises for producer risk
- Guided exercises for consumer risk
- Sampling risks in a sampling plan

## Sampling and Inspection of Packaging Materials

- Regulations and guidance for packaging and labeling control
- Primary packaging: containers and closures:
  - What is inspected?
  - Challenges in inspecting packaging materials
- Secondary packaging: labels, leaflets and folded boxes:
  - What is inspected?
  - Challenges in inspecting packaging materials
  - Sampling in printing house
  - Sampling in manufacturer's site
  - Defects in labels

## Risks in Sampling

- Probability of acceptance
- Operating curve
- Misconceptions of sampling
- Determining product and consumer risks in a sampling plan

## Sampling according to the WHO

- Sampling of starting materials
- Full testing vs. testing for identity
- Qualified supplier vs. unreliable supplier
- n, p and r plans
- Criticism of the sampling plans

## Sampling of Powders (APIs and excipients) and Tools for Sampling in a Pharmaceutical Plant

- Regulatory requirements
- Risk assessment for sampling
- Sampling plans/sampling schemes
- Training for sampling
- Retention/reference samples
- Starting material Identity testing
- Sampling for the purpose of assay
- Sampling of raw materials
- Techniques of drawing samples
- Prerequisites/requirements for correct sampling
- Sampling devices and containers

## √N rule: its Uses and Misuses

- Origin of the rule
- Uses and misuses
- How confident is it?

## How to effectively reduce the Amount of Samples to be tested? (incl. Practical Examples)

- Reduced testing concepts – how to apply?
- Internal testing vs. external testing
- Using the supplier's CoA instead of in-house testing
- Use of devices to reduce sampling / testing (e.g. Rapid ID)
- Use of risk assessment to reduce sampling / testing
- Practical example walkthrough

## Skip-Lot Testing

- What is skip-lot testing?
- Sampling plan SkSP-1 for raw materials
- Sampling plan SkSP-2 for attributes
- Skip-lot testing of excipients (USP <1040>)
- When skip-lot testing is justified

## Reference/Retention Samples and Good Quality Practice around Sampling Plans

- Reference/retention samples
  - Regulations on reference/retention samples
  - Which and how many samples to take?
  - Retention periods for GMP and clinical samples
- How to document the sampling system within the company? (SOPs, specifications, LIMS)
- What you should discuss with the supplier
  - Tailgate/satellite samples and pre-delivery samples
  - How to certify homogeneity of materials

## Charting and Trending Nonconformities and Nonconforming Items

- Run chart and control chart
- Charting the number of non-conforming items (p chart and I-MR charts
- Charting the number of nonconformities (c chart and I-MR charts)
- Detecting a trend in your inspection quality
- Determining your process average
- Does your inspection data confirm your AQL?

## Sampling for Visual Inspection of Particles in Parenteral Drugs

- Regulations for sampling for visual inspection
- Types of particles
- Probability of detecting a particle
- Procedure of manual visual inspection (Ph. Eur. 2.9.20 and USP <790>)
- Types of visual inspections
- Inspection of hard-to-see
- AQL sampling after 100% inspection
- Policy of sampling and inspection

## Video Demonstration of Sampling activities

- Explained videos on sampling and sampling tools

## Q&A Sessions

- Participants are invited to ask questions

# 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 Gerald Kindermann
GxP Consulting, Switzerland

Dr Kindermann was Product Quality Manager at the Global Quality Group at Roche working on quality systems. Before that he was Group Leader Quality Control and Quality Manager for the Supply Center. He worked as a Senior Pharma Consultant at AGIDENS AG and Capgemini Engineering, Switzerland. In May 2023, he joined GxP Consulting, in Basel, Switzerland as a Senior Consultant in the GMP area.

## Philip Lienbacher
Takeda, Austria

Philip Lienbacher has a MSc in Biomedical Engineering Sciences and works for Takeda since 2008. He has held several different roles in site based- and global quality organizations in the company focused on QC/QA activities. His current role is being the Head of Analytical Services & Support where he oversees a number of different expert groups that provide guidance and leadership to the Takeda site network in regard to analytical topics while being responsible for execution of operational activities as well (reference standards, particle LCM, stability, digitalization & LIMS, specifications).

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## Internationally Acknowledged Certificate from ECA Academy


The EU GMP Guide requires:
„... All personnel should be aware of the principles of Good Manufacturing Practice that affect them and receive initial and continuing training,...". This is why you receive an acknowledged participant certificate, which lists the contents of the seminar in detail and with which you document your training.

## Date of the Live Online Training
Tuesday, 07 May 2024, 09.00 – 18.00 h
Wednesday, 08 May 2024, 08.30 – 17.30 h
All times mentioned are CEST.

## Technical Requirements
We use Webex for our live online training courses and webinars. At www.gmp-compliance.org/training/online-training-technical-information you will find all the information you need to participate in our events and you can check if your system meets the necessary requirements to participate. If the installation of browser extensions is not possible due to your rights in the IT system, please contact your IT department. Webex is a standard nowadays and the necessary installation is fast and easy.

## Fees (per delegate, plus VAT)
Non-ECA Members € 1,890
ECA Members € 1,690
APIC Members € 1,790
EU GMP Inspectorates € 945
The conference fee is payable in advance after receipt of invoice.

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

## Presentations/Certificate
The presentations will be made available to you prior to the Live Online Training as PDF files. After the event, you will automatically receive your certificate of participation.

## 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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Reservation Form (Please complete in full)

EU GMP-/FDA-compliant Sampling, Live Online Training on 07/08 May 2024

Title, first name, surname

Department | Company

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

City | ZIP Code | Country

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2. If you have to cancel entirely we must charge the following processing fees:
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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 conference (receipt of payment will not be confirmed)! (As of July 2022).
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