

# Particles in Parenterals

## UPDATE: changes due to the revision of Annex 1

With an optional Pre-Conference Course: **Fundamentals of Visual Inspection & AQL Testing** on 9 October 2018

Bonus for the participants of this course:  
**The AQL Inspector's Rule** - A tool for conducting AQL Testing.



### SPEAKERS



**GABRIEL ANDERSON**  
*Novartis*



**DR MARTIN BECKER**  
*Siegfried Hameln*



**MARTIN DEARDEN**  
*PaxVax Berna*



**DR HELMUT GAUS**  
*Winsol, previously  
Boehringer Ingelheim*



**AL GOODWIN**  
*Amgen*



**ALAN KELLY**  
*Sanofi*



**FELIX KRUMBEIN**  
*Roche*



**CHRISTOF LANGER**  
*OSConsulting*



**DR TOBIAS POSSET**  
*Roche*



**DR HEINO PRINZ**  
*Rommelay AG*

All participants receive the current version of ECA's Best Practice Paper on "Visual Inspection" for free.



Image: Seidemader

10-11 October 2018, Hamburg, Germany

### HIGHLIGHTS:

- Regulatory and GMP requirements for the inspection of parenterals
- Trending and Monitoring and batch release with respect to inspection data
- Re-inspection of defect fractions
- New techniques for CCI and particle detection
- Inspection of plastic and BFS containers
- Case study Sanofi: Manual visual inspection
- Case study Roche: Detection at the limit of visibility
- Case study Novartis: Fully automated inspection
- Impact of the Annex 1 revision on the testing of parenterals



**Optional pre-conference course  
"Fundamentals of Visual Inspection & AQL  
Testing" on 9 October 2018**

The training course on visual inspection which takes place the day before the Particles Conference gives you an understanding of the fundamentals of visual inspection of injectable products, applicable to manual and automated inspection. You will also learn how to implement an automated system on the basis of the manual inspection. The course also includes an AQL training, that is you will learn how to use AQL tables to set defect limits and how to evaluate batch inspection data.



**For that purpose all participants of the Pre-Conference Course receive the AQL Inspector's Rule as tool for AQL testing for free.**

The rule covers a wide range of AQL's with Normal, Tightened and Reduced inspection for both single and double sampling plans according to ISO 2859-1 (1999). **The practical usage of this tool will be shown during the course.**

Skills you will develop through the course:

- Ensuring GMP compliance in manual inspection
- Setting up a qualification strategy for automated systems
- Usage of statistical tools for assessing inspection data
- GMP-compliant routine operation of automated systems

Content of the course in detail:

#### **General requirements**

- Requirements of the Pharmacopeia
- Defect categorisation
- Test kits for training, qualification and routine

#### **Manual Inspection**

- Qualification and training of personnel
- Standardisation of working conditions
- AQL in the manual inspection

#### **From Manual to automated inspection**

- Usage of the Knapp and the modified Knapp test
- Cross validation during the PQ phase

#### **Automated inspection**

- Importance of particle detection rates
- System-Suitability, Requalification and revalidation

Course Trainer:

DR HELMUT GAUS, *WinSol & former Director Quality Control at Boehringer Ingelheim*

DR TOBIAS POSSET, *Head of Production Support Roche Diagnostics*

## **Particles in Parenterals**

10-11 October 2018, Hamburg, Germany

### **Objectives**

Main topic of this conference is the detection of particles in injectables and their evaluation during batch release and continuous process improvement. Besides the current regulatory requirements with regards to particulate matter, routine 100% inspection of injectables will be addressed. Manual inspection as well as automated inspection systems will be covered, including training, AQL testing, trending, inspection equipment and batch release considerations.

### **Background**

In most cases particles found in parenteral medicines will lead to a quarantined product or even to the recall of the product – as we have seen in the last years in the cases of several pharmaceutical companies. Responsible staff in charge will have to start root cause analysis to find the source of the particles and will have to do an evaluation of batches already shipped.

There is still confusion within the global pharmaceutical industry with regard to the requirements for testing for visible particles. After the USP chapters <790> and <1790> were published, things have become much clearer, at least for the US. But still, lots of questions arise, e.g. concerning re-testing, detection capabilities and revalidation of inspection systems.

Furthermore there has been a recognisable trend towards automated inspection machines throughout the last years. The challenge for pharmaceutical companies is to find a suitable machine for their products and to determine reasonable inspection parameters during qualification and validation. But also during routine process there are questions arising like re-testing and the usage of test-sets, doing AQL-Testing as well as the adjustment of parameters of the vision systems.

We will address those topics during the conference and discuss and answer questions on

- The latest compendial requirements concerning particulate matter
- Training in the manual visual inspection
- Qualification and operation of an automated inspection system
- Threshold studies and the border of visibility
- Trending and monitoring of visual inspection data
- Limitations of the AQL test
- New inspection technologies
- Re-inspection of defect fractions

### **Target Audience**

This conference is directed at specialists and executives from sterile operations, that is manufacturing, quality assurance and engineering. But also suppliers of primary packaging materials and inspections technology are target group of this conference.

### **Moderator**

Dr Tobias Posset, Roche Diagnostics, Chairman of the ECA Visual Inspection Group

### **Regulatory Requirements for the visual inspection of parenterals**

- Compendial Requirements
  - 100% visual inspection & AQL testing
  - PharmEur, USP, JP - similarities and differences
- News from the Annex 1 revision
- GMP Expectations
  - Manual inspection
  - Automated Inspection
- Risk Management Considerations



### **Presentation and discussion of the ECA Best Practice Paper on Visual Inspection**

The best practice paper has been originally developed by the advisory board of the ECA Visual Inspection Group. Much rather than a strict requirement document, this paper is intended to be a reference for controversial issues. The first version of this paper has been published in September 2014 in Copenhagen. It has gained a broad acceptance in the industry afterwards.

The current version as well as planned updates will be explained and discussed in Hamburg.

### **Particle testing and the correlation with trending and Batch release**

- Why do we Monitor (What is it all about)
- Data and Measurement
- The AQL trap
- Improvement Process Map
- Investigation and Routine Analysis
- Release Process: "To AQL or not to AQL that is the Question"
- Product Release: "Falling off a log"

### **Re-inspection of defect fractions in visual inspection**

Different scenarios will be covered such as:

- Re-inspection or additional inspection of "grey-channel" units from (semi-) automated inspection
- Re-inspection in case of exceeding alert limits or AQL failures
- Focused re-inspection
- Inspection approaches in case of investigations due to unexpected particles (e.g., to determine frequency of occurrence of visible particles when particles are found during release/stability testing)

### **Advanced techniques for particle detection and laser inspection process for vial CCIT**

- Standard machine vision particle detection use only three or four algorithms. Already available and used in multiple industries are powerful algorithms which start to give you more information about the particle that has been detected. Using real case studies it will be shown how these new tools are adopted in the most recent automatic visual systems.
- Present vision inspection systems that are used for CCI checking of vials work with 2D images which are analysed by the vision software. This can lead to false fails because the closure condition is extrapolated from a 2D image. Using more advanced 3D laser profiling results in more human like data available to make judgments. Example what crimp angle is optimal and how far have we crimped the vial. This data is available real time and speeds can match the fastest AVI available at present.

### **Automated visual inspection of large volume parenterals – 360 degree approach for container quality control**

A new technique for particle detection in LVP containers will be presented with very low bubble influence combined with detailed detection and monitoring of process related quality aspects for container integrity and cosmetic defects. Includes an outlook using the technique as an application for IV Bags.

### **Case Study Sanofi: Manual visual inspection**

- Preparation of defect sets
- Sensitivity / threshold studies
- PQ & Knapp-Test studies
- Training and qualification of MVI operators

### **Case Study Novartis: Fully automated visual inspection**

- Implementation of the system
  - Qualification concept
  - Knapp studies & test sets
- Routine use of the system
  - AQL testing
  - Re-inspection
  - Re-validation of the system

### **Manual detection of particles at the border of visibility**

- General requirements
  - USP 1790: Composition of test kits for training, qualification and routine
  - Inspection conditions (inspection time, illumination, etc.)
- Manual Inspection:
  - Training and qualification of manual operators
  - Modified Knapp-Test
- Threshold study under different inspection conditions

### **Impact of the Annex 1 revision on the testing of parenterals**

- The final draft for comments of Annex 1
- Contamination Control Strategy
- New requirements on process simulation
- PUPSIT
- Container Closure Integrity requirements
- New expectations on Visual Inspection

### **Visual Inspection and Health Authority Expectations & Observations**

- Observation at the AIM qualification
- Comments to the 5000 test
- Dealing with particles & complaints



#### **Best-Practice-Paper**

All participants receive the current version of ECA's Best Practice Paper on "Visual Inspection" for free.



#### **Social Event**

In the evening of the first conference 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.

## Speakers

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**GABRIEL ANDERSON**, Novartis

Gabriel is going on 10 years of experience in the field of visual inspection of injectable products. He has a chemical engineering degree and joined Novartis Vaccines in the US in 2011 as a production engineer responsible for setting up the visual inspection program and validating an automated inspection machine. In 2014 he moved to Basel to take on a global role within Novartis in the manufacturing, science, and technology (MS&T) group and to co-lead Novartis's visual inspection expert network.



**DR MARTIN BECKER**, Siegfried Hameln

Dr Becker studied Chemistry and is actually Head of Technical Operations and Head of Production Sterile Operations at Siegfried Hameln (formerly hameln pharmaceuticals). He previously held different positions in analytical development, quality assurance, and production at IDT in Dessau and San-do in Austria.



**MARTIN DEARDEN**, PaxVax Berna GmbH

Martin has over 25 years of experience in the Pharmaceutical Industry with over 20 years concerned with the manufacture of sterile products and Biologics. Martin holds Degree level qualifications in Applied Biology and also Immunology and Microbiology. He was Senior Director at UCB S.A. and as the UCB Corporate Microbiologist responsible for microbiological standards, policy and strategy. Now he is Vice President of Quality for PaxVax Berna in Switzerland.



**DR HELMUT GAUS**, WinSol & former Director Quality Control at Boehringer Ingelheim

Dr Gaus was Head of Quality Control Service at Boehringer Ingelheim, Biotechnology. He has also been working as Vice President Quality Control and Qualified Person for Novartis Generics, Vetter-Pharma and Rentschler Biotechnologie where he gained an extensive knowledge in the field of visual inspection. In 2018 he founded his own company WinSol.



**AL GOODWIN**, Amgen

From the Headquarters of Amgen in California, Al specifies and supports globally all of Amgen's AVI systems for vials, syringes, plastic cartridges and drug delivery devices. Al has 25 years of experience in optical inspection systems. He has also worked in Japan for 5 years on optical test measurement systems. In the last 15 years he has worked closely with key International Machine Vision Software design companies and has used this experience in areas of Particle detection, Glass flaw detection and improvements and evaluation of Vision Algorithm Robustness in the pharmaceutical industry.



**ALAN KELLY**, Sanofi

Alan Kelly is a Senior Process Engineer currently working in the Technical Services Department at Sanofi in Ireland.



**FELIX KRUMBEIN**, Roche Diagnostics

Felix Krumbain studied optoelectronics and image processing. He worked for Scanware and for Laetus as head of the group identifications systems where he was responsible for the implementation of GMP-compliant imaging tools. Since 2011 he is working for Roche as head of Inspections-Systems-Support. He is responsible for the qualification of visual inspection systems in the GMP environment.



**CHRISTOF LANGER**, OSConsulting

Christof Langer studied Biotechnology and is certified Risk Manager as well as a Lean Six Sigma Black Belt. He has been working as Managing Director at Baxter BioScience, responsible for Operations. Since 2009 he runs his own consultancy business.



**DR TOBIAS POSSET**, Roche Diagnostics GmbH

Tobias Posset studied Biochemistry and Chemistry. He is heading the Production Support unit in the Pharma Production at Roche Diagnostics in Mannheim. Herein he is responsible for the IPCs, the particle laboratory, the automated visual inspection and the coordination of the manual inspection training. He is also the chairman of the ECA Visual Inspection Group.



**DR HEINO PRINZ**, Rommelag AG

Dr Prinz was in charge for research and development at Wilco in Wohlen, Switzerland and changed to Rommelag in 2014 where he has the position of the Director Inspection Devices.

## Easy Registration

 **Reservation Form:**  
**CONCEPT HEIDELBERG**  
P.O. Box 10 17 64  
69007 Heidelberg  
Germany

 **Reservation Form:**  
+ 49 6221 84 44 34

 **e-mail:**  
info@concept-heidelberg.de

 **Internet:**  
www.gmp-compliance.org

### Date

**Pre-conference course:**  
**Fundamentals of Visual Inspection**

Tuesday, 9 October 2018,  
10.00 to approx. 17.00 h  
(Registration and coffee 09.30 – 10.00 h)

### Particles in Parenterals Conference

Wednesday, 10 October 2018,  
09.00 – 17.30 h  
(Registration and coffee 08.30 – 09.00 h)  
Thursday, 11 October 2018,  
08.30 to approx. 15.45 h

### Venue

Barceló Hotel Hamburg  
Ferdinandstrasse 15  
20095 Hamburg, Germany  
Phone +49 40 22 63 62 0  
Email hamburg@barcelo.com

### Fees (per delegate plus VAT\*)

**Pre-Conference Course: Fundamentals of visual inspection (9 October)**  
ECA Members € 790  
APIC Members € 890  
Non-ECA Members € 990  
EU GMP Inspectorates € 495  
The conference fee is payable in advance after receipt of invoice and includes lunch and all refreshments.

### Particles in Parenterals Conference (10-11 October)

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 dinner on the first day, lunch on both days and all refreshments.

### Saving opportunities

Book also the pre-conference course on 9 October and save € 300 in total (not valid for EU GMP Inspectorates)

### 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 event. Reservations should be made directly with the hotel. Early reservation is recommended.

### Conference language

The official conference language will be English.

### Organisation and Contact

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

CONCEPT HEIDELBERG  
P.O. Box 10 17 64  
D-69007 Heidelberg, Germany  
Phone +49 (0)62 21/84 44-0  
Fax +49 (0)62 21/84 44 34  
info@concept-heidelberg.de  
www.concept-heidelberg.de

### For questions regarding content please contact:

Dr Robert Eicher (Operations Director) at +49(0)62 21 / 84 44 12, or per e-mail at eicher@concept-heidelberg.de.

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

Mr Rouwen Schopka (Organisation Manager) at +49(0)62 21 / 84 44 13, or per e-mail at schopka@concept-heidelberg.de.

Please note that there **will not be any print-outs at the conferences**. Instead you will receive all presentations prior to the event as Downloads as well as after the event, in the case of updates.

\* VAT is reclaimable

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

Reservation Form (Please complete in full)

 +49 6221 84 44 34

- Pre-Conference Course "Fundamentals of Visual Inspection & AQL Testing",  
9 October 2018, Hamburg, Germany
- Particles in Parenterals Conference, 10-11 October 2018, Hamburg, Germany
- Pre-Conference Course AND Conference, 9-11 October 2018, Hamburg, Germany

Mr  Ms

Title, first name, surname

Company

Department

**Important: Please indicate your company's VAT ID Number**

**Purchase Order Number, if applicable**

Street / P.O. Box

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E-Mail (Please fill in)

### 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 %  
- until 1 week prior to the conference 50 %  
- 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 responsible for discount airfare penalties or other costs incurred due to a cancellation. **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 cancellation 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 you have received your payment, you are entitled to participate in the conference (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](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.