QP CONFERENCE

Druga QP konferencija:

# Izazovi QP-a u savremenom farmaceutskom poslovanju

1. i 2. oktobar 2015. godine
Beograd, Srbija

The second QP conference:

# QP challenges in modern pharmaceutical trading

1st and 2nd of October, 2015
Belgrade, Serbia

## Organizaciju konferencije su pomogli
## Sponsored by

PHARMASWISS
A Valeant Pharmaceuticals International, Inc. company

PHARMANOVA

ALKALOID
SKOPJE

ZDRAVLJE
Actavis company

## Organizacioni odbor
## Organizing Board

Biljana Stupar

Katarina Popović

Ljiljana Solomun

Nataša Knežević

Slavica Kojić

Snezana Tvrdorjeka

Sonja Georgieva Jovanović

Svetlana Ibrić

Valentina Marinković

Zorica Vujić

## Registracija i organizacija skupa
## Registration and organisation

**SMART TRAVEL PCO**
Email: smarttravelpco4@smarttravelpco4.rs
www.smarttravelpco4.rs

## Zvanični jezici konferencije

Srpski i engleski

| | |
|---|---|
| 09.00-10.00 | Registracija učesnika |
| 10.00-10.30 | **Pozdravni govor i otvaranje skupa**<br>**Prof. dr Berislav Vekić**, državni sekretar u Ministarstvu zdravlja Republike Srbije<br>**Prof. dr Zorica Vujić**, dekan Farmaceutskog fakulteta, Univerzitet u Beogradu |
| 10.30-11.15 | **Update on the EU GMP Regulations**<br>**Dr Bernd Renger**, Renger Consultancy |
| 11.15-12.00 | **OOS results; regulatory expectations and remediation approaches**<br>**Dr Christopher Burgess**, EQPA |
| 12.00-12.30 | *Pauza za kafu* |
| 12.30-13.00 | **The role of QP in assuring the GMP compliant APIs**<br>**Andrej Ferlan**, Solutiones d.o.o., Consulting, Education and Training, Ljubljana, Slovenia |
| 13.00-13.30 | **Strateški plan razvoja Agencije za lekove Republike Makedonije**<br>**Marija Darkovska**, Direktor Agencije za lekove Republike Makedonije |
| 13.30-14.00 | **Diskusija - Svi predavači** |
| 14.00-15.00 | *Ručak* |
| 15.00-16.30 | **Modern Data and Documentation Management and recording.**<br>**State of the art Data and Document Structuring: Data Integrity -Electronic Signatures vs. digital Signatures.**<br>**Electronic Signature Law and requirements on signing electronically**<br>**Stephan Dresen**, Actavis, Weiterstadt, Germany |
| 16.30-17.00 | **The revised Annex 16 of the EU GMP Guide and is Implications for QPs**<br>**Dr Bernd Renger**, Renger Consultancy |
| 17.00-17.30 | **Diskusija - Svi predavači** |
| 20.30-23.30 | **Svečana večera**<br>**Restoran Malevilla**<br>Kej Oslobođenja bb, 11080 Zemun |

09.00-09.30 **Kontinuirana proizvodnja i puštanje leka u promet**
**Mate Poropat**, Jadran Galenski Laboratorij d.d., Hrvatska

09.30-10.00 **PAT i Real Time Release**
**Doc. dr Jelena Đuriš**, Farmaceutski fakultet, Beograd

10.00-10.30 **What QPs need to know about statistics?**
**Dr Christopher Burgess**, EQPA

10.30-11.00 *Pauza za kafu*

**TRI PARALELNE RADIONICE**

11.00-12.30 **RADIONICA 1**
**Upravljanje rizicima tokom transporta lekova**
Moderatori:
**Nataša Knežević**, mag.farm.spec., Head of quality and QP, JGL d.o.o.
**Katarina Popović**, mag.farm.spec., QP, Pharmanova d.o.o

**RADIONICA 2**
**OOS u studijama stabilnosti**
Moderatori:
**Dr sci. Ljiljana Solomun**, spec. QC, Ivančić i sinovi
**Slavica Kojić-Marinković**, mr ph spec. QP Pharmaswiss

**RADIONICA 3**
**Uloga QP-a u upravljanju konfliktnim situacijama**
Moderatori:
**Doc. dr Valentina Marinković**, Farmaceutski fakultet, Univerzitet u Beogradu
**Snežana Tvrdorijeka**, mag.farm.spec., QP, Direktor kvaliteta, Sektor kvaliteta, Zdravlje Actavis

12.30-13.30 *Ručak*

13.30-15.00 **RADIONICA 1**
**Upravljanje rizicima tokom transporta lekova**
Moderatori:
**Nataša Knežević**, mag.farm.spec., Head of quality and QP, JGL d.o.o.
**Katarina Popović**, mag.farm.spec., QP, Pharmanova d.o.o.

**RADIONICA 2**
**OOS u studijama stabilnosti**
Moderatori:
**Dr sci. Ljiljana Solomun**, spec. QC, Ivančić i sinovi
**Slavica Kojić-Marinković**, mr ph spec. QP Pharmaswis

**RADIONICA 3**
**Uloga QP-a u upravljanju konfliktnim situacijama**
Moderatori:
**Doc. dr Valentina Marinković**, Farmaceutski fakultet, Univerzitet u Beogradu
**Snežana Tvrdorijeka**, mag.farm.spec., QP, Direktor kvaliteta, Sektor kvaliteta, Zdravlje Actavis

15.00-15.30 *Pauza za kafu*

15.30-17.00 **RADIONICA 1**
**Upravljanje rizicima tokom transporta lekova**
Moderatori:
**Nataša Knežević**, mag.farm.spec., Head of quality and QP, JGL d.o.o
**Katarina Popović**, mag.farm.spec., QP, Pharmanova d.o.o

**RADIONICA 2**
**OOS u studijama stabilnosti**
Moderatori:
**Dr sci. Ljiljana Solomun**, spec. QC, Ivančić i sinovi
**Slavica Kojić-Marinković**, mr ph spec. QP Pharmaswiss

**RADIONICA 3**
**Uloga QP-a u upravljanju konfliktnim situacijama**
Moderatori:
**Doc. dr Valentina Marinković,** Farmaceutski fakultet, Univerzitet u Beogradu
**Snežana Tvrdorijeka**, mag.farm.spec., QP, Direktor kvaliteta, Sektor kvaliteta, Zdravlje Actavis

17.00-17.15 **Zatvaranje skupa i podela sertifikata**

| | |
|---|---|
| 09.00-10.00 | Registration |
| 10.00-10.30 | **Welcome speech**<br>**Prof. dr Berislav Vekić**, Secretary of State, Ministry of Health<br>**Prof. dr Zorica Vujić**, Dean, Faculty of Pharmacy, University of Belgrade |
| 10.30 – 11.15 | **Update on the EU GMP Regulations**<br>**Dr Bernd Renger**, Renger Consultancy |
| 11.15 – 12.00 | **OOS results; regulatory expectations and remediation approaches**<br>**Dr Christopher Burgess**, EQPA |
| 12.00 – 12.30 | *Coffee break* |
| 12.30-13.00 | **The role of QP in assuring the GMP compliant APIs**<br>**Andrej Ferlan**, Solutiones d.o.o., Consulting, Education and Training, Ljubljana, Slovenia |
| 13.00-13.30 | **Strategic development plan for Drug Agency of Republic of Macedonia**<br>**Marija Darkovska**, Director of Macedonian Drug Agency |
| 13.30-14.00 | **Discussion - All speakers** |
| 14.00 - 15.00 | *Lunch* |
| 15.00-16.30 | **Modern Data and Documentation Management and recording.**<br>**State of the art Data and Document Structuring: Data Integrity -Electronic Signatures vs. digital Signatures.**<br>**Electronic Signature Law and requirements on signing electronically**<br>**Stephan Dresen**, Actavis, Weiterstadt, Germany |
| 16.30-17.00 | **The revised Annex 16 of the EU GMP Guide and is Implications for QPs**<br>**Dr Bernd Renger**, Renger Consultancy |
| 17.00-17.30 | **Discussion - All speakers** |
| 20.30 -23.30 | **Dinner**<br>**Restaurant Malevilla**<br>Kej Oslobođenja bb, 11080 Zemun |

09.00-09.30 **Continual production and certification procedure by QP**
**Mate Poropat**, Jadran Galenski Laboratorij d.d., Croatia

09.30-10.00 **PAT and Real Time Release**
**Doc. dr Jelena Đuriš**, Faculty of Pharmacy, Belgrade

10.00-10.30 **What QPs need to know about statistics**
**Dr Christopher Burgess**, EQPA

10.30-11.00 *Coffee break*

**THREE PARALLEL WORKSHOPS**

11.00-12.30 **Workshop 1**
**Risk management during drugs transportation**
Moderators:
**Nataša Knežević**, mag.farm.spec., Head of quality and QP, JGL d.o.o.
**Katarina Popović**, BSc.Pharm.spec., QP, Pharmanova d.o.o

**Workshop 2**
**OOS in stability studies**
Moderators:
**Dr sci. Ljiljana Solomun**, spec. QC, Ivančić i sinovi
**Slavica Kojić-Marinković**, mr ph spec. QP Pharmaswiss

**Workshop 3**
**QP role in managing conflict situations**
Moderators:
**Ass. prof. Valentina Marinković**, Faculty of Pharmacy, University of Belgrade
**Snežana Tvrdorijeka**, BSc.Pharm.spec., Site Quality Head, QP, Quality department, Zdravlje Actavis

12.30-13.30 *Lunch*

13.30-15.00 **Workshop 1**
**Risk management during drugs transportation**
Moderators:
**Nataša Knežević**, mag.farm.spec., Head of quality and QP, JGL d.o.o.
**Katarina Popović**, BSc.Pharm.spec ., QP, Pharmanova d.o.o

**Workshop 2**
**OOS in stability studies**
Moderators:
**Dr sci. Ljiljana Solomun**, spec. QC, Ivančić i sinovi
**Slavica Kojić-Marinković**, mr ph spec. QP Pharmaswiss

**Workshop 3**
**P role in managing conflict situations**
Moderators:
**Ass. prof. Valentina Marinković**, University of Belgrade, Faculty of Pharmacy
**Snežana Tvrdorijeka**, BSc.Pharm.spec., Site Quality Head, QP, Quality department, Zdravlje Actavis

15.00-15.30 *Coffee break*

15.30-17.00 **Workshop 1**
**Risk management during drugs transportation**
Moderators:
**Nataša Knežević**, mag.farm.spec., QP, JGL d.o.o.
**Katarina Popović**, BSc.Pharm.spec., QP, Pharmanova d.o.o

**Workshop 2**
**OOS in stability studies**
Moderators:
**Dr sci. Ljiljana Solomun**, spec. QC, Ivančić i sinovi
**Slavica Kojić-Marinković**, mr ph spec. QP Pharmaswiss

**Workshop 3**
**QP role in managing conflict situations**
Moderators:
**Ass. prof. Valentina Marinković**, University of Belgrade, Faculty of Pharmacy
**Snežana Tvrdorijeka**, BSc.Pharm.spec., Site Quality Head, QP, Quality department, Zdravlje Actavis

## Bernd Renger

Dr. Bernd Renger has more than 35 years industry experience in different managing positions in API Manufacturing and Pharmaceutical Industry. He started his professional career with Hoechst AG as a Research and Development Chemist.

Since than, he has held positions as Head of Quality Control at Mundipharma (Limburg/Germany), Head of Quality Control Unit at Byk Gulden/Altana Pharma (Konstanz/Germany), Facility Quality Management Representative in Baxter BioScience (Vienna/Austria) and Vice President Quality Control in Vetter Pharma Fertigung (Ravensburg/Germany).

He holds a degree in Organic Chemistry from the University in Giessen, Germany and is an appointed Qualified Person according to the European regulations and has acted as a Qualified Person in the EU for more than 27 years. He is an expert in Quality Systems and Quality Risk Management System design, development and implementation.

In 2011, Bernd Renger Consulting is established, with consultancy services for the Pharmaceutical Industry, Medical Devices Manufacturing, API and Excipient Manufacturing, Packaging Material production and Analytical Services.

## Christopher Burgess

Dr Christopher Burgess is an internationally recognised expert in the qualification and validation of instrumentation and systems, analytical method development &validation, process validation and the statistical interpretation of data. In addition he has extensive experience in quality systems design and auditing the whole supply chain and has acted as a Qualified Person within the EU for more than 28 years.

He has

- 41 years experience in management and consulting positions within the pharmaceutical, biopharmaceutical and medical device industries. 20 years with Glaxo in Analytical R &D, Quality Control and Quality Assurance.
- MSc and PhD degrees from Loughborough University in Analytical Chemistry.
- Been involved in more than 200 ECA training courses since 2001 which have had over 8000 attendees from 75 countries.

Dr. Burgess has published over 100 papers, articles and books in analytical chemistry and analytical science. He is the author of Aberrant and Atypical Results and (in part) methods for determining limits of detection and quantitation in Method Validation in Pharmaceutical Analysis; A guide to best practice, (Eds Ermer and Miller) in 2005 [ISBN 3-527-31255-2] also a contributor to the 2nd Edition by Wiley –VCH (2015). He was a member of the PDA (USA) Expert Working Group on OOS results. He writes the Statistical Solutions column for Pharmaceutical Technology.

## Andrej Ferlan

Andrej Ferlan is an expert in Quality Control, Quality Systems, Quality Standards and Good Practices. He was Head of Pharmaceutical Inspection at Medicinal Products and Medical Devices Agency of Republic of Slovenia.

At beginning of 2009 he founded a company for consultiong and education dealing with quality systems and Good practices: Solutiones d.o.o., Consulting, Education and Training in Ljubljana, Slovenia.

## Marija Darkovska-Serafimovska

Marija Darkovska – Serafimovska is Director of Macedonian Agency for Medicines and Medical Devices. Her field of expertise is quality control, batch release and pharmacology. She participate in the following science projects: (1) Establishment and standardization of a technology for production of redy to use kit formulation of conjugated monoclonal antibody and peptide based radiopharmaceuticals (Faculty of medical science, University Goce Delcev, Shtip, Macedonia) and (2) Building of a national strategy for fight against couterfeiting medicines, Faculty of pharmacy (University St.Cyril and Metodius, Skopje).

## Stephan Dresen

Stephan Dresen is Director Quality of the Actavis/Allergan group cooperation and as Regional Head responsible for the production sites in Serbia (Zdravlje / Leskovac), Greece (Specifar / Athens) and Germany (Warner Chilcott / Weiterstadt). In Germany he has overall responsibility for the Quality areas of the production site at Weiterstadt. Before he had been in charge of the Third Party Manufacturing (TPM) Quality area in Europe for the Procter & Gamble Pharma (P&G Pharma later Warner Chilcott). He has started his career in the pharmaceutical industry within Abbott Laboratories as Global Head of Change Control and Standards Center in the established products division.

Since August 2003 he is managing partner and owner of D|Consulting GmbH (Baden-Baden). A company specialized in dealing with pharmaceutical and medical knowledge management. Among others his company has developed a neuronal network based software to automatically analyze SPCs (Summary of product characteristics of pharmaceutical products) and infer / deduce this data into an ontology based knowledge processing system letting doctors and pharmacists retrieve (knowledge retrieval) coded (LOINC, MedDRA, ICD10) information for defining medical therapies. It is used in the "Gelbe Liste".

Stephan has studied Chemistry starting at the University of Heidelberg and finished his studies in Trinity College in Dublin, Ireland, on Ph.D. level.

## Mate Proprat

Mate Proprat is Executive director of Pharmaceutical and Technical operations in JGL d.d. Rijeka, Croatia. His field of expertise is Production, Quality Control, Quality systems, Material management, Technical support. In "Jadran" Galenski laboratorij d.d., Rijeka, he started as assistant to production manager in 2000, then as production manager, operations manager, and finally, from 2010 to present, he is pharmaceutical and technical operations director.

## Jelena D. Đuriš

Jelena D. Đuriš graduated at the University in Belgrade – Faculty of Pharmacy in 2007, and in 2010 she defended her PhD thesis in the field of pharmaceutical technology. In 2011 she completed academic specialization studies in Industrial pharmacy.

Since 2007 she is employed at the Faculty of Pharmacy as: teaching associate (2007-2008), teaching assistant (2008-2012), and assistant professor (2012 to date). She is involved in teaching activities (practical classes and lectures) in integrated academic studies, specialization and doctoral studies. From 2008 to date she is engaged in projects of technological development coordinated by the Faculty of Pharmacy. Jelena Đuriš is also author of number of papers published in international and national journals, and she also presented her research in international and national meetings.

## Nataša P. Knežević

Nataša Knežević gradueted on Faculty of Pharmacy, University of Belgrade in 2000. where she specialized in drug control and was assigned the title "specialist in drug control" in 2006. In 2013. she finished the specialization for QP, releasing the products to the market.

Form 2001-2008. she worked in pharmaceutical company Srbolek a.d as Associate in Regulatory Affairs. From 2008. to 2014. she worked in Galenika a.d. on several positions, starting as Senior Associate in QC, QC manager, Quality Division manager, QP and the last position R&D, Regulatory and Quality Division Manager. From 2014. to date she has worked on start-up project for Jadran Galenski Laboratorij d.o.o. Belgrade-Sopot as Head of quality and QP.

The main focus in her professional career is quality including testing in QC labs as well as QA and regulatory activities.

## Katarina V. Popović

Katarina Popović graduated from the Faculty of Pharmacy at the University of Belgrade in 2001. She finished post graduate specialization and acquired the title of specialist in testing and control of medicines in 2010, and she ended academic specialization Release of finished products to the market in 2014.

Katarina began her career in 2002 at the Institute of Pharmacy of Serbia, then in Medicines and Medical Devices Agency of Serbia, where she worked for 8 years on various responsible jobs within the National Control Laboratory and Licensing Department.

Since 2010 she has been working in the pharmaceutical company Pharmanova d.o.o.. as a Regulatory Affairs Manager and Qualified Person.

She is the author or co-author of 11 expert papers and communications.

## Ljiljana Solomun

Ljiljana Solomun, graduated BSc at Faculty of Pharmacy, University of Belgrade. Msc obtained at the same Faculty, in the field of pharmaceutical chemistry, and PhD in the field of pharmaceutical technology. She completed Specialization in Quality control in 1985, and Specialization in QP in 2014.

She established her experience in pharmaceutical industry mostly in "Hemofarm" A.D. at the different positions. More than 20 year she spent in R&D department, more than half of that period as a Project manager. Her professional background includes:

- Registration of the medicines (dossier compilation for the EU countries as well as the USA);
- QA/QC activities (management of the quality system);
- Stability testing (compatibility, stress and formal stability testing in accordance with the ICH guidelines);
- Packaging development (especially contact packaging materials);
- Activities connected with internal and external audits (including MHRA and FDA);

She is the author or co-author of more than 40 publications in the scientific and professional literature. The last few months she is the Head of Quality Control at "Ivančić i sinovi".

## Slavica Kojić-Marinković

Slavica Kojic graduated from the Faculty of Pharmacy, in Belgrade, in 1985.

She finished post graduate Specialization in Medicines Analysis and Quality Control, in 1999.

She finished post graduate Specialization in Release of finished products to the market, in 2014.

From 1989 to 1999 she worked in physics-chemical laboratory of Quality Control department, in Galenika as associate and independent associate. During 1999 and 2000 she worked as manager in physics-chemical laboratory of Quality Control Department. From 2000 she continued to work in Quality Assurance Department. She was in charge of job of qualified pharmacist for raw materials release. From 2008 she started to work in Pharmaswiss as Quality control manager and qualified person for finished products release to the market. The major part of her professional career she dedicated to analytical work of chemical control of raw substances and drugs, as well as introduction and development of quality system in Quality Control and Assurance Departments.

## Snezana Tvrdorijeka

Snezana Tvrdorijeka, a Msc of Pharmacy, is a Quality Director in Zdravlje Actavis company in Leskovac. She graduated from the Faculty of Pharmacy at the University of Belgrade in 1995, where she successfully completed the specialist education in drug releasing and became a Qualified Person. Snezana has 20 years of experience in pharmaceutical industry, working with Zdravlje Actavis on various challenging and responsible jobs, such as product formulation and management of production process. Following her true commitment to quality of pharmaceutical products, Snezana devoted the most significant part of her individual and professional development to this key role in the pharmaceutical industry. Snezana also has a significant experience in the areas of validation, quality assurance, continuous improvement and risk management. Since 2010, Snezana has been working as the Quality Director in Zdravlje Actavis, responsible for GMP Compliance and leading the processes of implementation and management of the Quality Systems in Zdravlje in compliance with the highest standards and requirements of Actavis, the third largest global generic pharmaceutical company.

## Valentina D. Marinkovic

Valentina D. Marinkovic completed her BSc, MSc, PhD degree at the Faculty of Pharmacy, University of Belgrade. Valentina Marinkovic's professional career built in two directions - academic and work in practice. She acquired title of Associate Professor at Faculty of Technology in Leskovac, University of Nis, and she established their practical experience in the pharmaceutical and chemical industries, Zdravlje- Actavis and Alvogen where she had the leadership positions. She has published more than 150 publications in scientific and professional literature. Valentina Marinković was head of the several courses of continuing education of pharmacists and a member of the European and international associations for quality, as well as for bioethics. Nowadays, she is Assistant Professor of Pharmacy, University of Belgrade, Department of Social Pharmacy and Pharmaceutical Legislation.

**Dr Bernd Renger**

## Update on the EU GMP Regulations

Based on the so called "Falsified Medicines Regulation" 2011/62/EU and its Delegated Acts, a number of new regulations have been introduced in the EU/EEA. These regulations introduce tougher rules and new harmonised, pan-European activities to ensure that trade in medicines and its starting materials, especially active pharmaceutical ingredients (APIs) is rigorously controlled.

These new activities include:

- An obligation to affix safety features on the outer packaging of the medicines
- Strengthened record-keeping requirements for wholesale and distributors
- Tougher rules on the controls, audits and inspections of producers and wholesalers of active pharmaceutical ingredients
- Risk based definitions of quality standards for manufacturing of excipients

In parallel, most of the chapters of the EU GMP Guidelines and some of the Annexes have been revised, to bring Guidance up to date and align with requirements of Falsified Medicines Directive and to implement new technologies (e.g. PAT, Quality by design).

In addition, the revisions are intended to include:

- Tougher requirements for the qualification of supplier and the supply chain
- Rigorous implementation of ICH Q9 "Quality Risk Management" principles
- Introducing elements of ICH Q10 "Pharmaceutical Quality System", especially for trending of data, and
- Clearer regulations when prevention of cross contamination will require dedicated facilities

A fundamental revision is also ongoing for Annex 16 to include these topics in the process of batch certification and release.

**Dr Christopher Burgess**

## OOS results; regulatory expectations and remediation approaches

The purpose of the talk is to put analytical results & reportable values in the context of a specified process and will include a discussion of regulatory requirements, specifications and distributions, measures of variability and statistical control vs process capability. The importance of definitions of OOS, OOT & OOE will be covered as well as procedures for retesting and evaluation of OOS results. Reference will be made to the ECA Analytical Quality Control Working Group, SOP on Laboratory Data Management; Out of Specification (OOS) Results v 2.1 August 2013 and the importance of appropriate investigational and statistical strategies.

**Andrej Ferlan**

## The role of QP in assuring the GMP compliant APIs

The role of QP is very important according to the EU legislation since it is the person who has to make aGMP certification before the release of the finished product. Compliance with the GMP is interpreted much more complexly today, than it was only a few years ago.

With the appearance of substandard APIs, that have had a significant impact on the patients in EU, USA and other countries, especially with the appearance of counterfeit APIs, the way of perceivingof APIs has changed.

The broad discussion in the European parliament has brought a conclusion; the legislation regarding APIs needs to be quickly changed. New guidelines and especially Directive 2011/62, dictate much stricter conditions for qualification of API suppliers for all member states.

Along the statement of conformity of API with the GMP guidelines, the new EMA template requires that the proof of conducted on-site GMP audit has to be presented to the authorities.

This applies to APIs and to intermediates, which broadens the audit activity range.

The directive states that all of these activities are bound to the manufacturer of finished products, though in practice, this comes down to the person generally responsible for the GMP certification of the batches - QP.

There are multiple ways of assuring the conformity of APIs with GMP guidelines. The first way is a personally conducted audit, which is the most relevant concerning finished products manufacture.The second way is the procedure in accordance with Annex 16 to GMP, which means that the statement of conformity by the responsible person at the manufacturing site is based on the findings of another responsible person (auditor).

The responsible person needs to actively participate in the API supplier audit; either as an auditor, or as the person that directly sets the requirements for the compliance check.

The prerequisites for the personally conducting theaudit for the responsible person are auditing knowledge and skills and also knowledge of the manufacturing process and related user requirements.

European Committee has identified high risks in the fields of critical excipients and distribution conditions, especially for APIs traveling long distances. The Committee has published detailed guidelines for both fields in March 2015, both based on the risk management approach.

Key Words: Active Pharmaceutical Ingredient, GMP Conformity of APIs, EU GMP, QP responsibility

**Marija Darkovska**

## Strategic plan for development of MALMED

Macedonian Agency for Medicines and Medical Devices (hereinafter: the Agency) on September 16 2014 has been established as an independent regulatory authority. Founder of the Agency is the Government of the Republic of Macedonia. Institutional building of the Agency is an important part of implementation of national medicines and medical devices policy aimed at ensuring access to medicines meeting recognized EU standards of quality, safety and efficacy as well as access to medical devices, meeting essential requirements set in EU legislation. It can be ensured by setting up efficient regulatory system, so the Agency should quickly develop its capacity in order to be able to ensure unimpeded transition from the Drug Bureau, to ensure its proper development and to play a key role in implementing the said aims. First strategic plan for

the development of Macedonian Agency is for the period 2015-2017. This is a key period of action of this institution because it sets the groundwork for future work of the new competent authority for medicines and medical devices, which is built on the foundations of the Bureau of medicines. Agency Strategic Plan reflects not only the present moment, but also our duty to make the best possible way we fulfill our mission and develop the Agency in accordance with our vision. The new legal organizational structure allows us professional independence and the necessary flexibility. The strategic plan of the Agency allows to be based on an analysis of the current situation and the vision of who we want to become at the end of a given period.

**Stephan Dresen**

## Modern Data and Documentation Management in Pharma Companies :: Data Integrity

Data integrity is the hot topic in pharmaceutical industry. Starting with critical MoH inspection observations, followed by a shut-down of sites in India and leading to new types of request during FDA, MHRA and other authorities, the demands are requiring new defense packages in the modern pharmaceutical industry. Data integrity refers to maintaining and assuring the accuracy and consistency of data over its entire life-cycle. Is is a critical aspect to the design, implementation and usage of any system which stores, processes, or retrieves data.

The lecture will show how data integrity can be strengthened by usage of digital signatures and XML technology.

Therefor a short inside in both technologies will be given (including a reference to the European digital signature law). The lecture will answer the questions:

What is a digital signature? How can it guarantee data consistency over the full life-cycle of f.e. a pharmaceutical product and its data? How will avoid a digital signature effectively manipulation of data? What is XML? How can it be used in document management over the life-cycle of product data? What is the benefit of XML in the light of our experiences with data integrity?

The term data integrity is broad in scope and may have widely different meanings depending on the specific context – even under the same general umbrella of computing. This lecture provides only a broad overview of some of the different types and concerns of data integrity.

**Dr Bernd Renger**

## The revised Annex 16 of the EU GMP Guide and is Implications for QPs

In parallel to the revision of most of the chapters of the EU GMP Guidelines the Annex "Certification by a Qualified Person and Batch Release" is under revision. The actual draft contains the following major changes when compared to the existing revision:

- A clarification of the term certification versus batch release
- New regulations concerning the sampling for EU reanalysis and release
- A better description of duties that have to be performed by the QP personally
- A clarification what tasks of the QP may be delegated within the Pharmaceutical Quality System
- Tougher rules and requirements on acceptance of third party audit reports
- A clear description how unexpected deviations affecting batches to be certified have to be handled

On main focus of the revision is the implementation of supply chain knowledge. The entire supply chain of the medicinal product including all starting and packaging materials must be documented and available for the QP, preferably in form of a comprehensive diagram.

Especially the supply chain requirements and the tougher regulations for sampling and testing for EU release will represent major challenges for the Pharmaceutical Industry.

**Mate Proprat**

## Continual production and certification procedure by QP

It is well known that companies in the manufacturing sector in every moment thinking about how to faster, better and in more efficient way make a products in order to survive in the market and to be competitive in general. The food industry is therefore a few decades ago introduced the continuous production, which is replacing the current batch or serial production. Such processes are well established in the production of liquid forms and biscuits which we consume very often.

In the past, the pharmaceutical industry did not follow those trends for two reasons, profit and strict regulations which did not allow such dramatic changes. However, a significant changes in pharmaceutical regulations started in 1985, when the first product is released to the market based on PAT, and after that introduction of Annex 17 Parametric release in 2002 as well as RTRT EMEA guidelines in 2012. In parallel FDA CDER (Center of Drug and research) gives recommendation that the pharmaceutical industry should have changed from rigid to agile in order to understand the process. All these regulations put the focus on the understanding of the processes and in process control parameters, instead of traditional approach of quality control of finished product.

JGL follows the trends and focus on implementation of three continuous production, in aerosols, sterile solutions and in solid dosage forms. The project aim is to increase process efficiency by 30% and to ensure 100% in quality of in process chemical and microbiological parameters. The first project of continuous production is almost fully implemented. The continuous mixer is installed and technical series were produced. The first physicochemical results show excellent homogeneity through the whole batch. Microbiological test results are still in progress but the preliminary data show microbial bioburden zero.

Certification of the batch manufactured in continuous production is based on Parametric release, Annex 17 GMP and RTRT guideline taking into consideration in process parameters. This is actually the heart of continuous production, which needs strict continuous control process parameters and constant checking those parameters from independent control systems.

Key Words: Continual production, Parametric Release, Real Time Release Testing

**Dr Jelena Đuriš**

## PAT and real time release

Modern pharmaceutical industry and quality systems are moving towards concepts that enable continuous monitoring of the product quality, in comparison to traditional end-phase quality testing. Process analytical technologies are the key tools for in-line, on-line or at-line monitoring of the critical process parameters and/or materials quality attributes that affect critical quality attributes of the product. PAT process monitoring tools most often applied are NIR and Raman spectroscopy.

Real time release is a system of batch release that gives assurance that the product is of intended quality, based on the information collected during the manufacturing process, through product knowledge and on process understanding and control. EU Commission recently issued revision of GMP Annex 17, pointing out the requirements for application of a Real Time Release Testing concept. Successful implementation of the real time release approach to batch release relies on the well-established control strategy and the added benefit is continuous process verification.

Key Words: process analytical technology, real time release, GMP annex 17, RTR guideline

**De Christopher Burges**

### What QPs need to know about statistics

Do QPs need to learn to love statistics? Well it depends! However perhaps the word love might be seen as mildly provocative or perhaps a bit too extreme. However being a QP was never an easy option was it? The days of a QP being expected to sit in an office in splendid isolation checking batch records and signing documentation are long gone. Some of us never did this anyway. Perhaps we were fortunate to work in organisations were the role of the QP was understood and who had resources to call upon including statisticians. Over the past 40 years many things have changed within the industry but the legal responsibility and professional duties have remained. The purpose of this talk is to present an overview of the statistical aspects the QP needs to be aware of in performing their routine duties. The topics of process control charting and the importance of process stability and capability are covered in more detail.

## Workshop 1

**Katarina Popović[1], Nataša Knežević[2]**

### RISK MANAGEMENT DURING DRUGS TRANSPORTATION

[1]Pharmanova d.o.o.; [2]JGL d.o.o.

Maintaining a good level of quality in global supply chains is a real challenge nowadays. Before a product even reaches the patient, it is likely that multiple ingredient manufacturers, suppliers, and distributors from different parts of the world have had a hand in making, storing, and handling the finished drug product. Multiply this complex chain of events by the number of available drugs and countries involved in both producing and consuming medicines and the vulnerable areas within the global pharmaceutical supply chain become quite evident. Drug products must be transported in a manner that ensures products will be maintained within an acceptable temperature range. Stability testing thus evaluates the effect of environmental factors on the quality of a drug substance or a formulated product which is utilized for prediction of its shelf life, determine proper storage conditions and suggest labeling instructions. A sound stability protocol not only eliminates unnecessary testing but also reduces manufacturing needs, cost and time.

Key Words: supply chain, product stability, good distribution practices

## Workshop 2

**Ljiljana Solomun[1], Slavica Kojić-Marinković[2]**

### OOS IN STABILITY STUDIES

[1]Ivančić i sinovi; [2]Pharmaswiss

OOS (out-of-specification) results within stability studies are even more complex than OOS results within release testing. Product on the market could be affected and this may lead to a recall. OOS investigation includes Phase I – laboratory investigation and Phase II – full investigation. Through Phase II all results gathered during previous stability studies of the same and similar products should be discussed. With regard to stability studies issue, it is important to make differences between OOS and OOT (out-of-trend) results. OOT results are a serious problem, neither scientific literature nor regulatory guidelines fully address them. OOS or OOT results could lead to change of storage conditions, shorter expiration date, change of release or shelf life specification, or even preformulation of the product.

## Workshop 3

**Valentina Marinković[1], Snežana Tvrdorijeka[2]**

### Conflict Management in QP Practice

[1]University of Belgrade, Faculty of Pharmacy, Belgrade, Serbia; [2]FHI Zdravlje a.d , Leskovac, Serbia

One of the biggest challenges of the Qualified Person in product release process is to react properly to the conflicts. Since the term conflict is a part of inter-personal relationships within which the conflicts are solved, communication is a central aspect of the conflict and its resolution. There are five basic styles of conflict management: competition, adaptation, avoiding, collaborating and compromising. Different styles of resolving conflicts are not evaluated, i.e. there are no better or worse, but they all have their place in the resolution of conflicts. One way to understand the conflict better is based on the analysis of what we know about that conflict and what we can find out if we are interested enough. This paper presents the analysis of conflicts related to the issue of rejection of products to the market. Conflict management, using appropriate tactics or techniques has been evaluated during the workshop.

Key Words: conflict management styles, qualified person, product reject