EDQM & European Pharmacopoeia: State-of-the-art Science for Tomorrow’s Medicines

International Conference organised by the European Directorate for the Quality of Medicines & HealthCare (EDQM), Council of Europe

19-20 June 2019, Strasbourg, France

Workshop on OMCL Network

Moderator
Dr Maria João Portela, Infarmed, Portugal
Official Control Authority Batch Release (OCABR), *human*: benefits, challenges, perspectives

Straßbourg, 19th June 2019

Volker Oeppling
Microbiological Vaccines
Head of Section

Topics

- Major Network Elements/Structures
- Timing of Official Control Authority Batch Release (OCABR) Testing
- Mutual Recognition of OCABR Test Certificates
- Benefits
  - system/network related
  - direct (assurance of product efficacy/safety and availability)
  - indirect
- Challenges
- Perspectives
**Major Network Elements/Structures**

- **OMCL Network**
  - (Official Medicines Control Laboratories)

**Pre-marketing activities**

- OCABR (Official Control Authority Batch Release)
  - Human Biologicals (doc+lab)
  - Veterinary products
  - OBPR (Batch Protocol Release)
  - GEON (General European OMCL Network)

**Post-marketing activities**

- Post-marketing Surveillance of MRP/DCP products
- Post-marketing Surveillance of Centrally Authorised Products (CAP)

**Timing of OCABR Testing**

- **Starting Material**
- Intermediate Stages
- Final Bulk Product
- Finished Product (FP) (Final Lot)
- Labelled Finished Product

**In process (release) testing**

- Ad. Subst./ Manufacturing
- Formulation
- Filling

- Parallel testing by OMCL (Final Bulk/Final Lot)
- EU Batch Release Certificate

- Manufacturer’s testing
- Testing by OMCL
Mutual Recognition of OCABR-Test Certificates

- One common system within EU/EEA+Switzerland+Israel (vaccines only). No duplication of batch release at national level
  - mutual recognition of testing within the network is mandatory by law (Art.114 Dir. 2001/83)

- Common (high) quality standard
  - OMCL needs QM certification (ISO 17025, Mutual Joint Audit)

- Sharing resources
  - Product groups accumulating in individual OMCLs
  - Subcontracting between OMCLs

Benefits (system related 1)
Benefits (system related 2)

- Focusing of expertise (+ technologies)
  - Expertise and also necessary equipment for special area of interest only (preparedness in case of quality defects)

- Risk based strategy applied by OMCLs
  - Batch release mandatory only for a subset of biological medicinal products (e.g. vaccines, blood products)
  - OMCL batch release guidelines foresee only retesting of some key elements (full testing by the applicant only)
  - Reduced in vivo testing strategies applicable for products "performing well"

Benefits (system related 3)

- Testing strategy chosen avoids delay of product release
  - "Parallel Testing"
  - Certification at the filling/lyophilisation lot level (not finally packed material)
Benefits (safety, efficacy, availability 1)

- **Identification of substandard lots (before product enters the market)**

  Some examples identified/highlighted by an OMCL:
  - Systematic shift in tetanus potency (20%) due to change in manufacturing (finally company went back to the former process)
  - Inhomogeneity in filling process; lower Antigen content towards the end of the filling process (equipment issue, correction of filling equipment)
  - Detection of substandard diphtheria potency (ongoing, probably a reference issue at the company)
  - Detection of systematic calculation errors (correction of SOP)

Benefits (safety, efficacy, availability 2)

- **Allows comparison between products (inter-company) by an independant body**
  - If fully identical method is applied across products/companies

- **Independent partner for the public with expertise in experimental producttesting**
  - E.g. to prove/disprove statements/test results published in the public domains
Benefits (indirect 1)

- **Major drivers/supporters of 3R activities (Refine Reduce Replace in vivo testing)**
  
  Some examples:
  - Replacement/deletion of „Histamin Test“ (test for residual pertussis toxin in mice)
  - Replacement of „NIH test“ (switch from lethal challenge in mice to serology in mice or even glycoprotein ELISA for rabies potency testing)
  - General Safety Test (recently complete deletion)
  - Diphtheria/tetanus potency by lethal challenge (switch to serology)
  - Deletion of test for reversion of tetanus toxoid (test in guinea pigs to be replaced by „Binacle ELISA“)
  - Switch from rabbit pyrogenicity to monocyte activation test (MAT)

Benefits (indirect 2)

- **Creates expertise within agencies**
  - Research in new testing technologies (including 3R)
  - Supports product assessment (experienced in product testing also including feasibility issues)
  - Partner in reference/methods development
  - Supports development in guiding documents (Ph.-Eur. monographs, guidelines)

- **Acceptance even outside the system**
  - EU-certificates frequently accepted by third countries
  - Even product assessed via Art. 58 (EU Reg., 726/2004) is tested by OMCLs
Challenges (1)

- Replacement of in vivo tests (towards full in vitro consistency concept)
  OMCLs are involved in e.g.:
  - VAC2VAC research activities
  - Glycoprotein ELISA for Rabies Potency

- More and more sophisticated technologies
  - NMR spectroscopy
  - Mass spectrometry
  - Raman spectroscopy
  - Multiplexing technologies (Luminex, Mesoscale)

- Optimisation of release process by companies (shorter time windows for OMCL release activities)

Challenges (2)

- Provide confidence to public about importance/functionality of the system
  - Identify and communicate benefits

- Mutual recognition of batch release outside EU/EEA
  - Currently also WHO has initiated a network (National Control Laboratories Network, WHO)
  - Requests for EU-certificates from non EU/EEA countries

- Optimize risk based concept
  - Intensify use of already existing test reduction opportunities
  - Think about extension of risk based concepts
Challenges (3)

- Need for new reference material (e.g. non-endotoxin pyrogens)
- Complex products (high valencies, e.g. 15/20-valent pneumococcal conjugate vaccines)
  - Improve communication between OMCL (contribution of several OMCLs for release of one individual lot)

Perspectives

- Specialization (strengthening individual OMCL in specific area)
- Method development (3R and others)
- New products
- Mutual Recognition agreements with additional countries
- World wide market
Thank you!

Questions?
Market surveillance studies: OMCL contribution to quality and safety of medicines on the market

Dr. Lone Stengelshøj Olsen, Head of the Danish OMCL

OMCL = Official Medicines Control Laboratory

- OMCLs are public institutions which support regulatory authorities in controlling the quality of medicinal products for human and veterinary use
- OMCLs test medicinal products independently from manufacturers
Role of OMCLs in Europe

- Post-marketing surveillance programmes
- Pre-marketing sampling and analysis
- Sampling and testing of generic medicines
- Analysis of unlicensed (unauthorised) medicines
- Analysis of counterfeit / illegal medicines
- Support in evaluation of the quality part of MA files
- Support of pharmacovigilance assessments
- Support of GMP inspections as experts
- Support in the framework of the European Pharmacopoeia
- Evaluation of quality defect reports

=> Public / animal health protection

Types of products analysed by OMCLs

- Medicines (finished pharmaceutical forms)
- Biological products (e.g. vaccines, blood derivatives)
- Active Pharmaceutical Ingredients (API)
- Excipients
- Herbals
- Radiopharmaceutical products
- Cosmetics
- Medical devices
- Diagnostic products
- Food
- etc.

Different responsibiltites in different OMCLs
General European OMCL Network (GEON)

– **1994**: the Commission of the EU and the Council of Europe decided to create a **Network of OMCLs**, to promote the collaboration in the area of quality control of marketed medicinal products for human and veterinary use.

**2019: 25th Anniversary of the GEON**

– **1995**: EDQM sets up the OMCL Network and acts as Secretariat => responsible for co-ordinating the Network activities and joint programmes, with the financial support from the EU. Work programmes are decided on an annual basis in collaboration with the National Authorities and, where applicable, the European Medicines Agency (EMA).

**2019: 24th Annual Meeting of the GEON**

Market Surveillance Programmes within the GEON

The EDQM coordinates voluntary collaborative programmes within the OMCL Network, with the aim of controlling the quality of medicinal products available on the European market.

“Classical” surveillance programmes are:

1. **MSS** (Market Surveillance Studies) – *nationally registered products*

2. **MRP/DCP** Post Marketing Surveillance Scheme (Mutual Recognition Procedure/Decentralised Procedure) – *generics*

3. **CAP** Sampling and Testing Programme (Centrally Authorised Products) – *biotech products*
Market Surveillance Programmes within the GEON

Incorporation of a risk based approach in market surveillance testing of OMCLs

- Planning and selection
- Sampling
- Testing
- Reporting
- Communication of results

A Risk Assessment Model is established

- Risk Factors Identified by the Quality Assessor During the Assessment of the Marketing Authorisation Application and Recommendations for Essential Quality Parameters to be Tested

- IT support for the collection of data ensuring data is available for users

The Identification (selection) of Post Marketing Risk Factors is pending to expand the model
An example of a risk based control project

The risk analyse of "Old" medicinal products (national approved)

- Review of variations
- Review of recalls
- Review of complaints
- Review of results from laboratory controls
- Review of non-conformities during inspections

One Marketing Authorisation Holder with many old products got a high risk score

The results

- The systematic risk based approach identified a huge gap
- All products are used in hospitals and most of them are critical for treatment of patients
- Close collaboration between the OMCL, the inspectorate, the assessors and the MAH to ensure the upgrade of the documentation according to a risk based working plan
Thank you for your attention
Active Pharmaceutical Ingredient Testing

how OMCLs can support the control of APIs?

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19 June 2019, Strasbourg

Agenda

- API context
- API testing, initiatives before 2011
- API Working Group
- An example of the OMCL Network collaboration
- API Projects organised by the API Working Group
- Conclusion
API context

- The worldwide threat of FALSIFIED OR SUBSTANDARD MEDICINAL PRODUCTS has indeed rapidly increased during the past decades.

- Any form of tampering or falsification that will affect the QUALITY OF AN API constitute a direct threat to patient health.

- Apart from falsification issues, significant GMP NON-COMPLIANCE ISSUES are identified via inspection activities.

Need for API testing by “independent” laboratories as OMCLs

API testing within the OMCL Network initiatives

- CAP Testing: API testing upon request by the rapporteur
- EDQM Fingerprint Projects: Falsified/low quality APIs detection
- Surveillance by some OMCLs: Programme, specific study, ... DK, FR, SE, ...
- CAP/MSS on Clopidogrel: API testing upon request by the rapporteur

FEW TESTING comparing to finished products.
Establishment of a **WORKING GROUP** dedicated to **APIs** within the **OMCL Network**

**WHO is involved?**
- Austria
- Belgium
- Cyprus
- Denmark
- France
- Germany
- Ireland
- Italy
- Luxembourg
- North Macedonia
- Norway
- Poland
- Portugal
- Sweden

**What is the MAIN GOAL?**
- To **DEVELOP STRATEGIES** and **PROGRAMMES** for the OMCL network.
- To contribute to the efforts of the European Health Authorities to **ENSURE THE HIGH QUALITY AND SAFETY OF API**s on the European market into the future.

**What is the WORKING PLAN?**
- **SUPPORT** a general **RISK ASSESSMENT TOOL** to focus market surveillance programmes on critical APIs.
- **ORGANISE** specific **MARKET SURVEILLANCE STUDIES** for determination of the **QUALITY** and **AUTHENTICITY** of APIs sources.
- **IMPROVE INFORMATION** and **SAMPLING SHARING** with respect to API testing in the OMCL Network.
DATABASE for OMCLs

- **DATA ENTRY** of the APIs each OMCL PROPOSES TO TEST with the main selected parameters.
- Possibility to **SHARE SAMPLES**.
- **INFORMATION** of all SOURCES and BATCHES tested, and the GLOBAL OUTCOMES are SHARED for each API.

About 40 to 50 different APIs CONTROLLED per year

**SAMPLES TESTED** come from ALL OVER THE WORLD, but mainly from:
- India, China: about 40%
- Spain, Germany, France, Italy, Ireland, Finland: about 30%
An example of the OMCL Network collaboration

**CONTEXT:** From June 2018

**N-Nitrosamines in Sartan APIs**

Contamination of Sartan APIs by Genotoxic N-Nitrosamines

- Candesartan
- Irbesartan
- Valsartan
- Olmesartan
- Losartan

WORLDWIDE CRISIS: EMA/EDQM - EUROPEAN AGENCIES – FDA – TAIWAN – CANADA ...

- CEP SUSPENSION
- ASMF REVIEW
- BATCH RECALL
- GMP INSPECTION

...
**ACTION PLAN:**

- Creation of **TESTING GROUP** of 13 OMCLs.
- **DEVELOP** and **VALIDATE ANALYTICAL METHODS**.
- Organise a coordinated **MARKET SURVEILLANCE**.

**Toxicological limits:**

<table>
<thead>
<tr>
<th>Active substance (max daily dose)</th>
<th>NDMA</th>
<th>NDEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan (32 mg)</td>
<td>96.0</td>
<td>0.300</td>
</tr>
<tr>
<td>Irbesartan (300 mg)</td>
<td>96.0</td>
<td>0.177</td>
</tr>
<tr>
<td>Losartan (150 mg)</td>
<td>96.0</td>
<td>0.640</td>
</tr>
<tr>
<td>Olmesartan (40 mg)</td>
<td>96.0</td>
<td>0.088</td>
</tr>
<tr>
<td>Valsartan (120 mg)</td>
<td>96.0</td>
<td>0.082</td>
</tr>
</tbody>
</table>

**ANALYTICAL METHOD TO DEVELOP:**

- **CHALLENGE OF SENSITIVITY** (target < 0.03 ppm)
  - Look for 1 mL in 33,000 L solution
- **9 DIFFERENT METHODS** developed by the OMCLs are **AVAILABLE** and **PUBLISHED** on EDQM website
  - For NDMA, NDEA, NMBA
  - By LC/UV, LC-MS/MS, GC-MS

**MARKET SURVEILLANCE BY THE NETWORK:** on 15/04/2019

- For **NDMA**: 249 APIs have been tested (and 2000 DP)
- For **NDEA**: 637 APIs have been tested (and 1007 DP)
**An example of OMCL Network collaboration**

*N-Nitrosamines in Sartan APIs*

**STRENGTHS**

- RAPID INVOLVEMENT of OMCLs.
- GOOD SHARING of standards, methods, samples.
- Good COORDINATION OF ACTIONS by EDQM.
- PROVISION OF RELIABLE ANALYTICAL METHODS, with satisfactory sensitivity for other OMCLs, industry, ...
- CONTROL of a LARGE NUMBER of APIs (and drug products).

The story is not over but it is GOOD EXAMPLE of how OMCLs can support the control of APIs.

**API Projects organised by API Working Group**

**Before 2011**

API Fingerprint Projects « feasibility »

**2013**

1st Study MACROLIDES AND STATINS

**2016**

2nd Study MORPHINE

**2017**

3rd Study OMEPRAZOLE

**2019**

4th Study SILDENAFIL

**LESSONS LEARNT:**

- Importance to have a HIGH NUMBER OF SAMPLES
- Limitation of a SINGLE-TECHNIQUE APPROACH by testing OMCL
- Importance of FINGERPRINTING METHODS to differentiate sources
Fingerprinting methods

What?

« An analytical method or a combination of analytical methods that reflect the chemical composition of a sample »

~ create a characteristic profile of a sample

Use?

- FT-IR (Ph. Eur)
- Herbal analysis
- Impurity profiling
- Differentiation of samples

Advantage?

- Highly informative
- Possibility to reveal differences between samples

Disadvantage?

- A lot of data
- Interpretability of the data

solution Chemometrics
MSSIFP03: Omeprazole

**What?**

- **Action**: Proton-pump inhibitor
- **Indications**:
  - Gastroesophageal reflux disease
  - Peptic ulcer disease
  - Zollinger-Ellison syndrome
  - Prevention of upper gastrointestinal bleeding
- **Forms**:
  - Base
  - Magnesium salt
  - Sodium salt

**Why?**

- A case of falsification detected by the German OMCL in Karlsruhe
- A lot of different manufacturer
- Challenge for the analysis

**Wherefore?**

1. MSS for related substances (Ph. Eur.)
2. Fingerprint information

**Ultimate goal**: expertise in fingerprinting for falsification detection

**Whom?**

<table>
<thead>
<tr>
<th>OMCL</th>
<th>Country</th>
<th>Samples Collection</th>
<th>Sample testing</th>
<th>Chemometric Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGES</td>
<td>Austria</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Scimens</td>
<td>Belgium</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>DKMA</td>
<td>Denmark</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>ANSM</td>
<td>France</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>CDQC</td>
<td>FYROM</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>LZG NRW</td>
<td>Germany, NW</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>CVUA</td>
<td>Karlsruhe</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>NIL</td>
<td>Poland</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>INFARMED</td>
<td>Portugal</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>MPA</td>
<td>Sweden</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>
MSSIFP03: Omeprazole

How?

1) Sampling:
   Each OMCL individually according to their sampling strategies
   Centralisation and dispatch through EDQM
   29 samples:
   - Aurobindo: 3
   - Quimica: 5
   - Lee: 3
   - Cadila: 6
   - Union: 5
   - Minakem: 2 (Mg-salt)
   - Miscellaneous samples: 5

2) Testing:
   - Monoethanolamine impurity by GC (LZG-NRW)
   - Related substances by HPLC (DKMA, CDQC)
   - Residual solvents by GC (MPA)
   - NIR (INFARMED)
   - Polymorphism by X-Ray diffraction (NIL)

3) Data analysis:
   ANSM, Sciensano and CDQC according to own chemometric protocols
   Comparison results with different:
   1) Pre-processing
   2) Algorithms
   3) Softwares
MSSIFP03: Omeprazole

Results:

Outline of the data

<table>
<thead>
<tr>
<th>29 samples</th>
<th>29 samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Impurity profiles (HPLC-DAD)</td>
<td>• Aurobindo: 3</td>
</tr>
<tr>
<td>• Residual solvents (GC-MS)</td>
<td>• Quimica: 5</td>
</tr>
<tr>
<td>• NIR spectra</td>
<td>• Lee: 3</td>
</tr>
<tr>
<td>• XRD spectra</td>
<td>• Cadila: 6</td>
</tr>
<tr>
<td>• NMR data</td>
<td>• Union: 5</td>
</tr>
<tr>
<td></td>
<td>• Minakem: 2 (Mg-salt)</td>
</tr>
<tr>
<td></td>
<td>• Miscellaneous samples: 5</td>
</tr>
</tbody>
</table>

MSSIFP03: Omeprazole

Results:

Data preprocessing

◆ Individual techniques:
  1) NIR + XRD: snv, data centering, second derivative, scaling
  2) Residual solvents: data centering and scaling
  3) Impurities: data centering
  4) NMR: no pretreatment

◆ Combined techniques: addition and mid level data fusion based on PCA
  1) XRD + RS
  2) XRD + NMR
  3) XRD + RS + NMR
  4) NMR + RS
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**Results:**

**Data processing**

1) Principal Component Analysis
2) Projection Pursuit
3) Hierarchical Clustering

**Results:**

**Individual techniques**

Impurity profiles (HPLC-DAD) vs NIR
MSSIFP03: Omeprazole

Results:

**Individual techniques**

![Graph showing results of individual techniques]
MSSIFP03: Omeprazole

Results:

Individual techniques

NMR

Combined techniques

- Based on the results of the individual techniques
  => Impurities and NIR are discarded

- Combined data sets:

  1) XRD + RS
  2) XRD + NMR
  3) XRD + RS + NMR
  4) NMR + RS

=> Obtained results = XRD
=> XRD dominates the data
=> combinations have no use
MSSIFP03: Omeprazole

Results:

Combined techniques

NMR + RS

Loadings:

1) aurobindo, Union and Minaken
   - NMR signal 4 (2-propanol), 9 (grease), 15 (acetate), 18 (aceton), 24 (Unknown)

2) Quimica, Lee, Minaken and Cadila
   - RS aceton and toluene
   - NMR signal 18 (aceton), 24 (Unknown), 26 (Unknown), 29 (Unknown)
MSSIFP03: Omeprazole

Conclusions:

◆ Individual techniques:
1) Good discrimination for XRD, RS and NMR
2) Only NMR differentiate between Cadila and Union

◆ Combined techniques:
1) XRD dominates when combined with RS and/or NMR
2) Best results NMR + RS
   ● Both types of data important
   ● Important variables are related (e.g. Aceton and NMR signal 18)

◆ General considerations:
1) Inclusion of NMR in future studies
2) Use of other spectroscopic methods (Mid-IR, Raman)?
3) Impurity profiles?

MSSIFP04: Sildenafil Citrate

What?

Action: Phosphodiesterase 5-inhibitor
Indications:
- Pulmonary arterial hypertension
- Erectile disfunction
Forms:
- citrate

Why?

- Viagra® is one of the most falsified medicines worldwide
- Sildenafil is a frequently encountered adulterant
- API with high risk of falsification
MSSI FP04: Sildenafil Citrate

**Wherefore?**

1) MSS for compliance to the Ph. Eur.
2) Fingerprint testing
   - Enhance differentiation between manufacturers
   - Detection of falsifications

**Context:**

- First combined CAP, MSS and API Fingerprint studies

For

- 1/ Synergies for the API sample collection
- 2/ Synergies in API testing

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**MSSI FP04: Sildenafil Citrate**

**Context:**

Programme

- **CAP**
  - Reference Products (including CTS)
- **API WG**
  - API
  - Finished Product
- **MSS**
  - API Fingerprint OMCLs (Enlarged Market Surveillance)
  - MSS programme OMCLs

Samples reception

- CAP programme OMCLs
- API Fingerprint OMCLs

Testing

- EDQM
  - API
- OMCL
  - Finished Product
MSSIFP04: Sildenafil Citrate

Context:

API testing:
- **Option 1:** the sampling OMCLs perform the tests on API according to the MSS protocol
- **Option 2:** the sampling OMCLs do not perform any tests on API and use the results from the API Fingerprint programme

MSS API – Proposed by the Scientific Advisor: Maria João Portela

- Compliance of the Sildenafil samples with the specification of the corresponding Ph. Eur. Monograph
  - Infrared spectroscopy (Mid-IR)
  - HPLC analysis for related substances-UV detection
  - Assay, Water, Impurity E (tbd)

MSS Finished Products (coated tablet, oral-dispersible tablet, powder for oral suspension)
- Identification, assay, related substances, dissolution

API – MSSFP – Proposed by the Scientific Advisor: Eric Deconinck

- Compliance of the Sildenafil samples with the specification of the corresponding Ph. Eur. Monograph
  - Infrared spectroscopy (Mid-IR)
  - HPLC analysis for related substances-UV detection
  - NIR
  - Raman
  - Residual solvents
  - XRPD
  - NMR
MSSIFP04: Sildenafil Citrate

**Context:**

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  - NIR
  - Raman
  - Residual solvents
  - XRPD
  - NMR

Potential synergies and resource savings

**Future perspectives**

1) Challenge:

2) Link with finished products:

**Lessons**
Future perspectives

How OMCLs can support the control of APIs

• Large MSS with repartition of the work throughout the network
• Analysis according to Ph. Eur. under certification/accreditation ISO17025 and OMCL guidelines
  => Results recognised across the Pan European OMCL network
  => Exchange of samples between OMCLs
  => access to state of the art methods
• Centralisation of the API testing in the network in the MRP/DCP database
• Network response in case of crisis cfr. Sartan
• Broaden fingerprint expertise within the network in case of falsifications
• Promoting Chemometrics in the network:
  ➢ position paper « benefits of chemometrics for OMCLs » in preparation
OMCLs Contribution against Falsified and Illegally-traded Medicines

Stephen Young, June 2019

Why?

Substandard and falsified medical products

31 January 2018

Key facts

- Substandard and falsified medical products may cause harm to patients and fail to treat the diseases for which they were intended.
- They lead to loss of confidence in medicines, healthcare providers and health systems.
- They affect every region of the world.
- Substandard and falsified medical products from all main therapeutic categories have been reported to WHO, including medicines, vaccines and in vitro diagnostics.
- Antimicrobials and antibiotics are amongst the most commonly reported substandard and falsified medical products.
- Both generic and innovator medicines can be falsified, ranging from very expensive products for cancer to very inexpensive products for treatment of pain.
- They can be found in illegal street markets, via unregulated websites through to pharmacies, clinics and hospitals.
- An estimated 4 in 10 medical products in low- and middle-income countries is substandard or falsified.
- Substandard and falsified medical products contribute to antimicrobial resistance and drug-resistant infections.
OMCLs Role

What? – expert analysis
What? – information sharing

EDQM Know-X database assists authorities in the fight against falsified medical products

As part of its activities against falsified medical products, the EDQM has put in place a database called Know-X. This database collates reports on falsified medical products that have been detected in Council of Europe member states.

The idea is to provide a user-friendly tool that will assist officials by expanding their knowledge and awareness of the problem of falsified medicines, provide a basis for the exchange of information, highlight and encourage collaboration between health and law enforcement authorities, and foster the sharing of analytical information on the testing of falsified and other illegal medicines within the Network of Official Medicines Control Laboratories (OMCLs).

What? – training/symposia

Previous Technical OMCL Falsified Medicines Training Sessions

14th and 15th Technical OMCL Falsified Medicines Training
16-17 October and 20-21 November 2018, Prague, Czech Republic

On 16-17 October 2018 and 20-21 November 2018, two technical training sessions for OMCLs on the testing of falsified and illegal medicines took place on the premises of the National Health Institute in Prague, the location of the Czech OMCL for human medicines (SUML). The sessions were the 14th and 15th in a series of hands-on training programmes for OMCLs co-organised by members of the GEON and the EDQM.
Example (UK, China)

A man has been jailed for eight years for his part in what has been described as the most serious fake medicine fraud in the UK. The fraud involved Peter Gillespie, a 54-year-old from Harfordshire, who was part of a £4.7m plot to bring two million doses of counterfeit drugs from China to the UK.

He was convicted of conspiracy to supply pharmaceutical products to pharmacists and members of the public and was sentenced by a jury at Gleaston Crown Court.

By removing authentic, properly manufactured and tested medicines, Gillespie and other fraudsters put public health at risk, the regulator, the Medicines and Healthcare products Regulatory Agency (MHRA), said.

Example (Turkey, Denmark, UK, US)

Fake Avastin Took Murky Path to U.S.

A recent case of a counterfeit cancer drug reaching the U.S. market is focusing attention on the role of overseas suppliers that are involved in bringing the medications to U.S. doctors. The FDA, the British National Health Service and the U.S. government all have been investigating the case. The fake Avastin was supplied by a company in Turkey, and the investigation is ongoing.

By Ben Reagen and Jimml Whelan

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Example (UK, Thailand)

Viagra gang members jailed for making £10million selling fake drugs
The gang could have caused "catastrophic damage" to the public

Example (UK, France, Switzerland)

Cancer ‘cure’ boss David Noakes jailed for 15 months

David Noakes said his company had 15,000 customers
Example (Germany)

German pharmacist gets 12 years for diluting cancer drugs

BERLIN (AP) - A court in western Germany has sentenced a pharmacist to 12 years in prison for diluting cancer drugs on a massive scale in order to finance his luxury lifestyle.

In its ruling Friday, the Essen regional court said defendant Peter S. had manipulated at least 14,000 drugs, the quality of which was "not insignificantly" diminished. The offenses took place in nearby Bottrop between 2012 and 2016.

Prosecutors accused the 48-year-old, whose forename wasn't provided for privacy reasons, of harming at least 27 patients, although earlier estimates put the number far higher.

The defendant allegedly obtained more than 50 million euros ($58 million) through the fraud, and used the money to build a villa with a large water sike.

He was arrested in November 2016 after pharmacy staff blew the whistle.

Example (Switzerland)

WHO says fake cancer drug Iclusig has been "traded globally"
Thank you for listening

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