Preventing counterfeit/falsified APIs
What role can pharmacopoeia play?

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Counterfeit/falsified APIs

- What is a counterfeit/falsified API
- How to prevent counterfeit/falsified API
- Is GDUFA (USA) the solution?
- Is the FMD (Europe) the solution?
- Can pharmacopoeia play a role?
- Take home messages
Counterfeit/falsified APIs

What is a counterfeit/falsified API?

- For some products it is easy to spot falsifications or to know that it is one

- Some salesmen don’t hide counterfeit...
Counterfeit/falsified APIs

What is a counterfeit/falsified API?

Any active substance with a false representation of:
(a) its identity, including its packaging and labeling
(b) its source, including its manufacturer, its country of manufacturing, its country of origin
(c) its history, including the records and documents relating to the distribution channels used.

This definition does not include unintentional quality defects and is without prejudice to infringements of intellectual property rights.

Counterfeit/falsified APIs

What is a counterfeit/falsified API?

• It is clear enough that counterfeit/falsified APIs are not recognizable as are the examples for watches and bags.
• But the consequences may be tremendous: One API batch => 10,000 - 200,000 patients.
Counterfeit/falsified APIs

What is a counterfeit/falsified API?

- Nobody has exact figures on API falsification
- Only one scientific study was done: On Gentamicin Sulphate API samples by the University of Würzburg (Published in 2003). Results indicate: From the API samples obtained from the market ca. 33% probably falsified, maybe even more than 60%

=> The problem is almost certainly “very large”, probably affecting millions of patients in Europe each year

Counterfeit/falsified APIs

How to prevent counterfeit/falsified API
Counterfeit/falsified APIs

How to prevent counterfeit/falsified API

• ENFORCEMENT

• Making laws, directives, guidelines etc is only effective when there is enforcement from the regulators. Putting responsibility in the hands of the users is in our view not that best solution.

• Performing world wide inspections (using e.g. ICH Q7A as the standard) and only allowing inspected API sites to deliver APIs would be a huge step forward.

• FDA (GDUFA) and EU (FMD) are taking actions. What about the rest of the world?

• Will there be a negative side effect from GDUFA and FMD, such as will patients outside EU and US get sub standard or even counterfeit APIs in their medicinal products?
Counterfeit/falsified APIs

Is GDUFA (USA) the solution?

- GDUFA= Generic Drug User Fee Application
- Fees paid will be used to
  * Hire additional reviewers
  * Hire additional inspectors
  * IT systems
  * Regulatory science

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Is GDUFA (USA) the solution?

- Planned results after 5 years:
  * backlog of ANDAs dealt with
  * ANDAs first review cycle back to 10 months
  * Parity between domestic and foreign inspections
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Is GDUFA (USA) the solution?
• Unfortunately no mutual recognition programmes for inspections with other regions/countries.
• That would save costs and would have as a result that inspections would be more harmonized as to the focus areas.

Counterfeit/falsified APIs

Is the FMD (Europe) the solution?
• FMD = Falsified Medicines Directive
• Per July 1, 2013 conditions for import of APIs into the EU will apply.
• Import of APIs from so-called “listed third countries” will be without restrictions. A third country can request to be on that list (so far, Switzerland has been approved, Israel and Singapore have been refused, Australia, Japan and USA are under assessment and Brazil has applied but has not yet sent information).
Counterfeit/falsified APIs

Is the FMD (Europe) the solution?

• For non-listed third countries:
  * a written statement from exporting authority

  or, exceptionally

  * GMP Certificate issued by EU authority following an inspection (Art 46b(4)) (waiver)

We believe that the written confirmation as to Article 46b(2)(b) does, by far, not constitute an adequate solution to ensure GMP compliance of active substances imported into the EU, especially originating from certain Asian countries. Doubts are deemed justified how such confirmations can be issued by authorities of third countries which themselves do not fulfill the prerequisites to be included on the list of equivalent countries as to Article 111b?
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Is the FMD (Europe) the solution?

• We believe it will take 5 to 10 years until some countries will comply with the requirements of Article 111b.

• As long as such countries are not on the list of the third countries with EU-confirmed equivalent regulatory system, export will depend on the “written confirmation” issued by local authority (Article 46b) → this might become a “loophole” for the EU to prevent drug shortages

• The actual “waiver”, Article 46b(4), would constitute the desirable option from European API industry view

What role can pharmacopoeia play?

• Today’s monographs consider product quality aspects and not manufacturing aspects (with some exceptions e.g. for biological products)

• The “new paradigm” states that quality should be built into the product and not be confirmed by (only) testing the final result. This is not reflected in today’s pharmacopoeia.

• The European Pharmacopoeia has adopted/included a number of the ICH Q-guidelines (e.g. Q3), but not those related to manufacturing/development aspects (Q7-Q11)
What role can pharmacopoeia play?

- Considering the definitions in the FMD, today’s pharmacopoeia would not contribute to preventing counterfeit/falsified APIs.
- There might however be options there, such as a general monograph on “manufacturing” referring to ICH Q7A

Take home messages

- Counterfeit/falsified APIs are a problem since they reach the patients through the legal supply chain.
- Issuing directives and laws is only effective when enforced.
- Pharmacopoeia could play a role, e.g. by having “manufacture conform ICH Q7A” as a prerequisite.