Opportunities for Improved Access to Safe and Efficient Medicines

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On behalf of IFPMA
Agenda

• Import testing – Background and current situation

• Is Import testing still needed?

• Import testing waiver

• Conclusions
What Is Import Testing?

Sampling and quality control (QC) testing required locally when products imported into country

- **Scope -** depending on the country
  - Pharmaceuticals, biological/biotechnology, vaccines
  - Active pharmaceutical ingredients (APIs), semi and finished products, and bulk drug products

- **Legal requirement**
  - In 35+ countries/market
    - (The European Union = 1 market)
Reality with Import Testing Today

• Delay in delivery to patients
  – Patients receive medicines with 4-133 days delay
  – Bounded stock in quarantine
  – Repeated tests along the global supply chain (a single drug product batch may be analyzed up to 32 times)

• Increasing the drug shortage risk
  – Blocked stock reduces the remaining shelf-life time (RST)
  – Risk of interrupted supply of medicines to patients (e.g. in case of investigation of false positive out of specification (OOS) results or other delays in testing)

• Misuse of resources
  – Under appropriate controls (discussed in subsequent slides), import testing does not reveal any additional risks to quality: 0.005% batch rejection rate*
  – Economic losses (about €3,000 in average per batch imported, full analysis)
  – Covering well controlled legitimate supply chain

*IFPMA survey: 1 out of 18,616 analysis; may be explainable by transport monitoring data
Import Testing Requirements Worldwide
Import Testing Requirements in Latin America

[Map showing the import testing requirements in Latin America with different colors indicating requirements: red for import testing, yellow for waivers/reduced testing, green for no import testing.]
Import Testing Requirements in North America
Import Testing Requirements in Europe
Import Testing Requirements in Africa
Import Testing Requirements in Asia
Why Additional Import Testing?

Historically, re-testing requirements may have been necessary:

• Mistrust of having quality products imported
  – Issues with the original product quality that may not have been found
  – The release testing was not performed adequately
  – Potential for disreputable suppliers to provide substandard product
  – Failure to detect deterioration on transportation

• Limited development of regulations and enforcement procedures
  – Failure to detect counterfeit finished products

• Other arguments
  – Loss of economic value in a country/region through the provision of employment
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Is Import Testing Still Needed?

• Re-testing (import testing) does not add any quality or safety benefits to patients
  – It covers the well controlled legitimate supply chain only

• Quality is controlled and maintained in the legitimate supply chain:
  – Product Development – quality is built in by application of control strategies developed specifically for products
  – Manufacturing - according to good manufacturing and distribution practices (GMPs and GDPs)
  – Validated processes and analytical methods
  – Quality management systems in place
  – Distribution risk assessment – risks are identified, monitored and effectively managed
**Controls and Oversight**

- GMP and product release
  - A holistic, independent release decision considers all available information on the performance in operations and that requirements for product specific monographs are met
- Control of suppliers and service providers (quality agreements, audits)
- Oversight by self-audits and regulatory inspections; domestic oversight most effective
- Stability studies
  - (ICH Q1 series; Q5C*)
  - Temperature excursion studies
- GDP and import/export operations

*Q5C – Stability Testing of Biotechnological/Biological Products*
Controls and Oversight (cont.)

- Quality check by the recipient upon importation – e.g. identification testing
- Safe and efficacious product for the patient
  - Uninterrupted control through the whole supply chain

Patients can receive medicines in real time
Refocus on Control of the In-country Supply Chain

Import testing covers only the well controlled supply chain
Considerations

Understanding the responsibilities and perform controls
- Release testing and supply chain oversight
- Quality management system (QMS)
  - GMP and controls by manufacturers and suppliers
  - Controls of the supply chain towards the market (GDP)

Procedural requirements
- Allowing reduced release specification upon importation
- QMS by national regulatory authorities (NRAs)
- Market surveillance studies (MSS)

Regulators

Industry

Protect patients

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Overview

If the manufacturer of a pharmaceutical, biotherapeutic or vaccine product:

– provides evidence that their product manufacturing, testing and storage/distribution systems are well controlled and validated;
– has implemented a proper quality system to assure compliance; and
– is under regular control of globally recognized inspectorates (e.g., PIC/S members) or the inspectorates of other competent NRAs,

there should be confidence by the importing NRA that the product is safe and effective and complies with registered specifications.

As a consequence, the manufacturer should be given the opportunity to obtain a waiver for redundant import testing.

*IFPMA Position Paper - Appropriate Control Strategies Eliminate the Need for Redundant Testing of Pharmaceutical Products, February 2016*
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Rationale to Support a Waiver for Import Testing

A rationale for a waiver application may contain, but is not limited to:

• Current control strategy at site(s) of manufacturing, packaging and testing activities and that each location is currently authorized to deliver product(s) meeting relevant GMP and GDP requirements and regulatory commitments

• Overview of NRAs which have inspected the specified locations and authorize the supply of the product(s) in scope provided by an independent authorized person/ responsible person/ qualified person
Rationale to Support a Waiver for Import Testing (cont.)

- A summary of the control strategy for product transportation and distribution to the countries to ensure the integrity of product quality from release to arrival in the country

- Checks made to consignments on arrival and mechanisms for assessing the impact of unexpected events (e.g., temperature excursions, if applicable) to deliver a conclusion that the integrity of shipment(s) has been maintained in the shipping channel and the quality attributes of product(s) have been maintained as confirmed in the Certificate(s) of Analysis (CoA) from the exporting manufacturing site
**Documentation to Support a Waiver for Import Testing**

Potential documentation to support the application may contain, but is not limited to:

- Specifications for the final product (country specific example)
- CoA for product(s) reflecting registered limits (country specific example)
Documentation to Support a Waiver for Import Testing (cont.)

- GMPs certificates for the sites of manufacture, testing, packaging and release; further certificates (e.g., WHO certificate of pharmaceutical product), as applicable
- Summary of shipping container/system qualification used and/or distribution risk assessment to support shipping
- Quality checks performed (e.g., identification, temperature monitoring) on in-bound shipments
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Implement quality risk management in the evaluation of supply of medicines to the market

- The level of effort, formality and documentation of the quality risk management process should be commensurate with the **level of risk**
  
  ICH Q9, Principle 2

Eliminate redundant import testing

- The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient
  
  ICH Q9, Principle 1

Consider surveillance testing

The illegitimate supply chain represents the greatest risk from counterfeit and substandard medicines
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For Further Reading


- S. Rönninger, J. Garbe, **Import Testing Turned into an Unnecessary Limitation of Patient Access to Medicines as Risks are Managed Effectively**, Pending publication
Thank You

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