WHA65.29
Addressing the Global Shortages of Medicines and Vaccines
CASE STUDY, PROGRESS AND ACTIVITIES
Case study

- Informal survey on shortages of lopinavir/ritonavir.
- Rapid root cause analysis noted planning issues with a sole source (product on patent) as the primary cause.
- Support from civil society to the DOH was provided to issue a voluntary compulsory license.
- Other manufacturers have not entered this market following the license. The patent holder dropped its price after the license was issued.
Progress to date

- Systematic review of the use of definitions related to shortages and stock outs of medicines and vaccines
- Mapping of vaccines market initiated
- Harmonized definition of shortages and stock outs drafted
- Initial observations from ICDRA, TBS on practices and solutions
- Schematic development for a reporting mechanism

http://apps.who.int/medicinedocs/en/d/Js22423en/
Key activities for 2017

- Identification, specifications developed for a global reporting mechanism
- Identifying medicines at high risk for shortages
- Assessing the severity of the problem
- Engaging the Health Data Collaborative efforts to identify core improvements in data quality
- Consultation on the development of a global reporting mechanism
- Engage in antimicrobial resistance monitoring efforts
- Collaborate with partners on surveys to estimate the magnitude of the problem
Observations from ICDRA

International Conference of Drug Regulatory Authorities

Cape Town

29 November - 2 December 2016

Workshop 6:
Shortages of medicines: what can regulators do to help?

Moderators:
Greg Perry, Medicines Patent Pool
Anban Pillay, DOH South Africa

Speakers:
Anders Vinther (Sanofi)
Gerald Heddell, UK
Ivan Knezevic, WHO

Discussion/ Recommendations:

• Government-owned manufacturing not commercially viable as a solution
• Further investigate financial influences, e.g., exchange rate fluctuations on API costs
• Promote transparency on cost of production
• Identify products or APIs at risk of shortage
• Promote dialogue between manufacturers, regulators and supply chain actors
• Promote transparency from industry on potential risk of shortages, especially through dialogue with regulators
• Continue with supply chain interventions
• Consider contingency stocks to mitigate risks for certain products
Collaborative efforts across WHO departments

*Essential Medicines and Health Products (EMP)*
*Immunization, Vaccines and Biologicals (IVB)*

<table>
<thead>
<tr>
<th>Vaccine-specific work (WHA69.25 &amp; SAGE 2016)</th>
<th>EMP Work on Definitions</th>
<th>Other Related IVB Work</th>
<th>Shortage Work Phases</th>
<th>Vaccine Specific</th>
<th>All essential Medicines tbc</th>
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</thead>
<tbody>
<tr>
<td><strong>Threats to Vaccine Supply</strong></td>
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<td><strong>Causes of Vaccine Shortages</strong></td>
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<tr>
<td><strong>Vaccine Demand Information</strong></td>
<td>EMP work on definitions plus other related IVB</td>
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<td><strong>Vaccine Supply Availability Information</strong></td>
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<tr>
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<tr>
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<tr>
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<td></td>
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<tr>
<td><strong>Shortage and Stock-out Technical Definitions</strong></td>
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<tr>
<td><strong>Magnitude and Nature of Shortage Problem</strong></td>
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<tr>
<td><strong>Global Medicine Shortage Notification System</strong></td>
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**Scope**

**EMP Work**
- Definitions

**Other Related IVB Work**
- Vaccine Specific
- All essential Medicines tbc

**Shortage Work Phases**

**Phase 1**
- Vaccine Specific
- All essential Medicines tbc

**Phase 2**
- Vaccine Specific
- All essential Medicines tbc

**Phase 3 tbc**
- Vaccine Specific
- All essential Medicines tbc

**Threats to Vaccine Supply**

- Vaccine-specific work (WHA69.25 & SAGE 2016)

**Causes of Vaccine Shortages**

- Vaccine-specific work (WHA69.25 & SAGE 2016)

**Vaccine Demand Information**

- EMP work on definitions plus other related IVB

**Vaccine Supply Availability Information**

- work on causes of vaccine shortages and WHO’s response all feed in to Phase 1 project work

**Current Mitigations**

- Based on directors’ feedback, Phase 2 work will make concrete proposals in terms of medium & long-term activities to pre-empt and mitigate shortages

**Set up Vaccine Exchange Forum**

- Phase 1 has focused on vaccine demand information, pricing, vaccine supply information and current actors’ activities

**Essential Medicines (WHA69.25)**

- Global Medicine Shortage Notification System is out of scope for Phase 1 and Phase 2, but could be addressed by EMP in Phase 3
DRAFT DEFINITIONS
**Core Definition Shortage:** The supply of medicines, health products, and vaccines identified as essential by the health system is considered to be insufficient to meet public health and patient needs.

**Core Definition Stock-out:** The complete absence of the medicine, health product or vaccine at the point of service delivery to the patient.

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<thead>
<tr>
<th>Supply Chain</th>
<th>Measurement</th>
<th>Variables</th>
<th>Considerations</th>
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<tbody>
<tr>
<td><strong>Demand</strong></td>
<td>Inventory Metrics Service Delivery Metrics</td>
<td>Developing vs Developed Member States Economic Considerations Quality Assurance Data Availability and Data Quality</td>
<td>1. Actors 2. Audience 3. Actions 4. Consequences</td>
</tr>
<tr>
<td><strong>Level 1 National</strong></td>
<td>Manufacturing: eg. Raw Materials, Active Pharmaceutical Ingredients, Products</td>
<td>Channels to Patients: eg. Central Stores, Health Facilities, Distribution Affiliates, Strategic Buffer</td>
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Initial definitions from systematic review

Supply, main findings from systematic review:
- mainly NMRA mechanisms with MA holders;
- focused on managing responses to problems;
- time-bound in terms of timeliness of reporting;
- linked to duration in terms of time to estimated resolution;
- targeting management of national level solutions for the public health system;

Demand, main findings from systematic review:
- referred mostly to procurement, planning and supply chain management related problems.
- included various types of disruptions at various levels;
- linked to the duration of the stock-out; however measured in terms of hours and days and not in terms of consequences to the patient of delayed treatment;

quality data cuts across all areas and reporting depends on clear definitions
Report to the EB : Definitions of shortages and stock outs of medicines and vaccines

On the supply side:
A “shortage” occurs when the supply of medicines, health products and vaccines identified as essential by the health system is considered to be insufficient to meet public health and patient needs. This definition refers only to products that have already been approved and marketed, in order to avoid conflicts with research and development agendas.

On the demand side:
A “shortage” will occur when demand exceeds supply at any point in the supply chain and may ultimately create a “stock out” at the point of appropriate service delivery to the patient if the cause of the shortage cannot be resolved in a timely manner relative to the clinical needs of the patient.

• Additional work will be needed to support reporting mechanisms.
• EMA is launching a coordinated approach across EU countries.
• Technical consultation proposed for July 2017.

EXAMPLES OF REPORTING MECHANISMS AND DISCUSSION
• Inventory of reporting mechanisms from FIP
• Underscores the need for a global reporting mechanism
• Descriptions show that most of the existing mechanisms are focused on specific markets (national, region and in some cases global)
• Mechanisms include NMRA, pharmacist associations, procurement networks and programs
• A shortage in one region may or may not affect other regions
• Publicly available information is mainly snapshot level

Case study

• Informal survey on shortages of lopinavir/ritonavir.
• WHO and others responded to identify root causes and noted planning issues with a sole source (product on patent) as the one of the causes.
• Support from civil society promoted a decision from the DOH to issue a compulsory license.
• Other manufacturers have not entered this market following the compulsory license.
Drug Shortages

Current and Resolved Drug Shortages and Discontinuations Reported

Search by Generic Name or Active Ingredient: Enter at least three characters

A drug receives Resolved status when the Drug Shortages Staff (DSS) determines that the market is covered, based on information from all manufacturers. The market is considered covered when supply is available from at least one manufacturer to cover total market demand. However, some manufacturers may not have all presentations available. DSS monitors the supply of products with Resolved status. For the most current supply information, contact the manufacturers.

Generic Name or Active Ingredient | Status
--- | ---
Asparaginase Erwinia Chrysanthemi (Erwinaze) | Currently in Shortage

Asparaginase Erwinia Chrysanthemi (Erwinaze)
Atropine Sulfate Injection

Currently in Shortage
Currently in Shortage
# Drug Shortages

## Current and Resolved Drug Shortages and Discontinuations Reported

**Report a Drug Shortage | Contact Us | FAQ | Background Info | Get Email Alerts | RSS Feed**

**Search by Generic Name or Active Ingredient:**

![Search bar](image)

**Start Over | Back to Previous Screen**

**Asparaginase Erwinia Chrysanthemi (Erwinaze)**

**Status:** Currently in Shortage

- **Date first posted:** 10/14/2016
- **Therapeutic Categories:** Hematology; Oncology; Pediatric

[Expand all](expand)

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**Jazz Pharmaceuticals, Inc. (Revised 05/01/2017)**

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Availability and Estimated Shortage Duration</th>
<th>Related Information</th>
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<tbody>
<tr>
<td>ERWINAZE 10,000 IU lyophilized powder supplied in a clear 3 mL glass vial 5 vial carton (NDC 57902-249-05)</td>
<td><strong>Currently in Stock</strong></td>
<td>Includes additional special handling instructions with product. Update to include for Intramuscular administration only, and use of 5-micron filter needle. Please see Dear Healthcare Provider Letter. Jazz will update <a href="http://www.Erwinaze.com">www.Erwinaze.com</a> at such time as they are able to provide an update on supply. Dear Healthcare Provider Letter</td>
</tr>
<tr>
<td>ERWINAZE 10,000 IU lyophilized powder supplied in a clear 3 mL glass vial 1 vial (NDC 57902-249-06)</td>
<td><strong>Currently in Stock</strong></td>
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</table>

**Shortage Reason (per FDASIA):**

- Other
Contents and structure of a reporting mechanism

• **Lessons learned from other applications:**
  – The more complex, the lower the response rates
  – User support is key to success in long term use

• Key components identified to date:
  – Product identifiers, but designed in the same manner as those in either adverse event reporting, SF reporting to support inter-operability of and analysis of data
  – Type of problem needs to address multiple situation from supply chain to quality recall to API shortage
  – Key information should include duration and extent e.g., estimated quantity
  – Clinical recommendations, where available, should be reported
Contents and structure of a reporting mechanism

• Public facing site with downloadable documents related to current shortages
• "Members only" section for reporting, limited to those trained or with an official capacity to report
• Downloadable data for trend analysis and other analytical capabilities
• Links to SF reporting and potentially AE reporting systems
• If possible, a future feature would be a country page that any reporting country could customize for national use
Future questions

• Aligning roles and responsibilities?
• How to encourage uptake of a reporting system that is global in nature, when many countries have limited national reporting?
• If better data on demand are available, will industry respond?
Essential Medicines and Health Products