EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Initiatives on Product Shortages Due To Manufacturing/GMP Issues

EMA Workshop on Shortages due to manufacturing and quality problems – Session 2

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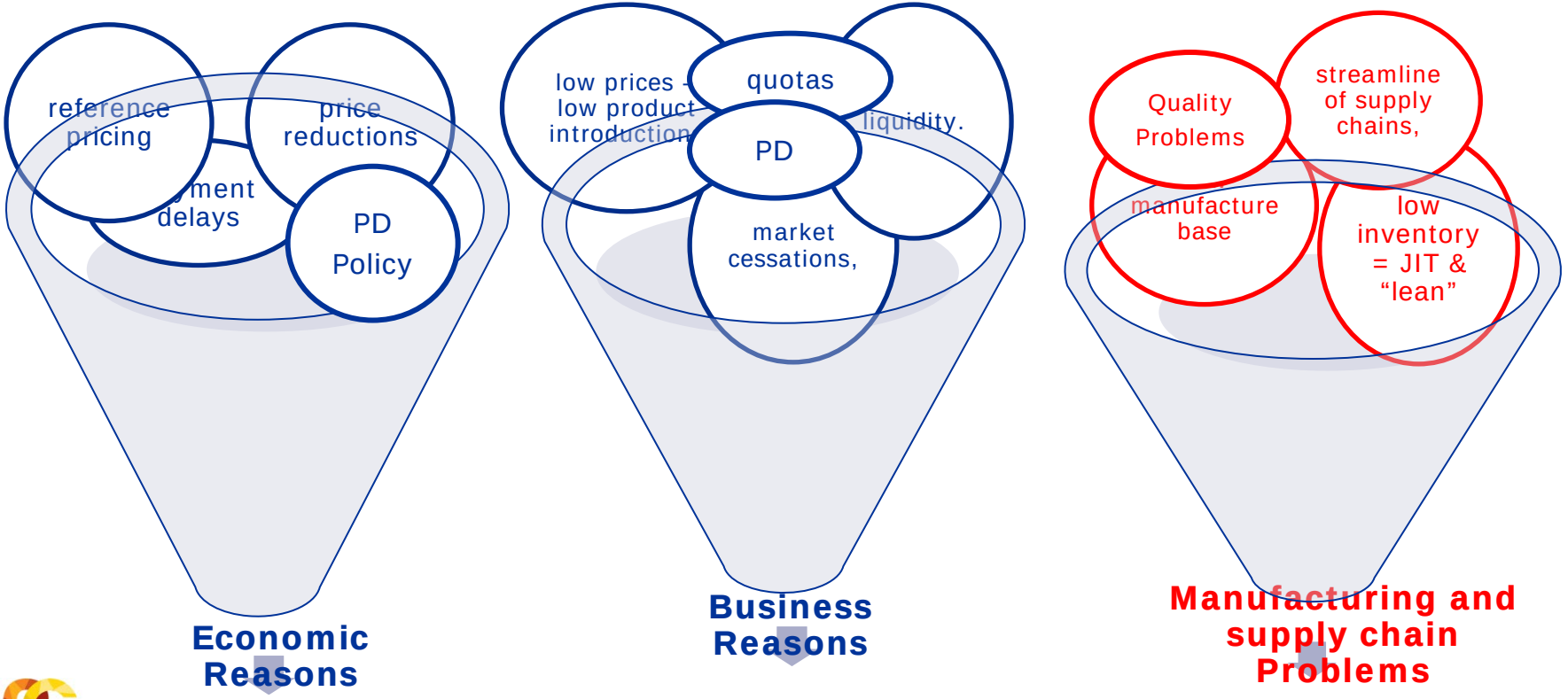
An agency of the European Union

Overview

- Background – EMA Reflection Paper
- Current Status; Communication and Prevention
- Points for discussion
- Structure of the day

Causes of Shortages of Medicines – From Birgli report



Why manufacturing and quality problems?

- Shortages due to manufacturing and quality problems usually present complex public health problem requiring multi-disciplinary team to assess risk-benefit.
- Flexibility sometimes needed to restore supply;
  - Restricted GMP certificates;
  - Accelerated assessment
  - Postponement of pre-approval EU inspection based on international partner inspection
  - Replacement and recall strategy
- Communication key aspect;
  - Patients – involvement of patients organisations on case by case.
  - Exchanging information with international partner Agencies.

Shortages – reflection paper

Reflection paper published November 2012.

- Virtual group on shortages created in January 2013
- First phase: Identify tools to assess reports of shortages
- Second phase: Industry to come up with proposed solutions

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22 November 2012
EMA/590745/2012
Patient Health Protection

Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice Compliance problems

1. Introduction

Ensuring the security and Good Manufacturing Practice (GMP) compliance of the manufacturing supply chain is an important responsibility of the Marketing Authorisation Holder (MAH) to ensure appropriate and continued availability of medicinal products for human use to meet the needs of patients in accordance with Article 81 of Directive 2001/83.

There is evidence that disruption in supply of medicines can lead to inter alia, a failure to treat; the use of less desirable, often expensive, unfamiliar alternative medicinal products; an increased potential for errors and poorer patient outcomes, caused by absent or delayed treatment or incidence of preventable adverse events associated with alternative medicinal products or dosage forms[1].

Recent unexpected disruptions to the manufacturing supply chain due to manufacturing/GMP compliance problems have resulted in acute and chronic shortages of important medicinal products in the European Union (EU) requiring changes to prescribing information, and initiation of patient allocation programs[2].

EU legislation currently requires mandatory pre-notification by MAHs of disruption of supply in the case of permanent or temporary cessations[3,4] and for manufacturers of medicines in the case of any defect that could lead to an abnormal restriction in supply[5].

In the United States (US), as a result of a high number of shortages of medicinal products, the Food and Drug Administration (FDA) have published at the end of last year a draft "Interim Rule" regarding

23 November 2012
EMA/708575/2012
Patient Health Protection

Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice compliance problems
Implementation plan 2012-2015

A Framework for assessment

- Developed common understanding of critical medicine/develop decision tree/clarify national input into EU advice/communication (public catalogue)
- Facilitate Benefit / Risk evaluation through template AR (points to consider) and closing AR (retrospective impact of shortage) plus resource guidance.
- Risk indicators for shortages (manufacturing and quality) developed to identify products at risk.
- Crisis situations resulting from product shortages addressed in context of EU Incident Management Plan (IMP)
- Develop international co-operation to foster sharing of information – quarterly multi-lateral TC.
- Revision of GMP Guide / Compilation of Community Procedures

Raising Awareness / Proactive approach

- Raise awareness of the impact of product shortages and stimulate industry reaction and improvement in Business Continuity Planning.

- Promote better and proactive risk management by Marketing Authorisation Holders – resilience in supply chains.

- Held a workshop with stakeholders

- http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2013/10/event_detail_000796.jsp&mid=WC0b01ac058004d5c3

Improving Quality of Pharmaceutical Operations –Better use of GMP / QRM

- *"The industry's risk management tends to be very reactive rather than proactive. Sustained pressure is needed to bring about a change in a manufacturer's approach to quality risk management and supply chain security". "Reflection paper on medicinal product supply shortages due to manufacturing and quality issues", EMA, 2011 .*
- *"Despite the proliferation and significant impact of risk events, most pharmaceutical companies still have not implemented comprehensive, forward looking programmes to proactively assess sources of quality and compliance risks and mitigate them before harm occurs". "Flawless, From Measuring failure to building quality robustness in Pharma", McKinsey and Co., 2014, p203.*

Points for Discussion today

1. Do we need to work on developing an identical trigger point for notification – **Workstream 3**
   - (a) agreed definition of a “meaningful disruption” to supply (b) triage process that evaluates the risk associated with a potential supply disruption.
   - A harmonised reporting content and format.
   - An agreed time-point and recipient of the information for all NAP’s and CAP’s.
2. Do we need a harmonised definition of “Drug Shortage” – **Workstream 2**
3. Do we need to develop harmonised principles for an agreed public communication plan (linked to current mechanisms for safety communication plan). – **Workstream 3**

See results of survey?

Points for Discussion today

4. How do we encourage industry to implement comprehensive, forward looking programmes to proactively assess sources of quality and compliance risks and mitigate them before harm occurs? Can we develop a “push/pull” approach with the PDA & ISPE documents. - **Workstream 1**

- Maintaining the positive engagement of the industry associations into the future;
- raising awareness of the industry to take up and use the documents developed.

5. Can principles apply to other parts of the supply chain; e.g better business continuity planning, application of GDP principles to distribution network. – **workstream 4**

Possible Action Items for Next Implementation Plan

6. How can we become more proactive in assessing supply chains and identify those that may be of higher risk to disruption in supply?

- Risk assessment
- Metrics
- Analysis of previous shortages

What do we see as the next steps after the workshop

- All presentations and a meeting report will be published on our web site.
- Update and publish the EMA Implementation plan.
- Continue with the virtual group on shortages;
- Continue with the inter-association task force.
- Intermediate tri-partite discussion on an ongoing basis to follow up on implementation.
- A follow up meeting in 2 years time.

Thank you for your attention

Any Questions?

Further information

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