



Shortages of medicines

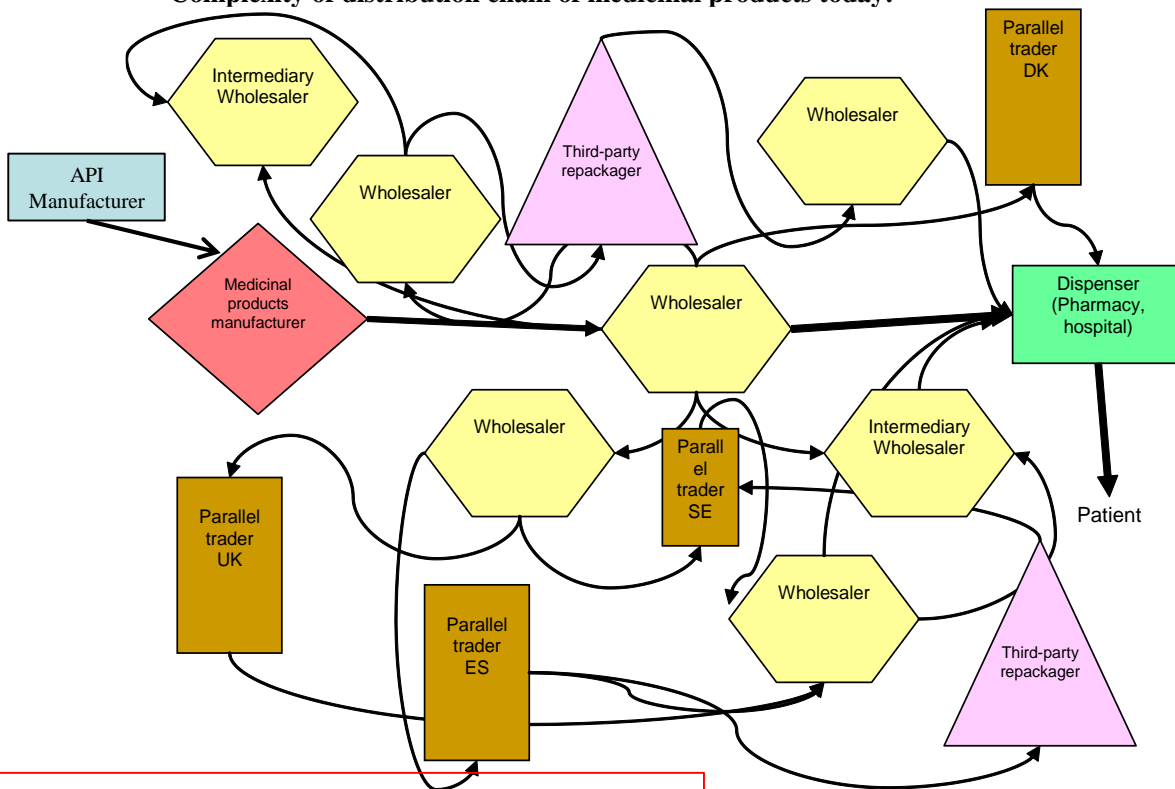
Responses to the Questionnaire on the Measures implemented in the MS territories in the context of Article 81 of Directive 2001/83/EC

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***Agnès Mathieu-Mendes
Deputy Head of Unit
DG SANTE - Unit B4: Medical products:
quality, safety, innovation
DG Health and Food Safety
European Commission***

Background

Complexity of distribution chain of medicinal products today:



Causes of shortage

- Manufacturing problems e.g. GMP
- Insufficient stock available for the market
- Economic reasons



- **Call of the Council and the European Parliament** to examine and monitor Article 81 of Directive 2001/83/EC
- **Goal:** exchange information to address more efficiently shortage of medicines
- **28 replies** (27 MS+NO)

Directive 2001/83/EC

➤ **Article 81**

Obliges the MAH of a medicinal product and the distributors of the said medicine to ensure, within the limits of their responsibilities, appropriate and continued supplies so that the needs of patients are covered.

➤ **Article 23a**

Obliges the MAH to notify the NCA if the product ceases to be placed on the market (at least 2 months in advance). Upon request by the competent authority, the MAH shall provide with all data relating to the volume of sales/prescriptions.

1. How is the obligation of continued supply transposed as far as MAH are concerned?

- Transposed in a literally sense by most of respondents.
Additional provisions:
 - Information about the amount of product that can be delivered, measures to prevent/overcome supply difficulties, pharmacies should be provided with the unavailable medicine within 48h...
- Five MS did not indicate that the national legislation requires the MAH to ensure continued supply.
- Purchasing policies also differ amongst health insurers possibilities to include items in contracts with the MAH (e.g. mandatory delivery, periodic report of supply, penalty, selection of another supplier as long as the shortage persists).

2. What are the responsibilities of WD stemming from the transposition of the obligation of continued supply (i.e. public service obligation)?

- WD are obliged to ensure continued and adequate supply in most MS. Varying additional requirements:
 - Distributor's right to request from the MAH a supply corresponding to its market share,
 - Maximum delivery time,
 - Notification and expected duration of the discontinuation,
 - Mandatory Stocks
- In general, MS do not distinguish between full-line and other distributors (only 4 MS make a distinction).

3. What are the limits of their responsibilities in your country?

Different limits reported:

- Availability from manufacturers or other WD (e.g. no API available);
- Responsibility of the WD limited by products they stock;
- Responsibility of the WD limited to certain products (reimbursed/with price agreement);
- Delivery time depends on the distance;
- Public service obligation applies only to full-line wholesalers;
- WD do not have to be proactive and investigate other ways of supply;
- WD and manufacturers may apply for exemption from obligatory storages in some situations.

4. What are the responsibilities of the manufacturers and how are they connected to the responsibilities of the MAH and the WD? Is consultation with the authorities and notification obligatory?

- In general, there are no specific responsibilities for manufacturers. Some MS require:
 - obligatory stocks
 - ensuring continuous supply
- Contracts between MAH or manufacturer and stock lists. One MS organises meetings between the different members of the distribution chain.
- Responsibility for notification is placed only on the MAH. In 4 MS, the manufacturers are also required to notify.

5. Is there a specific definition of product supply disruption or shortage in your national legal order or other regulatory guidance? Is it linked to a specific medicinal product and to a specific territory? Is it linked to the public service obligations referred to under questions 1 and 2?

- Most MS do not have a specific definition in their national legislation.
- 3 MS have a definition and 4 MS have definitions/classifications in their internal procedures:
 - Linked to a product/reference group/territory sometimes
 - Not linked to the public service obligations (2 MS)

6. Are there specific legal and/or other regulatory measures for critical or essential medicines? Do you have a definition of critical or essential medicines? Do you use the WHO list of essential medicines or apply another solution?

- 13 MS have no specific legal and/or regulatory measures, 6 MS have some measures: buffer stocks, specific legislation/special monitoring for life savings or essential medicines.
One MS applies a decision tree.
- 5 MS have a definition of critical/essential medicines, 4 MS use the definition adopted by the EMA.
- In general, each MS has its own list (based on the WHO list sometimes).

7. Which other actions (not mentioned under questions 1 and 2 and not related to Article 23a) are the MAH, distributors, or pharmacies required to take when anticipating or experiencing product supply disruption? Which legal or regulatory measures are in place?

- Prevention/mitigation plans for critical medicines with measures to be taken (security stocks, alternate production sites...)
- Agreements between different stakeholders,
- Pharmacies are obliged to deliver the product to the purchasing part/to hold stocks corresponding to its usual customer needs,
- Information to hospitals/pharmacies/healthcare professionals,
- One MS has developed best practice guidelines on shortages.

8. With regards to Article 23a: Do you make this information available to WD or pharmacies? Is there any other compulsory reporting of interruption of supply to the NCA/WD/pharmacies or to patients? Is this information publicly available? Are there penalties for non-compliance?

- Information available to distributors/pharmacies
 - Notification tools
 - Emergency call centres

- Other compulsory reporting measures:
 - Notification at least one year in advance if critical medicines
 - WD obliged to provide with data on sales volumes
 - MAH should notify its intention to withdraw the product from a third country.

- Information publicly available at NCA's websites

- Sanctions for non-compliance in most MS

9. Do you have any specific export restrictions in place to mitigate the shortage or the risk of shortage of medicines? If yes, what is their precise scope and what criteria are they based on? (e.g. prior notification for shipments within a certain timeline, dynamic list of products...)

- No specific restrictions in 16 MS.
- Export restriction measures in 11 MS:
 - In the same way for exports to the EU/third countries in 8 MS,
 - General and/or individual measures,
 - Substitutable medicines are taken into account in 7 MS,
 - Part of public service obligation in 7 MS,
 - List of specific medicinal products with availability problems/mandatory reserves in most MS.

10. How are you determining and monitoring the shortage situation (e.g. by comparing supply and consumption data) for a particular medicinal product?

- Most common practices involve:
 - Contacts with the industry
 - For monitoring the shortage situation, MS compare supply and consumption from the concerned MAH
- Linked to export restrictions in 6 MS. Not linked in 8 MS.
- More than half of the respondents is considering the use of the EU secure repository system.

11. Are there specific penalties for interruption of supply/shortages? If yes, did you impose sanctions during the last 10 years ? Have the penalties for shortage resulted in reluctance from the MAH to inform you about shortages, or in deregistration of the medicinal product?

- Most authorities foresee sanctions:
 - Not applied in the last 10 years in most cases. Some exceptions for non reporting of interruption of supply or for non-compliance to the public service obligation leading to warning letters, suspensions of authorisation or financial penalty.
 - No reluctance from the MAH to inform the authorities/deregistration has been reported.
- 8 MS have no specific sanctions for interruption of supply.

12. In the case of a MAH informing you of its plans to discontinue the marketing of a medicinal product, where no other alternative is available, what actions are taken? Is there a dialogue with the MAH?

- Dialogue with the MAH is most cases (1 MS has a dedicated working group),
- Other actions:
 - Shortage impact and substitution assessment
 - Essential medicines cannot be withdrawn until an alternative solution is identified (1 MS),
 - Special/exceptional import and manufacturing authorisations,
 - Fee reduction for the MAHs of essentially important products under discussion (1 MS),
 - Information to different actors and healthcare professionals (3 MS).

13. Can you describe some real life examples on how to act on shortage of essential medicinal products, in order to minimize the consequences of the shortage? What has worked, and what has not worked?

- Examples provided by 24 MS. Successful actions reported by MS can be summed up as follows:
 - Open dialogues with companies and shortage impact assessment,
 - Increasing stocks, exceptional import and manufacturing authorisations, export restrictions,
 - Limitation of the quantities distributed to ensure a uniform supply,
 - Restriction of use, priority given to hospitals supply,
 - Short time assessment of a linked regulatory request,
 - Communications to healthcare professionals,
 - Informing the EMA/other international regulatory authorities,
 - Fee reductions.



Thank You