



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Patient Health Protection

## Decision tree on escalation from national to European level

Shortages due to GMP non-compliance/quality defects

### 1. Introduction

GMP non-compliance/quality defects may lead to a shortage of a medicinal product, if it is decided that it is necessary to prohibit importation and/or release of a batch or to withdraw batches from the market. Though in general such action based on GMP non-compliance/quality defects is good precautionary practice and at the discretion of the Member States when products are authorized nationally, there might be incidents where it is necessary to elevate the discussion to agree on a harmonized risk management strategy at a Union level in order to protect public health.

The principles set out in this paper may also apply when shortages due to other reasons are encountered, at the Member States' discretion.

### 2. Problem statement

Supply incidents caused by GMP non-compliance/quality defects may be managed and controlled with the aid of the EU regulatory network incident management plan for medicines for human use.

At the moment there are no standardised criteria in determining whether the EU regulatory network incident management plan for medicines for human use should be initiated for supply shortages due to GMP non-compliance/quality defects.

HMA has requested EMA to develop a set of criteria that could be used by Member States to decide if a discussion on a European level is necessary. The current document sets out a decision tree which would facilitate the decision on when such escalation to a European level could be considered.



## 3. Decision Tree

### 3.1. *No escalation to European level is required if:*

- a. shortages are limited to a single Member State (although noted that this situation may change over time);
- b. the duration of the shortage is limited and not considered relevant from a clinical point of view (e.g. for vaccines, vaccination may be postponed for a few weeks), although this situation may evolve over time.

### 3.2. *Escalation to a European level may be considered if:*

- a. the product is considered to be a critical medicinal product in a Member State and there is evidence that indicates that the shortage will affect more than one Member State. It is possible that there may be differential supply of GMP compliant/GMP non-compliant product between Member States;
- b. a decision to keep a suspected defective product on the market may have possible safety implications (e.g. sterility is not guaranteed) that may indicate the need for Union advice on appropriate risk minimization measures to be taken to allow continued use of the suspected defective product;
- c. the product at issue is considered to be non-critical but the concern is due to critical GMP non-compliance/quality defects which may affect other products on the Union market;
- d. the product is considered to be non-critical but shortages may have an impact on public health (e.g. owing to the number of users or the characteristics of the patient population).

Discussion should always take place on the lowest possible level and only be escalated for further discussion a European level in case there is an interest at Union level identified.

## 4. Actions at Union level

Once a Member State or several Member States have decided that an escalation to Union level is necessary, the following principles should be followed in determining which Committee at the Agency should take the lead in the assessment and communication strategy. It is proposed that shortages only affecting centrally authorised products (CAPs) as well as shortages affecting both CAPs and non-CAPs are subject to the CHMP's review. Should more than one Rapporteurship be affected, a lead Rapporteur will be nominated by the Committee. Should a shortage only affect non-CAPs, the Member State(s) should escalate the issue to the CMD(h) for a harmonised response at Union level. PRAC will be consulted by the Committees as necessary.