

Analysis report on root-causes

Work Package 5

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List of abbreviations

API	Active Pharmaceutical Ingredient
CHESSMEN	Coordination and Harmonization of the Existing Systems against Shortages of Medicines – European Network
EC	European Commission
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
GMP	Good Manufacturing Practices
HMA	Heads of Medicines Agencies
MAH	Marketing Authorization Holder
MS	Member State of the European Union
NCA	National Competent Authority
SPOC	Medicine Shortages' Single Point of Contact
TFAAM	HMA/EMA Task force on Availability of Authorised Medicines for human and veterinary use
TWG-1	Thematic Working Group 1
WP	Work Package
wp	Working Party

Introduction

Medicine shortages are a growing issue in the European Union (EU) and present a major problem for the quality and continuity of patient care ⁽¹⁾. Treatment regimens, health of EU citizens and, ultimately, the resilience of health systems in Member States (MS) are affected by this issue ⁽²⁾, as it increases workload for healthcare professionals and has economic repercussions ⁽³⁾. Medicine shortages have been a serious concern in the EU for several years and have increased during the COVID-19 pandemic ⁽⁴⁾. The European authorities are particularly involved in improving the availability of medicines and numerous initiatives have been launched in recent years. For instance, the new EU Pharma Strategy, adopted in November 2020, specifically aims to secure the supply of medicines across the EU and avoid shortages. The European Medicines Agency (EMA) is also focused on improving the availability of medicines authorised in the EU and leads several dedicated initiatives such as the Task Force on the Availability of Authorised Medicines for Human and Veterinary Use (TFAAM), jointly with Heads of Medicines Agencies (HMA) or the Medicine Shortages Single Point of Contact (SPOC) working party, that is responsible for monitoring and reporting events that could affect the supply of medicines in the EU ⁽⁵⁾.

The CHESSMEN Joint Action (Coordination and Harmonisation of the Existing Systems against Shortages of Medicines – European Network), co-funded by the European Commission (EC), was created to strengthen the European coordinating structure in relation to identifying, managing and preventing medicine shortages, as well as optimising the use of the available resources of all Member States ⁽⁶⁾. CHESSMEN officially started on January 16th, 2023, and one of its main objectives is the identification of the root causes of medicine shortages.

The identification of the root causes of medicine shortages is essential to address their mitigation and help prevent future ones. Enhancing the comprehension of the situation that has led to a shortage, allows Member States to implement practical measures to ensure medicine availability and/or to devise strategies to reduce the risk of shortages. E.g. if the shortage is due to a problem with the active pharmaceutical ingredient (API) manufacturer and a new API manufacturer has been proposed, the National Competent Authority (NCA) could expedite the variation to include that new manufacturer in the dossier. The identification of the root causes might also allow the Marketing Authorisation Holder (MAH) to take appropriate measures to secure medicine's supply, minimise the duration or reduce the severity of the shortage.

In most EU countries it is mandatory for the MAH to report medicine shortages to the NCA ⁽⁷⁾ and most have a national shortage notification system for this purpose ⁽⁸⁾. This report is usually done through a shortage notification form and the reason of the shortage is one of the mandatory fields included in most of them ⁽⁷⁾. Moreover, several national shortage notification systems include a template with predefined categories of root causes, so the MAH can select from ⁽⁷⁾. In this manner, NCAs record the root causes of shortages and proceed to assess their impact, alongside the rest of the provided information within the shortage notification. The information of the reason of the shortage is also a mandatory field in the shortage notification template proposed by HMA/EMA TFAAM in the *Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders (MAHS) in the Union (EEA)* ⁽⁹⁾, which reinforces the importance of having this information when addressing medicine shortages. However, despite the fact that in most cases the cause of the shortage is indicated, the information provided is often quite general and does not specify the underlying root cause behind. Another challenge faced when analysing the root causes of medicine shortages is the absence of standardised concepts, as each NCA has its own way of operating. Consequently, in 2019, the SPOC working party (named SPOC network

prior to the adoption of the *Regulation (EU) 2022/123 of the European Parliament and of the Council of 25 January 2022 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices*), defined and categorised the different shortage root causes to enhance harmonisation among EU Members ⁽¹⁰⁾. The eight defined root causes are listed in Table 1.

Quality issues	Unforeseen disruptions within the manufacturing process leading to quality defects (API or finished product), including recalls.
Manufacturing issues	Unforeseen disruptions within the manufacturing process caused by GMP compliance problems (API or finished product). Manufacturing issues also include capacity issues.
Regulatory issues	When requirements or obligations relating to the grant of the authorisation have not been fulfilled after authorisation and ‘placing on the market’, e.g. Brexit. Failure to implement safety features, i.e. MAH failure to implement the unique identifier and the tamper evident features on the pack are also considered regulatory issues.
Safety and efficacy issues	If the medicinal product lacks therapeutic efficacy (or decrease efficacy), there are new safety risks identified requiring precautionary action, or the risk-benefit balance of the medicine is no longer favourable.
Unpredicted major events or natural disasters	May indirectly lead to shortages of medical products, e.g. the ongoing swine fever in China or the earthquake in Japan in 2011.
Unexpected increased demand	Due to previous Qdefects, due to market cessation/shortage of alternative products (e.g. generics), due to great awareness about a specific disease prevention or new treatment guidelines and/or recommendations of physicians’/veterinarians’/other healthcare professionals’ organizations, change in reimbursement conditions, change in epidemiology.
Distribution issues	Distribution channel structures, parallel trade (also includes export to outside of the EU), quotas, supply chain policy (e.g. DTO), logistic issues.
Commercial reasons	Company-driven decisions linked to business aspects such as pricing negotiations; discontinuation; change in reimbursement status; low sales (i.e. low number of patients); business strategies prioritising other markets.

Table 1. List of definitions and classification of different shortage root causes made by SPOC working party in 2019.

Work Package 5 activities

Work Package 5 (WP5) of CHESSMEN Joint Action is responsible for carrying out the identification of root causes of medicine shortages in EU and European Economic Area (EEA) countries. Therefore, as a preparatory task, a review of documents identified with relevant information on root causes of medicine shortages was carried out to find out what information was available in literature and what information needed to be collected. The results are included in the deliverable 5.2. *Review on existing documents or information relating to root causes of medicines shortages in the EU* and stated that medicine shortages were caused mainly by manufacturing issues, followed by commercial reasons and unexpected increased demand. Shortages were also driven by distribution and regulatory issues to a lesser extent, according to the information provided by literature. However, the information on the underlying root causes that originated these issues was scarce in the documents reviewed. One of the most relevant studies on this subject is the study on medicine shortages commissioned by the EC and published in 2021, Technopolis study, which carried out an in-depth analysis of medicine shortages and the root causes behind them. A more detailed analysis of the root causes collected in countries such as Portugal and Ireland was conducted but information on other countries was missing.

WP5 also launched a survey in August 2023, via SPOC working party, to gather information on the management of medicine shortages in the different Member States and their definition. One of the questions included was whether it was mandatory to report the cause of the shortage when notifying the NCA and if so, whether a template is provided with different cause-options for the MAH to choose from. The results of the survey, to which 21 out of the 29 EU/EEA countries responded, are included in deliverable 5.1 *List of key definitions relating to shortages of medicines* and showed that it is mandatory to indicate the root cause when reporting the shortage in most countries (19/21). Moreover, 17/21 (80,9%) countries confirmed that they have a template for MAHs to indicate the reason of the shortage. However, categories included in each template differ considerably between countries, so a more in-depth analysis was needed. Therefore, this report aims to explore in detail the information included in the templates as the way the information is collected influences the root causes recorded in each country.

Additionally, it should be taken into account that there is an interconnexion between the different technical work packages of CHESSMEN. Below is an outline of the deliverables of WP5 and their relation to other technical packages (Figure 1).

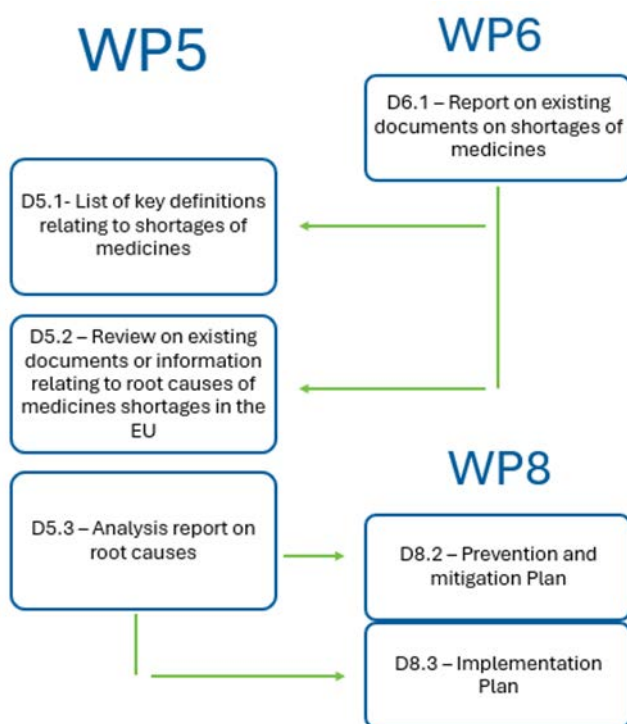


Figure 1. Flow chart of WP5 activities and their interconnexion with the other technical work packages of CHESSMEN.

Objectives

This report aims to delve deeper in the identification and analysis of root causes of medicine shortages in EU/EEA countries. Based on the review conducted in the previous deliverable, an accurate analysis and categorisation of the identified root causes will be performed.

In order to achieve this goal, the root causes included in the national shortage notification systems and their frequency of occurrence will be analysed. In addition, relevant stakeholder perspectives will also be taken into consideration to complete the analysis.

Methodology

1. Analysis of the root causes of medicine shortages extracted from national shortage notification systems

The analysis of the root causes of medicine shortages extracted from national shortage notification systems has been carried out by analysing the results of two surveys. Firstly, WP5 launched a survey to EU Member States, Iceland and Norway (29) via SPOC working party (Annex I). The results are included in the deliverable 5.1 *List of key definitions relating to shortages of medicines*. However, the responses to the question “Is it mandatory for the MAH to inform the cause of the shortage? Yes/No. If yes, do you have a template to mark the cause?” included in the aforementioned survey have been further analysed within this report given that the findings hold significant value for the analysis of root causes. 21 countries initially responded. Clarifications were requested via email from some NCAs with the collaboration of Thematic Working Group 1 (TWG-1) of the HMA/EMA TFAAM. In addition, the NCAs that had not initially responded to the survey were contacted again to increase sample size. This enabled the gathering of responses from six additional countries, which resulted in a high rate of response (27/29), and a total of 17 root cause’s templates used by NCAs to gather information on the root causes of medicine shortages during the shortage notification were obtained.

Subsequently, a second survey was designed to collect data on the frequency of the different root causes in EU/EEA countries. This enabled new templates to be collected, bringing the total to 24 (Figure 2). [The details of the survey will be described in section 2.1].

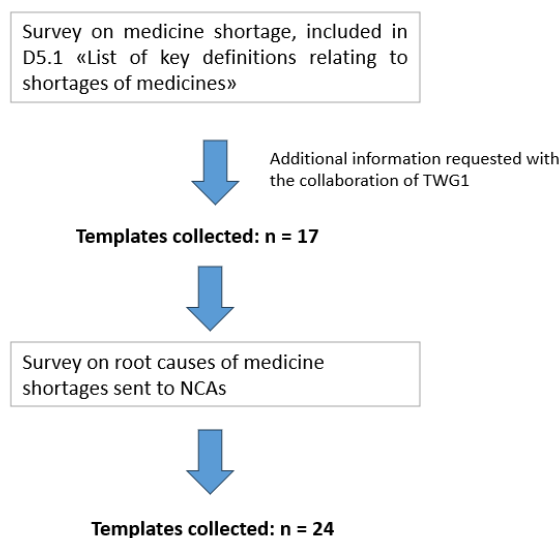


Figure 2. Flow chart of the process followed to collect information on the templates used by NCAs to collect information on the root causes of medicine shortages.

Data analysis

A descriptive analysis was carried out to identify the main characteristics of the templates used to register the root causes of shortages during the shortage notification. This involved the analysis of the number of categories included in the templates, calculating measures of central tendency, as well as the analysis of the type of root causes included. To simplify the responses obtained, some categories were merged or renamed. Given the wide range of options and the challenge of comparing the information between countries, the different root causes included in the templates were grouped according to the classification of root causes proposed by SPOC working party in 2019. The category “other” was analysed too.

2. Analysis of the root causes of shortages in EU/EEA countries in 2022 and 2023

Two surveys were designed to collect information on root causes of observed shortages in EU/EEA countries in the last two years (2022 and 2023).

2.1. Survey on root causes on medicine shortages sent to NCAs

The survey on root causes of medicine shortages sent to NCAs in EU/EEA countries was designed to extract information on the frequency of the reported root causes in each Member State based on their national-root cause classification system. On the one hand, confirmation was sought as to whether the root cause-options included in their template had been correctly interpreted by WP5, as the root causes obtained in the previous survey were pre-populated and those very similar were grouped or renamed. Furthermore, a free text field was included to add any information they considered necessary. On the other hand, NCAs were asked to provide the frequency (%) of root causes of reported shortages in their countries in 2022 and 2023, as well as the total number of shortages reported per year. Additionally, they were asked whether the information on the classification of root causes and number of shortages shared was public or confidential. The instructions of the survey are provided in Annex II.

The survey was sent to EU Member States, Iceland and Norway, via SPOC Working Party on May 30th, 2024. All countries (29) responded but only 27 shared data on the root causes of their shortages. Clarifications were requested via email from some NCAs.

Data analysis

The analysis of the frequencies (%) of the root causes of medicine shortages was carried out using the data provided. However, data from countries were excluded if the total of the frequencies provided did not add up to 100%, allowing for a 5% margin of error (95-105%). Countries that did not provide the total number of shortages were also excluded from the frequency analysis, as this omission prevented obtaining the absolute numbers necessary for a comparative analysis. It should also be mentioned that the analysis included data provided by countries that, despite not having a template, still recorded the frequencies.

After application of the selection criteria, frequency data from 23 countries in 2022 and 24 countries in 2023 were included in the analysis and the frequencies provided (%) were converted to absolute numbers to allow for analysis of all countries combined. Please note that for a certain country only the data from 2023 could be analysed as data for 2022 was not available. Furthermore, data was grouped according to the root cause classification

proposed by SPOC working party in 2019, resulting in a total of eight groups. The category “other” was also included since it was incorporated in most templates.

Additionally, the grouped root causes were analysed by region, according to the geographical classification defined by the European Union (EuroVoc/ EUR-Lex) (11). The classification followed is detailed below:

- **Northern Europe:** Denmark, Estonia, Finland, Latvia, Lithuania, Sweden, Norway and Iceland.
- **Western Europe:** Germany, Austria, Belgium, France, Ireland, Luxembourg and The Netherlands.
- **Southern Europe:** Spain, Greece, Italy, Cyprus, Malta and Portugal.
- **Central and Eastern European Countries:** Bulgaria, Croatia, Slovakia, Slovenia, Hungary, Poland, Czechia and Romania.

2.2. Survey to Industry EU Trade organisations

An additional survey was conducted to get the pharmaceutical industry's view on what were the root causes responsible for medicine shortages in EU/EEA countries. In order to narrow down the responses, respondents were asked to rank from 1-8 the frequency of the root causes of medicine shortages defined by SPOC working party: 1 being the most common root cause and 8 the less common root cause. In addition, a free text field was included to add any other causes not covered by the aforementioned classification. The survey is provided in Annex III.

The survey was circulated to 14 Industry EU Trade organisations via EMA Stakeholders and Communication Division on June 5th, 2024.

Data analysis

The responses were categorized into four groups based on the responses received: 1-2 “very frequent”, 3-4 “frequent”, 5-6 “infrequent” and 7-8 “very rare”.

3. Limitations of the analysis of root causes

Data analysis has several limitations due to the significant differences in data collection across various countries. Besides, it is assumed that all shortages share the same characteristics, even though the definition and reporting criteria differ significantly across countries. Other characteristics such as the number of marketed medicines per country, the population, or the price of medicinal products, have also not been considered when comparing the shortages by region. Moreover, when grouping root causes according to the SPOC working party classification, some errors could have appeared due to subjectivity in their inclusion and also because certain countries categorise multiple root causes under a single category. In addition, an error was assumed when converting the frequencies’ percentages to absolute numbers since not all of them sum up to 100% (5% margin of error allowed). In certain cases, the percentages could not be converted as the total number was not available. Regarding the analysis of responses from Industry EU Trade Organisations, there are also limitations. Not all organisations responded and among those who did, some did not adequately rank the indicated root causes from 1-8.

Results

1. Analysis of the root causes of medicine shortages extracted from national shortage notification systems

After sending out the surveys, responses were collected from 29 NCA in the EU countries, Iceland and Norway, which resulted in a 100% response rate. The responses indicated that the national shortage notification systems of 24 (82,8%) countries included a template with pre-defined categories of root causes to register them during the notification of the shortage. However, 5 countries do not have in place this system and collect the root causes mostly through a free text field (Figure 3).

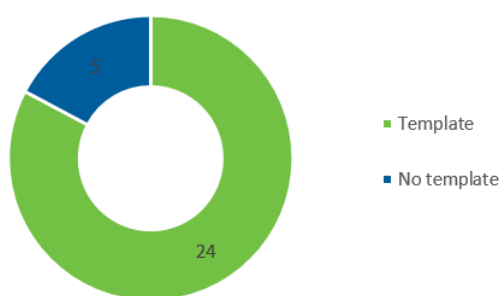


Figure 3. National shortage notification systems with and without a template to register root causes of medicine shortages.

The templates from the aforementioned 24 countries have been further analysed. The analysis revealed that the pre-defined categories of root causes included in templates vary among countries, as well as the number of categories included, ranging from 2 to 39 (Figure 4). The mean value of categories per country was 12, with the median at 10 and mode at 6.

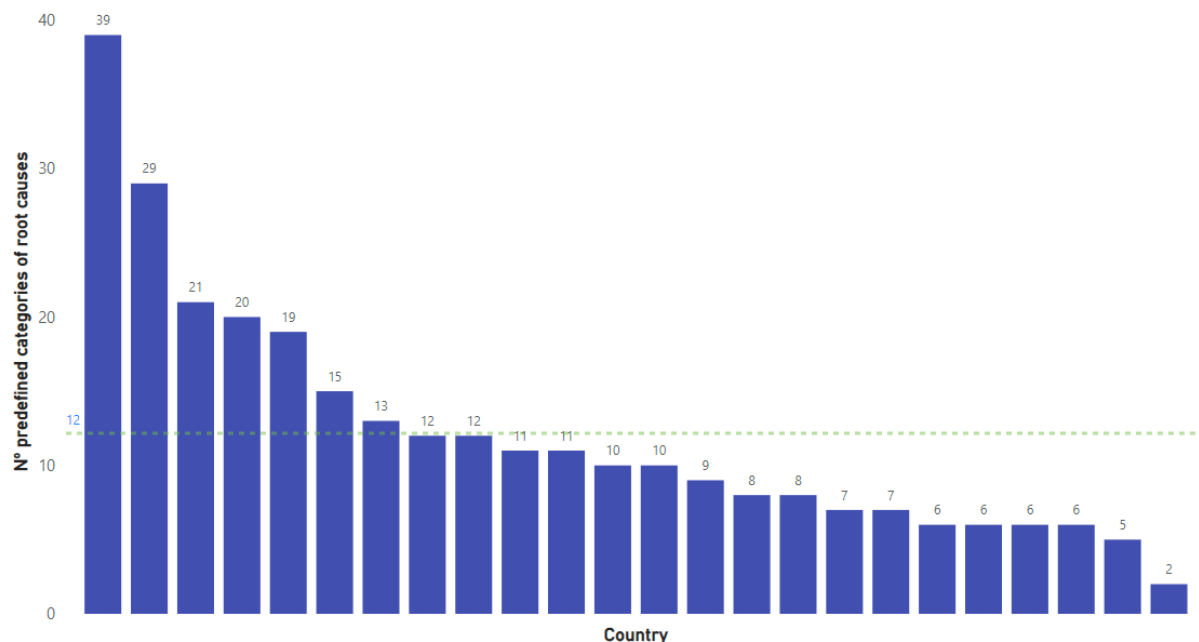


Figure 4. Number of predefined categories of root causes included in each template.

The categories included in the 24 templates were grouped according to the SPOC working party root cause classification. The category “other” was also added (Figure 5). The grouping visualises that all NCAs (24/24) include manufacturing related issues in the categorisation of root causes in their national shortage notification systems. Additionally, the majority (87,5%) includes distribution issues and unexpected increased demand. To a lesser extent, commercial reasons, regulatory and quality issues categories are included in around 75% of templates, 62,5% of the templates include a section to register other issues. Finally, it is worth mentioning that categories of unpredicted major events/natural disasters and safety and efficacy are only included in seven and three of the templates analysed, respectively.

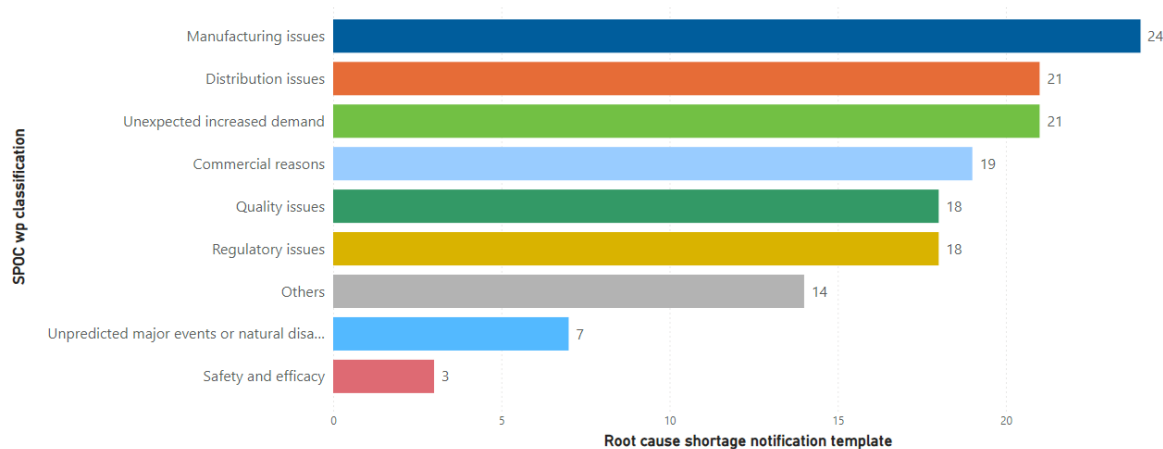


Figure 5. Type of categories of root causes included in the analysed templates according to SPOC working party classification.

2. Root causes of medicine shortages recorded by NCAs in the last two years

The survey on root causes of medicine shortages sent to NCAs was designed to extract information on the frequency of the reported root causes in each Member State based on their national-root cause classification system. Of the 29 countries surveyed, 27 shared the frequency data for the different root causes that led to medicine shortages in 2022 and 2023. However, three countries were excluded from the analysis for not meeting the criteria set out in the methodology. In total, root causes of 83.266 shortages (36.454 in 2022, 46.812 in 2023) from 24 countries have been further analysed in this report.

To analyse the root causes of the medicine shortages over the past two years, data was grouped according to the root cause classification agreed within the SPOC working party in 2019 (see Table 1). Eight major groups were obtained, and the category “other” was also added since it was present in most templates. The results per country are shown in Figure 6, where it is observed that, in most countries, the main root cause was manufacturing issues. Notable exceptions are M71 where the most common reported cause were distribution issues, and F89 and C44 where the most common were commercial issues. Unexpected increased demand was also quite frequent in most countries in both years.

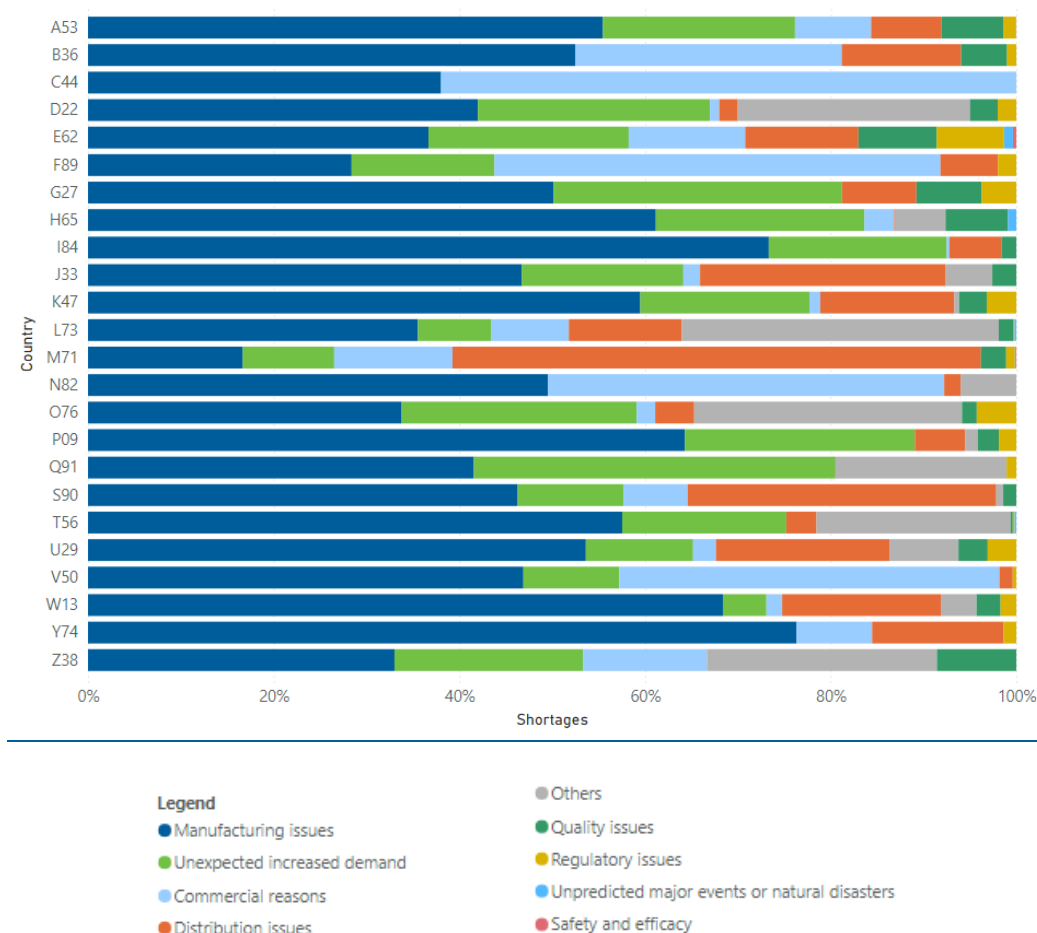


Figure 6. Frequencies of root causes of medicine shortages per country in 2022 and 2023 grouped according to SPOC working party classification.

2.1. Analysis of root causes of medicine shortages in 2022 and 2023

The results of the analysis of the total shortages for 2022 and 2023 (Figure 7) showed that manufacturing issues were responsible for half of the shortages notified (50,6%), followed by unexpected increased demand (16,7%), commercial reasons (11,2%) and distribution issues (10,6%). To a lesser extent shortages were caused by quality (2,6%) and regulatory issues (1,3%). Shortages caused by safety and efficacy issues, and unpredicted major events were virtually unaccounted for in the various national shortage notification systems. In addition, it is noteworthy that 6,9% of shortages were due to other issues.

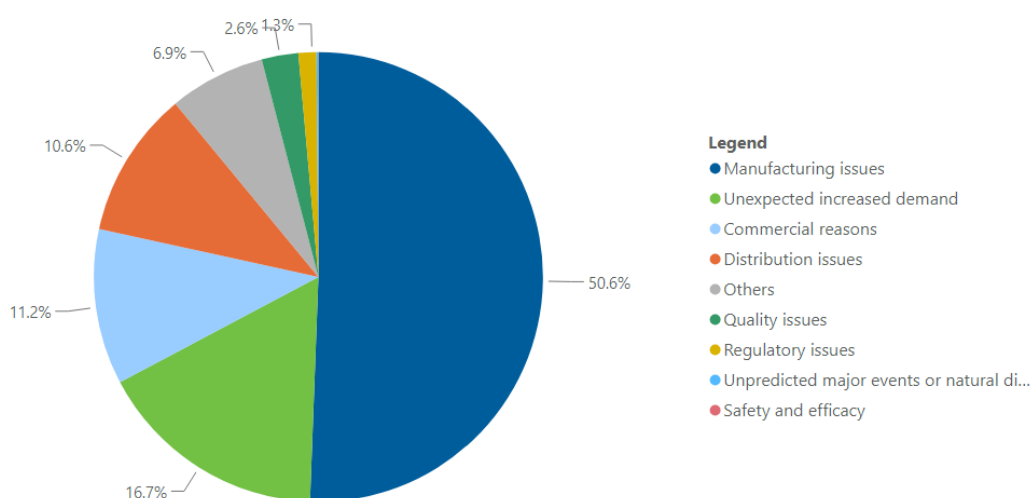


Figure 7. Root causes of medicine shortages in 2022 and 2023 in EU/EEA countries, grouped according to SPOC working party classification.

A closer examination of the shortages per year (Figure 8) revealed that the distribution of root causes was very similar in 2022 and 2023. The exceptions were commercial reasons, which went from the fourth most common root cause in 2022 to the third most reported in 2023, and distribution issues which dropped from third to fourth place.

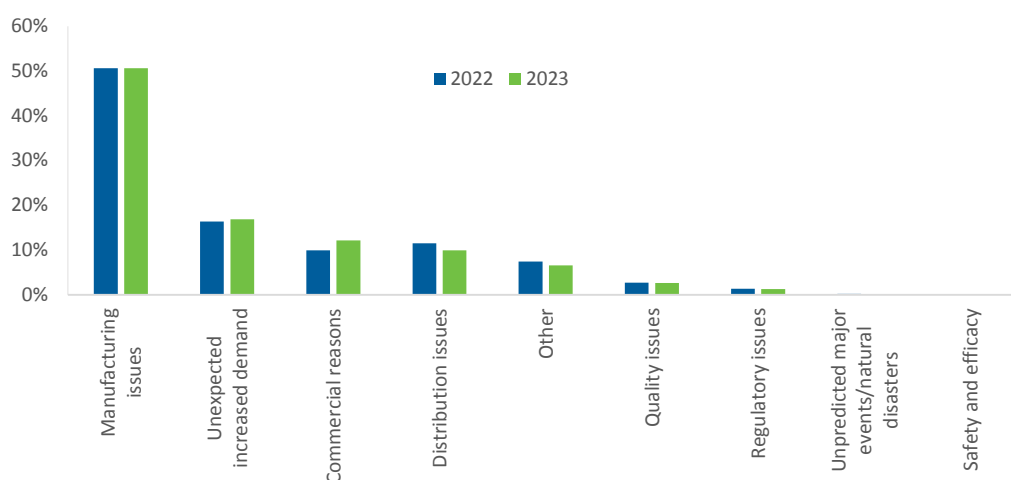


Figure 8. Root causes of medicine shortages in 2022 and 2023 in EU/EEA countries, grouped according to the SPOC working party classification.

Manufacturing issues

Manufacturing issues were the main root cause of medicine shortages in the countries analysed (50,6%). Moreover, all responding countries have indicated that they register this root cause in their national shortage notification systems. However, the record of these issues varies greatly between countries. Some follow the SPOC working party classification and collect these issues in a general way under the name of manufacturing issues (22,5%), while others include more manufacturing-related root causes such as capacity constraints, delay in manufacturing or API not available, which represented 14,0%, 7,6% and 2,4% of total shortages, respectively. To a lesser degree, countries include additional root causes in their templates which represented a very low percentage of the shortages analysed (< 1%). Table 2 shows the 16 different root causes grouped under manufacturing issues in the countries analysed, the number of these shortages under each root cause during 2022 and 2023 and the number of countries whose template includes that root cause. Change of the pharmaceutical form is included in the template of one member state but was not reported in any of the analysed years.

SPOC WP classification	Shortages		Shortages (%)		Total Shortages 2022 & 2023 (%)	N° templates including the root cause	
	2022	2023	2022	2023			
Manufacturing issues	18.412,5	23.332,8	50,6%	50,6%	50,6%	24	100%
Manufacturing issues	8.422,7	10.114,5	23,1%	21,9%	22,5%	19	79%
Capacity constraints	4.758,0	6.767,8	13,1%	14,7%	14,0%	11	46%
Delay in manufacturing	2.686,4	3.584,4	7,4%	7,8%	7,6%	6	25%
API not available	891,4	1.071,4	2,4%	2,3%	2,4%	13	54%
Delay/ Issue in the release of the finished product	659,0	559,0	1,8%	1,2%	1,5%	7	29%
Raw materials/ Ingredientes not available	294,8	397,2	0,8%	0,9%	0,8%	4	17%
Packaging materials not available	165,9	213,6	0,5%	0,5%	0,5%	4	17%
Problems at other manufacturer	181,4	141,5	0,5%	0,3%	0,4%	2	8%
Change of manufacturing procedure	86,9	161,7	0,2%	0,4%	0,3%	2	8%
Site transfer	93,0	118,4	0,3%	0,3%	0,3%	3	13%
Excipients not available	101,4	101,5	0,3%	0,2%	0,2%	3	13%
GMP non compliance	55,5	85,1	0,2%	0,2%	0,2%	6	25%
Changes on the manufactured product	12,5	3,2	0,0%	0,0%	0,0%	0	0%
Planning issues	1,1	12,1	0,0%	0,0%	0,0%	2	8%
Change of the pack size	2,5	1,5	0,0%	0,0%	0,0%	1	4%
Change of the pharmaceutical form	-	-	0,0%	0,0%	0,0%	1	4%

Table 2. Root Causes related to manufacturing issues (2022-2023).

Unexpected increased demand

Unexpected increased demand was the second most common root cause of shortages in EU/EEA countries, accounting for 16,7% of analysed shortages. This category is included in most templates (21/24) and no subcategories have been included in any country. Only three countries do not register unexpected increased demand as a root cause for medicine shortages.

Commercial reasons

Commercial reasons were responsible for 11,2 % of analysed shortages. This category is included in most templates (19/24) and sub-categories are often included to detail what the root cause is. By examining the categories listed in the various templates and the reported shortages in 2022 and 2023, it was observed that the most frequent ones, in addition to commercial reasons, were marketing discontinuations (4,5%). However, it is only recorded in nine of the 24 EU/EEA countries for which the templates were analysed. Four countries also

registered temporary marketing cessations as root causes of shortages. To a lesser extent, shortages were originated due to changes of MAH or price. It is worth mentioning that price is only included in three templates. Table 3 shows the seven different root causes grouped under commercial reasons in the countries analysed, the number of these shortages reported under each of these root causes during 2022 and 2023 and the number of countries whose template includes the root cause.

SPOC WP classification	Shortages		Shortages (%)		Total Shortages 2022 & 2023 (%)	N° templates including the root cause	
	2022	2023	2022	2023			
Commercial reasons	3.613,47	5.608,93	9,9%	12,2%	11,2%	19	79%
Commercial reasons	1.630,1	3.334,8	4,5%	7,2%	6,0%	17	71%
Marketing Discontinuation	1.787,0	1.936,5	4,9%	4,2%	4,5%	9	38%
Price	134,0	229,1	0,4%	0,5%	0,4%	3	13%
Temporary marketing cessation	46,9	84,1	0,1%	0,2%	0,2%	4	17%
Change of the MAH	10,4	22,9	0,0%	0,0%	0,0%	6	25%
Prioritisation of supply to other countries	3,8	1,5	0,0%	0,0%	0,0%	2	8%
Insolvency proceedings of the manufacturer or MAH	1,3	-	0,0%	0,0%	0,0%	1	4%

Table 3. Root Causes related to commercial reasons (2022-2023).

Distribution issues

Distribution issues represented 10,6% of analysed shortages and it is a category included in most templates (21/24), although the denomination and sub-classification vary considerably between countries. Most of the templates analysed do not have the root cause of the distribution issue divided into more categories, they usually include only one category to register all types of these issues. However, the templates of some Member States do incorporate more than one sub-category to register other root causes related, such as delivery quotas, logistic issues or import/export ban or delay. In total, seven different root causes were grouped under distribution issues.

A closer examination of the medicine shortages caused by distribution issues, based on the information provided, revealed that delay/issues in delivery were responsible for 5,1% of shortages, logistic issues for 1,1% and delivery quotas for 0,4% (Table 4).

SPOC WP classification	Shortages		Shortages (%)		Total Shortages 2022 & 2023 (%)	N° templates including the root cause	
	2022	2023	2022	2023			
Distribution issues	4.171,3	4.560,1	11,5%	9,9%	10,6%	21	88%
Delays/ Issues in delivery	1.927,3	2.289,7	5,3%	5,0%	5,1%	4	17%
Distribution issues	1.420,8	1.584,3	3,9%	3,4%	3,6%	11	46%
Logistic issues	497,6	443,6	1,4%	1,0%	1,1%	6	25%
Delivery quotas	239,0	131,7	0,7%	0,3%	0,4%	2	8%
Transport problem	78,3	100,1	0,2%	0,2%	0,2%	3	13%
Import/export ban or delays	8,2	10,7	0,0%	0,0%	0,0%	4	17%
Storage issues	-	-	-	-	-	1	4%

Table 4. Root Causes related to distribution issues (2022-2023).

Quality issues

Quality issues were responsible for 2,6 % of analysed shortages. The denomination of quality issues is broadly shared by most countries, which usually have only this category to indicate the cause of the problem (17/24). In addition, four Member States add recalls as an additional root cause. Of the total number of shortages grouped under quality issues, only a small percentage were recorded as recall (0,1%) (Table 5).

SPOC WP classification	Shortages		Shortages (%)		Total Shortages 2022 & 2023 (%)	N° templates including the root cause	
	2022	2023	2022	2023			
Quality issues	982,2	1.195,8	2,7%	2,5%	2,6%	18	75,0%
Quality issues	936,2	1125,7	2,6%	2,4%	2,5%	17	70,8%
Recall	46,1	70,1	0,1%	0,1%	0,1%	5	20,8%

Table 5. Root Causes related to quality issues (2022-2023).

Regulatory issues

Regulatory issues were only responsible for a small proportion of analysed shortages (1,3%) but eight different types of root causes have been observed within this group (Table 6). Most of the templates analysed do not have the root cause of the regulatory issue divided into more categories, they usually include only one category to register all types of these issues. Regulatory issues included problems caused by administrative reasons (0,07%), falsified medicines directive (0,01%) or marketing suspension by the Authority (0,02%). Brexit and patent dispute have also been included in this category, but they are only reflected in the templates of two countries and no shortages caused by Brexit were reported in 2023.

SPOC WP classification	Shortages		Shortages (%)		Total Shortages 2022 & 2023 (%)	N° templates including the root cause	
	2022	2023	2022	2023			
Regulatory issues	495,4	572,5	1,4%	1,2%	1,3%	18	75%
Regulatory issues	457,0	503,4	1,26%	1,09%	1,16%	16	67%
Administrative reasons	16,5	44,9	0,05%	0,10%	0,07%	1	4%
Requirement for product information not fulfilled	10,2	6,5	0,03%	0,01%	0,02%	1	4%
Marketing suspension (by the Authority)	4,7	11,2	0,01%	0,02%	0,02%	1	4%
Falsified Medicines Directive (Serialization)	3,0	3,6	0,01%	0,01%	0,01%	2	8%
Patent Dispute	3,0	2,8	0,01%	0,01%	0,01%	1	4%
Brexit	1,1	0,0	0,00%	0,00%	0,00%	1	4%
Non compliance with legal requirements	0,0	0,0	0,00%	0,00%	0,00%	1	4%

Table 6. Root Causes related to regulatory issues (2022-2023).

Unpredicted major events or natural disasters

Only seven templates include unpredicted major events or natural disasters as root cause of medicine shortages. These issues represented a very low percentage of the shortages analysed, there were less than 100 cases registered during 2022 and 2023.

Safety and efficacy issues

Safety and efficacy issues are severely under-represented in the different national shortage notification systems. Only three countries include this root cause within their templates. In the period 2022-2023, 14 shortages were caused by these issues according to the information provided.

Other

The category “other” is included in more than half of the templates (14/24), allowing for the inclusion of causes that do not fit into any of the predefined categories. Within this category “cybercrime” has been included, classified only by one Member State’s template.

In general, medicine shortages classified under “other” category accounted for 6,9% of analysed shortages but the percentages of shortages caused by “other” varied greatly between countries. Some had less than 5% of shortages attributed to this category, while in other Member States, they were responsible for more than 15% of shortages (Figure 9).

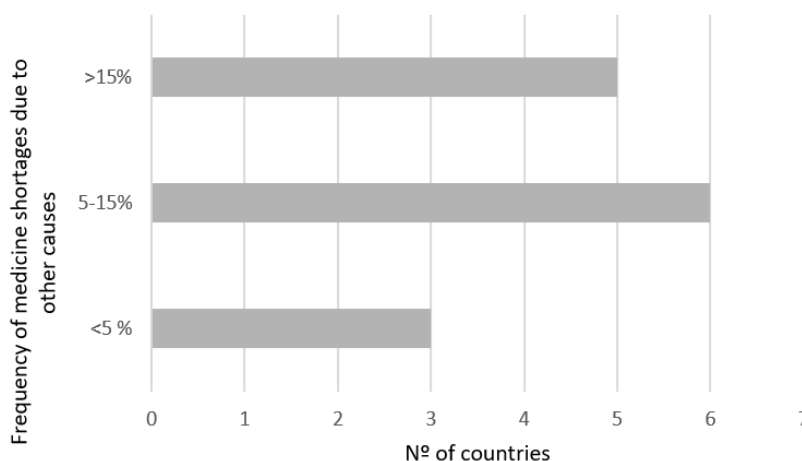


Figure 9. Frequency of medicine shortages due to other causes (2022-2023).

When analysing the templates and the root causes of medicine shortages of the last two years provided by EU/EEA countries, it was assessed whether having more options to choose from in the template reduced the percentage of the category “other” by providing more specific choices. To verify this hypothesis, the number of options included in the shortage notification templates were compared to the shortages due to other issues reported. Figure 10 depicts the templates analysed within the category “other” (grey bars) against the average of medicine shortages attributed to other issues during the years 2022 and 2023 (blue bars). As illustrated, some countries, with over ten categories in their templates, showed a very low percentage of medicine shortages attributed to other issues (< 5%). However, in most cases, an increase in categories number did not result in an inversely proportional relationship.

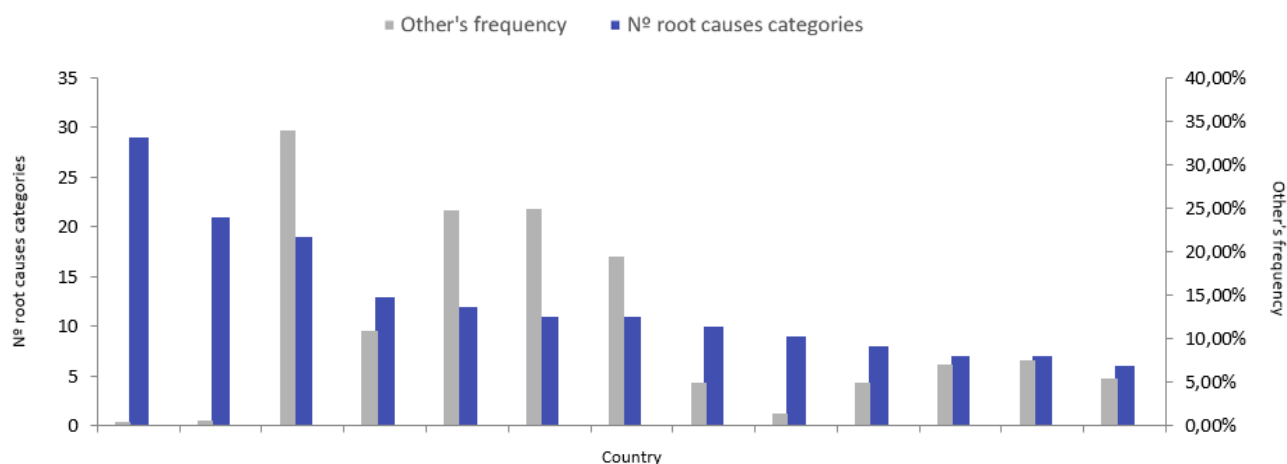


Figure 10. Number of root causes categories and frequency of “other” (2022-2023).

2.2. Analysis of root causes of shortages per region

Data provided was also analysed according to the classification defined by the European Union (EuroVoc/ EUR-Lex)⁽¹⁰⁾ to study whether the location of the country affects the cause responsible for the medicine shortage.

- **Northern Europe:** Denmark, Estonia, Finland, Latvia, Lithuania, Sweden, Norway and Iceland.
- **Western Europe:** Germany, Austria, Belgium, France, Ireland, Luxembourg and the Netherlands.
- **Southern Europe:** Spain, Greece, Italy, Cyprus, Malta and Portugal.
- **Central and Eastern European Countries:** Bulgaria, Croatia, Slovakia, Slovenia, Hungary, Poland, Czechia and Romania

As observed (Figures 11-14), manufacturing issues were the main cause of medicine shortages, close to 50%, regardless of their region. However, differences were observed in the frequency of shortages caused by other issues. For example, distribution related shortages were less frequent in Western Europe countries (4,5%) versus the mean value (10,6%) while unexpected increased demand was less frequent in Central and Eastern Europe (4,9%) compared with the average (16,7%). Additionally, shortages caused by commercial reasons (11,2% of mean value) varied greatly from one region to another. For example, in Western Europe these issues represented 0,5% of shortages while in Northern Europe they reached up to 5,3%, 18,4% in Central and Eastern Europe and 21,8% in Southern Europe.

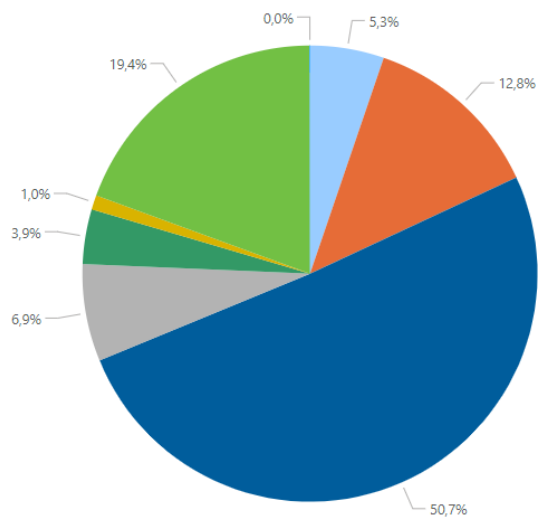


Figure 11. Root Causes in Northern Europe (22-23.)

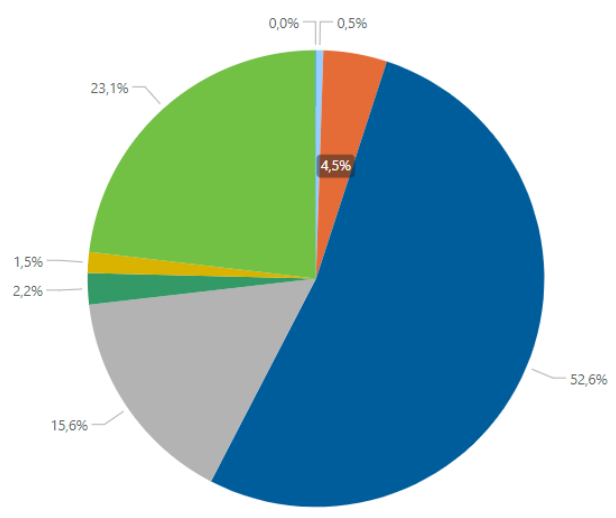


Figure 12. Root Causes in Western Europe (22-23).

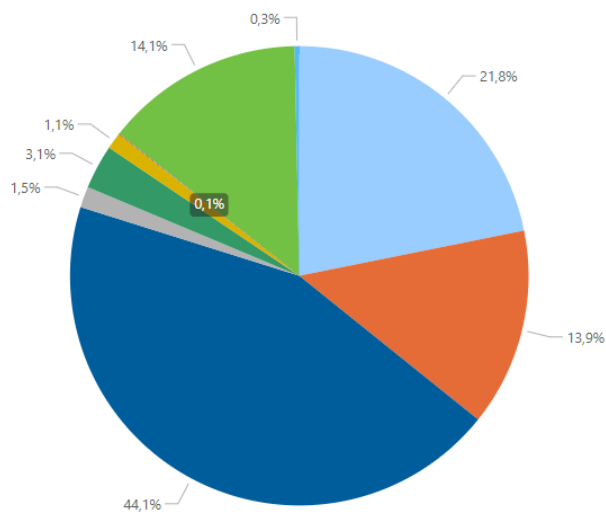


Figure 13. Root Causes in Southern Europe (22-23).

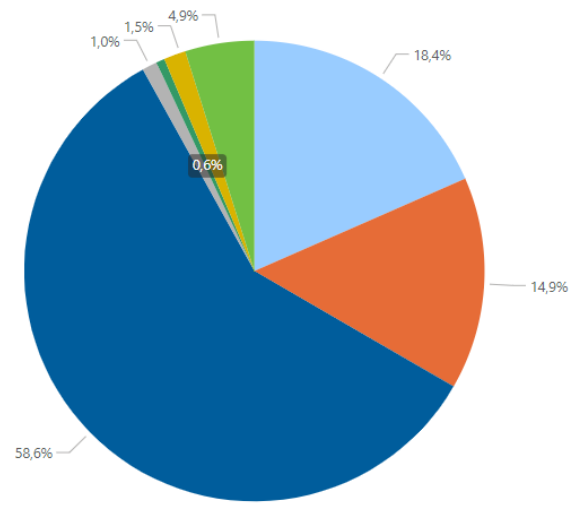


Figure 14. Root Causes in Central and Eastern Europe (22-23).

Legend:

- Commercial reasons
- Distribution issues
- Manufacturing issues
- Others
- Quality issues
- Regulatory issues
- Safety and efficacy
- Unexpected increased demand
- Unpredicted major events or natural disasters

3. Feedback from industry organisations

Several Industry EU Trade organisations were contacted to participate in the study on root causes of shortages and eight responses were received. However, one of these organisations informed that they did not face any shortage during 2022 and 2023, so they were not able to complete the survey.

The organisations that responded to the survey ranked the root causes responsible for shortages, from the most frequent (1) to least frequent (8). The responses (Figure 15) showed that manufacturing issues and unexpected increase demand are the most frequent root causes of medicine shortages, followed by quality issues and commercial reasons. Shortages caused by distribution and regulatory issues are uncommon while safety and efficacy issues and unpredicted major events are the least frequent root cause of medicine shortages, according to the respondents.

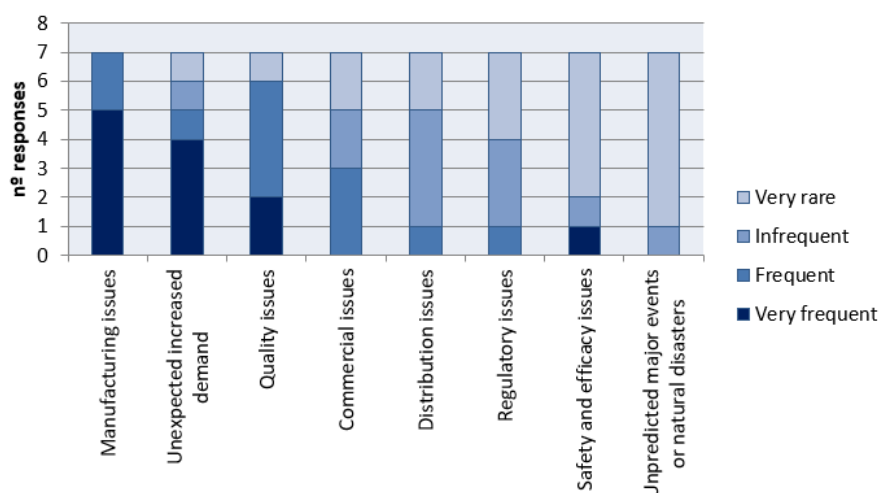


Figure 15. Frequency of root causes of medicine shortages according to Industry associations responses.

Additionally, several associations provided feedback on other root causes they also considered to be responsible for medicine shortages in Europe. Some pointed out that supplier's issues and lack of API and raw materials were very common root causes of shortages, as well as changes in reimbursement and parallel trade. One organisation also indicated that national stockpiling requirements were commonly associated with shortages, as well as no profit on the medicine. Other distribution-related factors and tender practices were also identified as being responsible for these issues. Furthermore, in specific cases, test on importation could also delay the supply of these medicines. Nonetheless, it was noted that this was not a frequent occurrence.

Discussion

The identification of the root causes of medicine shortages is essential to address the underlying issues and to implement tailored measures of prevention or mitigation of their impact. Previous reports have analysed medicine shortages in Europe, but most did not explore the root causes in detail. The most remarkable study on this subject is the study on medicine shortages commissioned by the European Commission and published in 2021 ⁽¹⁾. However, one of the main conclusions of that study was that there was still a need for a better understanding of the root causes of shortages. There is limited information available, and reporting of root causes is generally reductionist, singling out most acute causes but without considering the underlying systemic issues ⁽¹⁾. Therefore, the main objective of the present report was to identify and analyse the root causes of medicine shortages in EU/EEA countries to further delve into them and add value to what is already known.

For this purpose, NCAs of EU/EEA countries were contacted and information on the root causes of medicine shortages described in their national shortage notification systems was collected, as well as the frequencies of the root causes of shortages registered in the last two years (2022 and 2023). Ultimately, NCAs consolidate all the information regarding medicine shortages occurring in their respective countries. It is important to note that, in most countries, MAHs are required to report medicine shortages and provide the reason that has originated them. This study focused on data from the past two years to provide a better reflection of the current situation and to avoid the bias caused by the COVID-19 pandemic during 2020 and 2021.

The data analysis was conducted, on one hand, by examining how different NCAs registered the root causes of medicine shortages in their national shortage notification systems, as understanding the origin of the information was crucial to properly draw conclusions. However, there are differences in reporting systems among Member States which may affect the types of root causes of registered shortages. The findings from the two surveys conducted with NCAs showed that 82,8% EU/EEA countries included a template in their national shortage notification systems with pre-defined options of root causes. Using a template enables a more thorough data analysis, as the responses are narrowed down and collected more uniformly but they also limit the ability to capture responses that do not fit perfectly into the predefined fields. The comparison of the different templates provided revealed significant variability, both in the root causes included and in the number of options each one presents. Some NCAs have 39 pre-defined root causes options within their templates while others only have two. In NCAs with a higher number of options within their templates, more detailed root causes are usually reported. Countries that do not have such templates usually collect this information through a free text field.

In terms of the type of root causes collected within the templates, the results showed significant differences among Member States. The most common were manufacturing-related issues, which were identified in all templates analysed. However, other root causes such as regulatory or quality issues have not been included in about 20% of templates, which prevents analysing the medicine shortages caused by these issues in those Member States. Additionally, when each root cause is analysed in detail, it is observed that the level of granularity of the collected information also changes. Regarding manufacturing-related issues, 16 root causes related have been identified within this report, among which are delay in manufacturing, API not available or capacity constraints. As observed, this group has identified a greater variety of root causes than others. This makes sense since manufacturing issues can occur on many different levels of medicine production. However, when analysing the data, it has been found that some Member States consolidate multiple root causes under manufacturing issues, making it impossible to discern the details of the reason that has led to the shortage. This must be taken into account when interpreting the results of the analysed root causes, as some like API not available or capacity constraints are probably underrepresented. Quality issues, which are unforeseen interruptions in the manufacturing process that affect the quality of the medicine, may also fall under the manufacturing issues category in some Member States, as 25% of analysed templates do not include a dedicated category for these

issues. Several root causes have also been identified within distribution, commercial and regulatory issues. However, in the case of distribution issues it is observed that this is mainly due to different denominations of this type of issue used by country: distribution issues, logistic issues and transport problems are generally used indistinctly. Only three countries differentiate between two types of distribution issues, for example, between logistic issues and delivery quotas. During the review of commercial reasons and regulatory issues included in the templates, seven and eight subcategories were identified, respectively. As opposed to the other groups of root causes, no further detail has been found in unexpected increased demand, safety and efficacy issues, and unpredicted major events. These categories do not include subcategories to add additional information. Regarding the category “other”, it captures root causes that are not covered by the above options. However, this study lacks the information included in this category, preventing a detailed analysis. Analysing the causes included in this category would be of great interest to assess which issues are not being considered. Moreover, it is worth noting that one country’s template included a category for unknown causes, which is surprising as it is expected that the MAH is aware of the reasons that have triggered the medicine shortage, as they are the final responsible of their medicinal product. Additionally, another aspect to consider when analysing the data extracted from the root cause templates is that some countries collect and analyse certain groups of root causes jointly. For example, in some countries capacity constraints and distribution issues are included under the same category, which complicates the separate analysis of these issues. As can be observed, despite most Member States using a template to register root causes of medicine shortages, the lack of standardization between countries complicates the analysis of information considerably and can lead to over or underestimating some root causes.

On the other hand, once the collection methods of the different root causes were studied, the frequencies of the root causes of 83.266 shortages from 24 countries in 2022 and 2023 were analysed in depth. In order to facilitate cross-country data comparison, all root causes included in the templates were grouped according to the root cause classification proposed by SPOC working party in 2019. Moreover, another category was accounted to analyse other issues, which appear in more than half of the templates. Overall, manufacturing issues were the most frequent root cause for medicine shortages in EU/EEA countries (50,6%) and, within this category, capacity constraints and delay in manufacturing accounted for 14,0% and 7,6% of the shortages analysed, respectively. It should be noted that there were other root causes responsible, albeit to a lesser extent, such as packaging materials (0,5%) or excipients not available (0,2%), site transfer (0,3%), planning issues (0,02%) or problems at other manufacturer (0,4%), but less than five countries registered them and were thus underrepresented. Knowing their frequency in other countries would likely reveal much higher numbers. The second leading root cause of shortages was unexpected increased demand, accounting for 16,7% of medicine shortages. The underlying root causes of the unexpected increased in demand were not captured in this study, as the provided data did not detail them. However, as the SPOC working party definition suggests, these increases in demand can be due to shortages of alternative medicinal products, new treatment guidelines or changes in epidemiology, among others. The third most frequent root cause of analysed shortages was commercial reasons (11,2%), with marketing discontinuation or cessation of the medicinal product accounting for 4,5% and temporary marketing cessation accounting for 0,2%. Only nine Member States include marketing discontinuation and four temporary marketing cessations in their templates. These root causes need to be further discussed across EU/EEA Member States, as they are changes in the commercialization status and should be kept separate from shortages. Several countries make a distinction between shortages and marketing discontinuations ⁽⁷⁾, therefore it would be necessary to agree on this approach to achieve harmonisation. Continuing with commercial reasons, it is also important to analyse the impact of the price of the product in medicine shortages. Only three countries referred to this factor in the template included in their national shortage notification systems. Incorporating this root cause in all templates would be very useful to know the reality of how price influences the availability of medicinal products in each Member State. In fourth place and with a percentage very near to commercial reasons, were distribution issues (10,6%) which refers to problems with distributors or transport, among others. Nevertheless, the analysis of the medicine shortages by year revealed that the root causes remained stable except for distribution issues, where it was observed that in 2022 the order was reversed, with distribution issues coming in third place. To a lesser extent were the shortages caused by quality (2,6%) and regulatory issues (1,3%). It is important to highlight that most countries recorded

regulatory issues without going into detail. If it were possible to break down the root causes for all regulatory issues, more comprehensive information could be gained. The more detailed root causes such as administrative reasons (0,07%), marketing suspension by the Authority (0,02%) or serialisation issues (0,01%) were only registered in some countries. The analysis of the shortages caused by safety and efficacy issues, and unpredicted major events showed that they remain largely unreported in the various national shortage notification systems. This is due not only to a small percentage of Member States recording them as root causes, but also to the absence of shortages attributed to these issues in the last two years. Undoubtedly, a review of the 2020 and 2021 data would likely show a significant change by including the medicine shortages caused by COVID-19. Finally, it is noteworthy that 6,9% of shortages were due to other issues for which no further information was available. This percentage represents the average frequency of shortages attributed to other issues out of all shortages analysed. However, upon examining the differences between Member States it is observed that in some cases, the percentage of others exceeds 30%. This could indicate that the templates used are incomplete and that new categories could be incorporated to better record the root causes. For this reason, WP5 evaluated whether having more categories included in the reporting template reduced the number of shortages included under the category of others (Figure 12). Apparently, it does not seem to be an inversely proportional relationship. Therefore a re-evaluation of the categories included in the templates would be worthwhile.

To complete the analysis, it was evaluated whether the root causes of shortages varied according to the country's geographical location. The root causes remained generally stable in the two years studied, there were no significant differences between the different regions. Nevertheless, a future deeper and exhaustive analysis, considering the particularities of each country, could be quite worthwhile in order to assess if true differences exist and why, or conversely there is bias.

In addition to contacting the NCAs of Member States to collect information on the root causes of the medicine shortages in their countries, Pharmaceutical Industry Organisations were also contacted to include their expertise on this topic. There was a great variability in the responses as there were significant differences between the organisations contacted. According to the information provided, manufacturing issues and unexpected increased demand are the most common causes of medicine shortages, which is consistent with the information provided by the NCAs. However, in contrast to the results obtained by NCAs, quality issues represent a frequent cause of shortages for Industry Organisations. They also highlighted other root causes that triggered shortages, besides the ones included in the SPOC working party classification, such as lack of materials or changes in reimbursement. Moreover, it is worth noting that one respondent indicated that cooperation to address shortages at EU level could be a trigger for medicine shortages. On the contrary, it is general believed that improving communication with industry's stakeholders and standardising the different root causes among NCAs, taking into account their feedback, would be of enormous help in improving root cause reporting and achieving more standardised results. This way, the reporting of medicine shortages would be harmonized, and the same root cause would be indicated across the different affected countries.

To conclude this analysis report on root causes, it is important to consider its limitations. One of the most significant issues stems from the differences in the reporting systems across different countries, leading to inconsistencies in the source information. For example, some record only shortages that last a certain time period or affect a certain type of medicinal product. Besides, during the data analysis, it was assumed that all medicine shortages shared the same characteristics, even though the definition deferred significantly. Therefore, global results are biased due to the aggregation of shortages without considering the particularities of each country in terms of shortage's definition and reporting criteria, nor were differences in prices of medicinal products or population size. Moreover, the comparison based on the categories defined by SPOC working party provides a general idea of the root causes responsible of medicine shortages in EU/EEA Member States but introduces some errors when analysing them all together due to subjectivity in their inclusion in the defined categories and also because certain countries categorise multiple root causes under a single category resulting in a loss of data. Additionally, the root causes included in Member States that do not granularise the information lead

to some root causes being either overestimated or underestimated. Lastly, an error was assumed when converting the frequencies' percentages to absolute numbers since not all of them sum up to 100% (5% margin of error allowed) and information was lost from countries that did not provide the total number of shortages.

Even though the main root causes of medicine shortages have been accounted for and it has been possible to study in depth how each member records the root causes within their national shortage notification systems, it is still necessary to thoroughly analyse the detailed root causes, especially in Member States that do not break down the information and only register the main categories of root causes in their systems. And also, it is necessary to examine the categories that are not included in some templates, as this omission can result in the loss of information about certain root causes. Besides, many concepts still need clarification to understand the root causes behind these issues. Therefore, it would be highly recommended that all Member States would share a common template to record root causes of medicine shortages during the shortage notification made by MAHs. This tool would be highly valuable to standardise concepts and to gain a better understanding of the root causes behind all the medicine shortages in the EU/EEA countries, thereby enabling the implementation of effective measures of prevention and mitigation to tackle this global challenge. WP8 of CHESSMEN Joint Action will address the latter in next deliverables.

Conclusion

Based on the information from the surveys conducted within the scope of this deliverable, and the consequent data processing and analysis that were carried out the main conclusion are:

- Most EU/EEA Member States have in place a template that facilitates shortages' root cause data collection and the subsequent analysis on the frequency of these root causes.
- There is a high variability between the different templates, some collect very detailed information while others are more general. The greater the granularity, the more accurate information is usually collected on root causes. However, to maintain a high-level oversight of root cause types that could be compared across EU, even granular categories should be grouped into bigger categories.
- The categories that included more subcategories and therefore provided more detailed information on the underlying root causes were manufacturing issues (16 subcategories) and regulatory issues (8 subcategories).
- There is a significant number of shortages caused by other issues and their comparison to the number of categories available within the templates shows no direct relation. This could indicate that templates are incomplete and a re-evaluation of categories should be done to reduce this percentage.
- The most frequent root causes of shortages during 2022 and 2023 were manufacturing issues, followed by unexpected increased demand, commercial reasons and distribution issues.
- The comparison of the root causes of shortages among Member States is very complex due to the lack of harmonisation on the root causes recorded by each of them.
- A second analysis should be carried out in the future, following the implementation of a common EU template that will allow a more unified comparison of root causes between Member States.

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Annex I

Shortage definitions of European Member States. We would like to have a better understanding of how MS apply in practice their shortage definition. See the example of Spain.

Country	Shortage definition	Source. Legislation if applicable.	Have you changed your national definition of shortage after the publication of Regulation 2022/123? If yes, please explain.	Is there a different definition of shortage for reporting shortages? Yes/no. If yes, please elaborate.	Criticality		Notification		Time frame	Publication	Do you consider a temporary suspension of a drug as a shortage? Yes/No.	Do you consider a permanent cessation or withdrawal of the marketing authorisation of a drug as a shortage? Yes/No	Do you distinguish between availability issues and shortages? Yes/No. If yes, please elaborate including a definition of availability.	Please add any other questions you could think of in order to understand the implementation of shortage definitions in MS.
					Do you have criticality categories? E.g. Minor/Serious/Critical? Yes/No. If yes, please elaborate.	Is it mandatory for the MAH to report shortages: A. Only for critical medicinal products. B. Prescription-only medicines C. All types of medicinal products - including non-prescription medicines	How long in advance does the MAH has to notify shortages?	Is it mandatory for the MAH to inform the cause of the shortage? Yes/no. If yes, do you have a template to mark the cause?	How long does the supply disruption need to be in order to be considered a shortage?	Are all shortages published? Yes/No If no, please elaborate.				

Annex II

INSTRUCTIONS

CHESSMEN WP5 has analysed the root causes classification systems of medicine shortages in the different EU/EEA countries. Therefore, after knowing how each country classifies the root causes of shortages, we would like to know the frequency of the reported root causes in your country, so that a depth analysis can be made. The information should be provided by filling in this file. We would like to thank you in advance for your contribution.

Sheet 2 "Template Confirmation" - We would really appreciate if you could check the row applicable to your country and confirm if the information you provided related to your classification of root causes of shortages has been correctly interpreted, so all the "x" have been placed in the correct excel cells. If you identify that a "x" is missing, please add it in **blue**. On the other hand, if you detect an incorrect "x", please colour it in **red**. Please note that in order not to create excessive columns, the options of root causes of shortages have been compiled. Nevertheless, an additional "Free text" column has been added at the end of the table to indicate any key missing category or other useful information. Additionally, please indicate if this information is "Confidential"/ "Public", in order to assess whether the data could be published or should be presented in an aggregated way. You should provide this information by filling the last column of the table.

Sheet 3 "Frequency"- Please provide the frequency (%) of each root cause of reported shortages in your country in 2022 and 2023 in the applicable excel cell, and indicate the total number of shortages reported per year in column [AS]. An additional "Free text" column has been added at the end of the table to include any useful information. Additionally, please indicate if this information is "Confidential"/ "Public", in order to assess whether the data could be published or should be presented in an aggregated way. You should provide this information by filling the last column of the table.

Please note that medicine shortages are defined as a situation in which the supply of a medicinal product that is authorised and placed on the market in a Member State or of a CE-marked medical device does not meet demand for that medicinal product or medical device at a national level, whatever the cause, as defined in the *REGULATION (EU) 2022/123 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 25 January 2022 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices*. Furthermore, reported root causes are the causes that have been indicated by the MAH when reporting the medicine shortage to your NCA.

Please, note that "Spain" row has been already fulfilled according to the instructions given, in order to provide an example. However, do not hesitate to contact us if you require further clarifications.

Annex III

BACKGROUND

CHESSMEN (Coordination and Harmonisation of the Existing Systems against Shortages of Medicines – European Network) is an EU co-funded Joint Action that aims to support European Member States to provide a harmonized response and to promote the use of best preventive practices to reduce shortages of medicinal products. The Action has officially started on 16 January 2023 and will be running for 3 years. CHESSMEN envisages strengthening the coordinating structure in relation to identifying, managing and preventing medicine shortages, as well as optimize the use of the available resources of all Member States, by both supporting the existing networks and initiatives already active in the field, such as the Medicines Shortages Single Point of Contact (SPOC) Working Party and the Heads of Medicines Agencies / European Medicines Agency Task Force on Availability of authorised medicines for human and veterinary use (TF AAM), as well as enhancing Member States cooperation. The Joint Action consists of 4 horizontal work packages (WP) and 4 technical work packages that support the implementation of the Joint Action objectives. WP5 is in charge of the identification of the root causes of medicines shortages and involves the participation of TWG1 from TF AAM.

In this context, WP5 has designed a survey to get Pharmaceutical Industry's feedback in order to analyse in depth the reported root causes of medicine shortages. Please, note that the information you provide within this survey will be treated confidentially and results will be published in an aggregated manner.

INSTRUCTIONS

We would appreciate if you could complete the survey by sorting the root causes of shortages from highest to lowest frequency ("1" will be the most common root cause) and providing the source from which the data was obtained, if available. In addition, please feel free to add any key missing option of root cause you identify within "Other Root Cause" excel cell or if you feel that more granularity needs to be included (e.g. types of manufacturing problems). Your feedback will be of great help to conduct a proper analysis of the root causes of medicine shortages in Europe. We would like to thank you in advance for your contribution.

In order to clarify some key concepts, please find below the classification of the different root causes of medicine shortages agreed by the SPOC network in 2019 and the definition of medicine shortages.

Medicine shortages are defined as a situation in which the supply of a medicinal product that is authorised and placed on the market in a Member State or of a CE-marked medical device does not meet demand for that medicinal product or medical device at a national level, whatever the cause, as defined in the REGULATION (EU) 2022/123 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 25 January 2022 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices.

Entity Name	
Type of entity (e.g. Pharmaceutical Manufacturing Industry, Generics Pharmaceutical Industry, Pharmaceutical distributors or wholesalers...)	

Root Cause	Frequency
Quality issues	
Manufacturing issues	
Regulatory issues	
Safety and efficacy issues	
Unpredicted major events or natural disasters	
Unexpected increased demand	
Distribution issues	
Commercial issues	
Additional root causes of medicine shortages	
Ej. Change in reimbursement.	

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