European Commission

Assessment of the supply chain vulnerabilities for the first tranche of the Union list of critical medicines:

June 2024

TECHNICAL REPORT

Health Emergency Preparedness and Response Authority

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BACKGROUND

The recently adopted Communication from the European Commission (EC)[1] on addressing medicine shortages in the European Union (EU) puts forward a broad set of short-term and longer-term actions to address shortages of medicines and enhance their security of supply in the EU. The aim is to develop coordinated actions with all relevant stakeholders to prevent or mitigate critical shortages at EU level, focusing on the most critical medicines for which security of supply needs to be assured at all times. The actions proposed build on work already under way and especially the proposed revision of the EU pharmaceutical legislation.

The continued availability of medicines is key in our European Health Union. To achieve this, the Communication emphasises that the EU needs to boost the resilience of its supply chains. This will require ensuring access to key capabilities at different levels of the supply chain, from sourcing of key input materials, active pharmaceutical ingredient (APIs), and precursor production to the actual manufacturing of finished products. At the same time, the EU needs to reconsider its manufacturing dependencies and enhance its strategic autonomy in health, by exploring the potential for expansion of its internal EU manufacturing capacity, while also building on strategic relations with neighbourhood countries and like-minded countries around the world.

In this context, in December 2023, the EC, the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) published the first version of the Union list of critical medicines[2]. The list features over 200 active substances deemed critical based on therapeutic indications and the availability of suitable alternatives.

Following the publication of the Union list, the Commission performed a pilot exercise to assess the supply chain vulnerabilities of a first tranche of 11 critical medicines from the Union list to guide coordinated actions at EU level if necessary.

The Commission collected data from marketing authorization holders (MAHs), Member States and EMA on the supply chains of the selected medicines. The outcomes of this pilot exercise outlined in this document will guide the discussions within the various fora which were involved in this work such as the MSSG or Joint industrial cooperation forum of Health Emergency Preparedness and Response Authority (HERA) and within the Critical Medicine's Alliance[3]. The aim is to provide recommendations and strategic advice to the Commission, Member States, and other EU decision-makers on how to address medicine shortages, including from an industrial policy perspective.

[1] commission.europa.eu/system/files/2023-10/Communication_medicines_shortages_EN_0.pdf

[2] First version of the Union list of critical medicines agreed to help avoid potential shortages in the EU | European Medicines Agency (europa.eu)

[3] Critical Medicines Alliance - European Commission (europa.eu)

SCOPE AND OBJECTIVES

This pilot exercise was undertaken jointly by two Commission services: Health Emergency Preparedness and Response Authority (HERA) and the DG Internal Market, Industry, Entrepreneurship and SMEs (GROW) with the purpose of:

Evaluating the proposed methodology and determining the scalability for the assessment of the entire Union list of Critical Medicines

Identifying structural vulnerabilities within the supply chains of the first tranche of Critical Medicines

Providing evidence-based insights for discussions within the various fora such as the MSSG or Joint Industrial Cooperation Forum of HERA and within the Critical Medicines Alliance[4].

The figure below outlines the framework followed to conduct this pilot exercise:

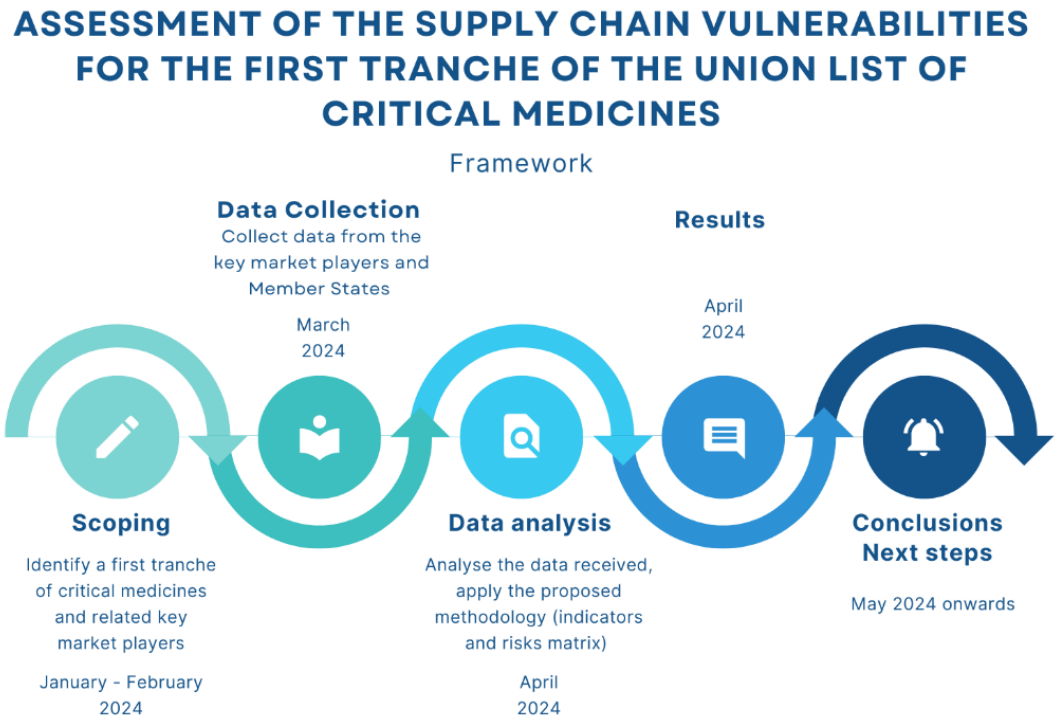

***Figure 1**. Framework to conduct the pilot exercise.*

SELECTION OF THE FIRST TRANCHE OF CRITICAL MEDICINES

The methodology to derive the first tranche of critical medicines followed a data-driven approach for identifying a subset of critical medicines from the HMA/EMA Union list, balancing public health need and potential supply chain vulnerability in the process. For this purpose, the Commission organized a workshop on 10 January 2024 with the participation of Member States, industry associations, the EMA and other Commission services to discuss the criteria for selecting the first tranche from the Union list to be subjected to the supply chains vulnerability assessment. Participants identified historical shortages as the most suitable criterion for a quantitative, data-driven selection procedure with respect to data availability and relevance. They also highlighted the importance of other criteria, such as the location of API producers and market concentration, for which data is not readily available. Based on the feedback from the workshop's participants and follow-up discussions with EMA, the Commission decided to follow a combination of

[4] Critical Medicines Alliance - European Commission (europa.eu)

quantitative and qualitative approaches for selecting of medicines included in the pilot exercise. The details are illustrated in Figure 2 and described in detail below.

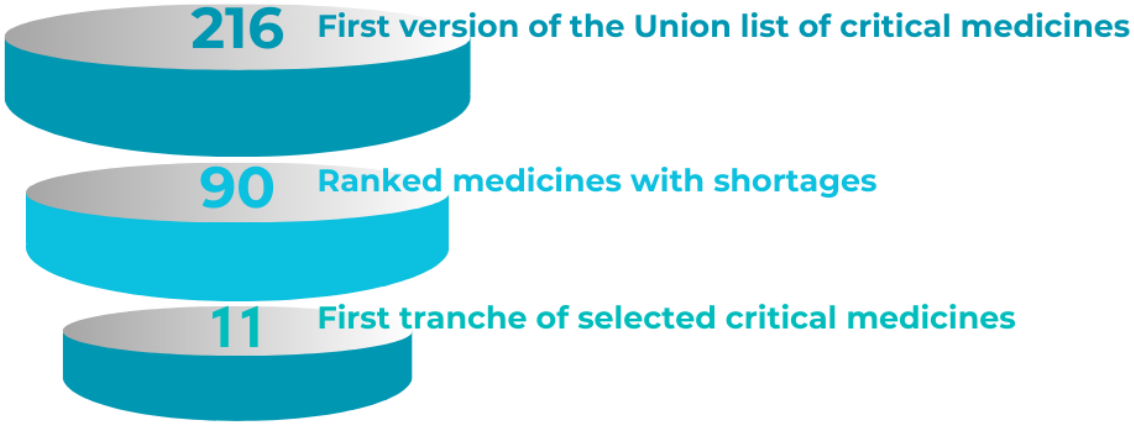

***Figure 2**. Process to select the 11 medicines in scope of this exercise.*

Specifically, the selection of the 11 medicines followed a stepwise approach as follow:

Step 1

Selection of the medicines from the Union List of critical medicines with shortages notified to the EMA between the years 2019 to 2023.

In this initial step, the Union list of critical medicines published by the EC/EMA and HMA was narrowed down by selecting the medicines for which the Member States had reported a notification of a shortage instance to the EMA between 2019 and 2023. As a result, the initial list of 216 critical medicines was reduced to 90.

Step 2

Ranking of the critical medicines with reported shortages based on quantitative criteria.

In this step, a quantitative assessment was applied to the selected medicines, considering the risk of a supply chain disruption and the public health impact of each medicine. The risk of supply chain disruption was evaluated using the total number of past and ongoing shortage notifications per medicine between 2019 and 2023 (i.e., frequency of shortage notifications), while the public health profiling was based on the assessment performed by the Member States during the development of the Union list under EMA's guidance[1]. Based on these two criteria, all medicines with reported past or ongoing shortages were ranked accordingly.

Step 3

Deriving a representative sample of critical medicines for the selected first tranche by applying qualitative factors.

The medicine list underwent enhancement by incorporating qualitative factors to increase sample diversity across various dimensions. These factors included specificities in the manufacturing process and geography, such as single sourcing versus multi-sourcing, the geographical location of API suppliers within the EU versus third countries, aseptic requirements, storage specifications, and transportation challenges. Additionally, product characteristics such as the target population (paediatric versus adult), substance type (biological versus chemical), economic considerations (cost, volumes), and demand patterns (seasonality) were considered.

[1] Methodology to identify critical medicines for the "Union List of critical medicines" (europa.eu)

Based on these qualitative considerations, the top-ranked medicines were selected to ensure coverage across a range of diversified aspects, thereby allowing to test the methodology with a sample of medicines covering a broad set of supply chain specificities.

This approach resulted in the following 1st tranche of critical medicines from the Union list: Alteplase, Amoxicillin, Amoxicillin/Clavulanic Acid, Benzathine benzylpenicillin, Clonazepam, Fludarabine, Glucagon, Hepatitis B vaccine, Rifampicin, Verteporfin, Vincristine.

It is important to stress that, by following this approach, these medicines are not to be regarded as 'at most risk of shortages/most vulnerable' but present a diversified sample with respect to therapeutic indication, manufacturing process and product specificities and thus appear suitable to serve the objectives of the pilot exercise.

SELECTION OF MARKETING AUTHORISATION HOLDERS (MAHs)

After the selection of medicines, the key suppliers for the medicines in scope were identified based on sales data from the year 2022 (most recent available) in EU/EEA using a commercial database.

Suppliers were ranked based on their market shares in each Member State (aggregated data). This step ensured a broad geographical coverage of the suppliers across the different Member States. Based on this ranking, suppliers covering at least 70% of the EU/EEA market were selected. This step ensured sufficiently high overall EU/EEA market share coverage and led to the identification of 49 key suppliers for the 11 selected medicines.

DATA COLLECTION

The data from marketing authorisation holders (MAHs) and Member States (MSs) was collected via dedicated questionnaires. Additionally, the EMA provided information regarding the shortages and manufacturing sites of centrally authorised medicines. The data requests to industry and Member States, as well as the data selection process, were discussed with industry associations, Member States, and the EMA at a dedicated in-person workshop on 10 January 2024 and follow-up online meetings on 9 February (with industry representatives) and 12 February (with Member States). The questionnaires and the processes were adjusted based on constructive input from the relevant stakeholders.

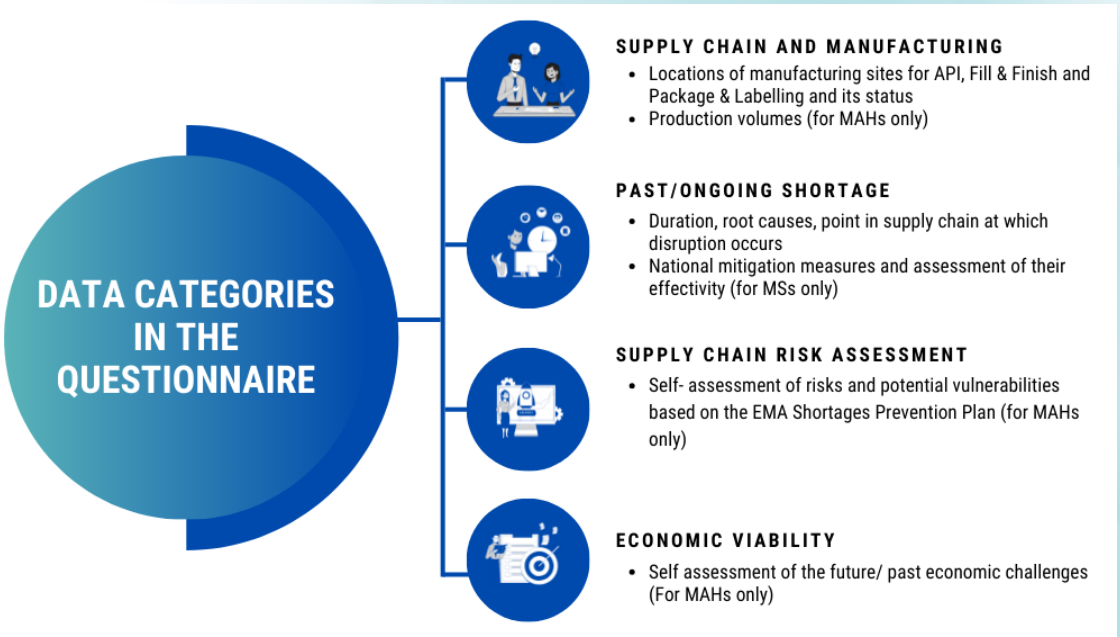

***Figure 3**: Illustration of the data categories presented in the questionnaires.*

DATA CATEGORIES COLLECTED FROM MAHS

Supply chain and manufacturing information, including location, the status of the production site (active/inactive and inhouse/contracted), production volume for the fill and finish process, packaging and labelling, and API production.

Shortage information covering the last three years (i.e., between 01/01/2021 and today), including the shortage status (resolved, ongoing, not applicable), duration of shortage, the root cause of shortage, and point of supply chain disruption. Information already transmitted to the EMA was not required to be reported to the Commission.

Supply chain risk assessment, including potential vulnerabilities based on the current draft of the Shortage Prevention Plan currently developed by the EMA in cooperation with the industry.

Past and expected economic viability based on the MAH's subjective assessment using a three-scale response option (high, medium, low).

DATA CATEGORIES COLLECTED FROM MEMBER STATES

Supply chain and manufacturing information, including information on the location and status (active/inactive) of the manufacturing sites for fill-finished processes, packaging and labelling and the API production.

Shortage information covering the last three years (i.e., between 01/01/2021 and today), including the shortage status (resolved, ongoing, not applicable), duration of shortage, the root cause of shortage, and point of supply chain disruption. Information already transmitted to the EMA, was not required to be reported to the Commission.

Shortage mitigation measures, including past national measures used to address shortage instances and national measures put in place to prevent future shortages.

Initially, stakeholders were given a 3-week deadline. However, to gather as much information as possible, the deadline was further extended, with the latest submission received on 15 April.

BILATERAL CALLS WITH MARKETING AUTHORISATION HOLDERS

Bilateral calls were organised with 15 MAHs that submitted information to this pilot exercise. The calls aimed to discuss the data received, as well as to providing MAHs the opportunity to provide feedback on the pilot exercise and for future analyses.

Main findings of these bilateral calls can be found in the results section of this document.

A summary of the main findings during these bilateral calls can be found in the results section of this document.

DATA ANALYSIS

The data analysis focused on two primary tasks: computing the six indicators presented in Figure 4 and applying the risk thresholds depicted in Figure 5.

COMPUTING THE INDICATORS

The quantitative measures that were adopted to capture the vulnerabilities of the supply chains and provide insights into different aspects of the dataset are the following:

EU industrial presence

Production in EU member states along the different supply chain tiers serves as an indication of the EU's resilience to scenarios where a higher degree of self-sufficiency may be required. In this regard, a higher proportion of extra-EU production signals higher vulnerability.

Diversification

Important threats to security of supply may stem from reliance on a sole supplier or suppliers located in only one geographical region. A lower number of manufacturing sites along the supply chain and a lower number of countries with manufacturing sites implies a smaller capacity to ramp up production and less flexibility.

Supply chain risks

This self-assessment indicator captures the perceived risks of supply chain disruptions as evaluated by the key MAHs. The indicator provides a comprehensive view of the vulnerabilities and resilience within the supply chain.

Market concentration

Even when production occurs within the EU or there is a high number of producers, a supply chain may still be vulnerable if production volumes are concentrated in few companies or countries, making it less resilient to single-point failures.

Unpredictable demand

A lack of demand visibility or unpredictable demand spikes may result in companies being unable to produce the necessary supply. The occurrence of past shortages or back orders serves to draw patterns on the likelihood of demand tensions happening again in the future.

Economic viability

Cost pressure and certain tendering or public procurement practices can lead to cost-saving measures affecting the security of supply. When manufacturers operate with slim profit margins or even at a loss, they may be compelled to adopt cost-cutting measures. This can manifest in practices like single sourcing, reduced investments, or ultimately ceasing production.

APPLYING THE RISK THRESHOLDS

The data from different MAHs per molecule have been analysed by applying predefined risk thresholds, which help categorise data points based on the level of risk they represent. These thresholds are presented in Figure 5.

The 'industrial presence' indicator indicates low risk if more than 70% of production is within the EU, medium risk if 30-70% of production is within the EU, and high risk if less than 30% is within the EU.

For a high-risk 'market concentration', the definition of the indicator requires more than 30% of production coming from one supplier or one country. Less than 10% of production from one supplier or one country indicates low risk.

The indicator of 'diversification' assumes low diversification, hence high risk, when there are less than 4 active manufacturing sites of the molecule and high diversification, hence low risk, when there are more than 6 different suppliers.

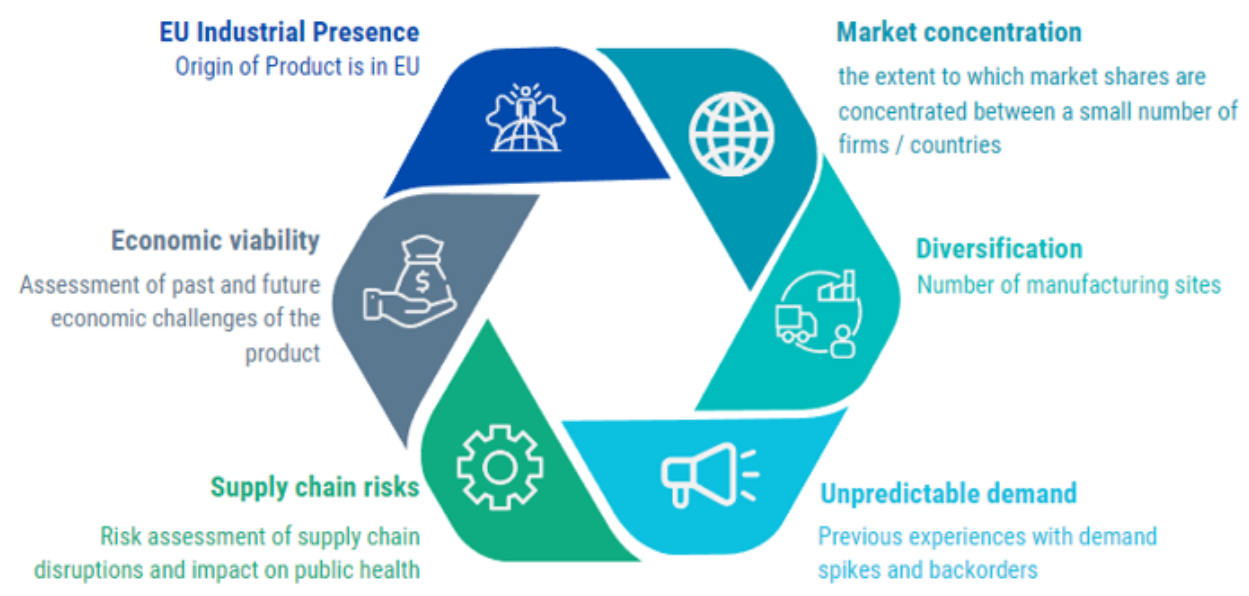

Figure 4: *Indicators.*

	LOW RISK	MEDIUM RISK	HIGH RISK
INDUSTRIAL PRESENCE	> 70% of production in the EU	30-70% of production in the EU	< 30% of production in the EU
MARKET CONCENTRATION	< 10% of production is from one supplier or one country	10%-30% of production is from one supplier or one country	> 30% of production is from one supplier or one country
DIVERSIFICATION	> 6 manufacturing sites	4-6 manufacturing sites	< 4 manufacturing sites
UNPREDICTABLE DEMAND	Expert assessment based on information received for root causes of shortages: frequency of "Unexpected increased demand", weighted by the market share of the MAH		
SUPPLY CHAIN RISK	MAH self-reported supply chain risk as 'Low'	MAH self-reported supply chain risk as 'Medium'	MAH self-reported supply chain risk as 'High'
ECONOMIC VIABILITY	MAH self-reported economic risk as 'Low'	MAH self-reported economic risk as 'Medium'	MAH self-reported economic risk as 'High'

Figure 5: *Risk thresholds/levels per indicator.*

The risk level of the 'unpredictable demand' indicator was attributed by assessing the frequency of 'unexpected increased demand' in the reported root causes of shortages, weighted by the market share of the reporting MAH.

The two self-assessment indicators, 'supply chain risks' and 'economic viability', report the weighted average of the assessments by MAHs.

RESULTS

Caveats

Data currency: information on MAHs sales relies on market share data for 2022 from commercial sources. This may significantly impact the quality and reliability of the results presented and the identification of current critical nodes in the supply chain (if key players in the market have changed since 2022).

Coverage limitation: The questionnaire respondents account (on average) for 70% of the market. There is a 30% segment of the market that is not represented in the data.

Data gaps: The questionnaire responses presented gaps, resulting in an incomplete dataset, therefore, critical vulnerabilities might be overlooked by this exercise.

Risk of inaccurate information: The data received has not undergone any validation process and relies on subjective self-assessment declaration provided by concerned MAHs.

Risk of inadequately defined **indicators**: The thresholds of the indicators are not based on (historical) data analysis and/or expert opinions; hence they may fail to accurately reflect the true levels of risk, leading to either overestimation or underestimation of potential supply chain issues.

Overall, given the coverage and data gaps and data currency limitations, the exercise's results are associated with a significant degree of uncertainty. It is crucial to exercise caution when utilising the results of this pilot exercise.

Response rate

The response rate for marketing authorisation holders in scope was circa 50%. In total, 19 marketing authorisation holders submitted data. Eight suppliers indicated they no longer supplied the product or are parallel importers.

The response rate for Member States was circa 64%. 18 Member States submitted data.

RESULTS FROM MARKETING AUTHORISATION HOLDERS' DATA

The traffic light risk matrix in Figure 6 shows the results of the assessment based on the indicators' risk matrix (Figure 5). The columns depict the substances and the sub-columns of the three different supply chain tiers: PL stands for packaging and labelling, FF for fill and finish and API for active pharmaceutical ingredient; and the risk level for each indicator. As a reminder, green depicts low risk, yellow is for medium risk and red/purple is high risk.

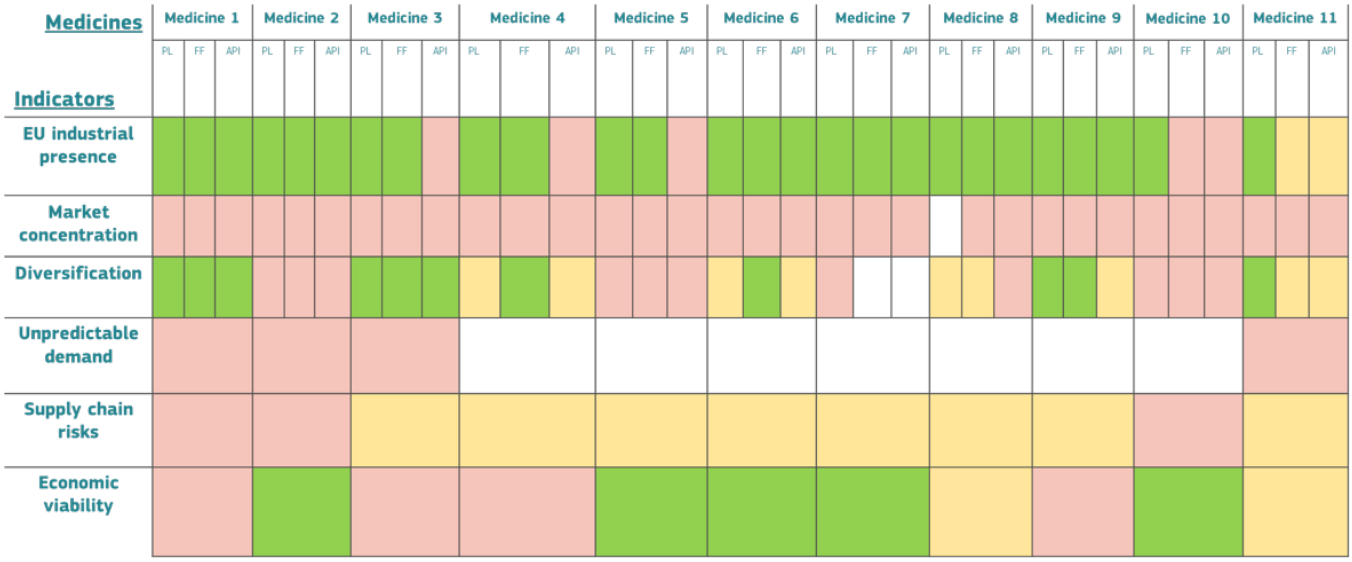

***Figure 6**: Traffic light risk matrix: results from the analysis of MAHs data. PL stands for packaging and labelling, FF for fill and finish and API for active pharmaceutical ingredient; Green depicts low risk, yellow medium risk and red/purple high risk.*

First, concerning the EU industrial presence, 4 out of 11 substances display high vulnerability, highlighting a significant dependence on Active Pharmaceutical Ingredient (API) production/supply sources outside the EU.

In the indicator of market concentration, all 11 molecules are categorised as having, on average, more than 30% of supply from a single country or single manufacturer.

The indicator of diversification of manufacturing sites shows mixed results, suggesting a variable degree of resilience. This is to be expected as the market development history of each assessed molecule is unique.

The indicator of unpredictable demand shows significant uncertainty in market dynamics; however, data is missing for 7 substances.

Supply chain risks are assessed as high by the MAHs for 3 molecules. There might be a link herewith low diversification as these MAHs are dependent on a limited number of suppliers across their supply chain tiers. The MAHs of the other 8 substances reported medium risks in their supply chains.

Lastly, the economic viability indicator points to pressing economic challenges for 4 substances. Here, the follow-up free text answers of MAHs in the questionnaires include economic challenges/aspects such as: cost/price pressures, high competition, energy costs and inflation, continuous delays, unsustainability of the market because product prices are below costs in certain MS.

RESULTS FROM MEMBER STATES' DATA

As previously mentioned in this report, information from Member States was collected for this pilot exercise regarding the manufacturing sites (of API, fill and finish, and packaging and labelling) under their supervision, as well as on the root causes of shortages of the medicines in scope between the years 2021 and to date (i.e. Q1 2024) and mitigation measures.

1. Spatial distribution of API, fill and finish, and packaging and labelling production sites

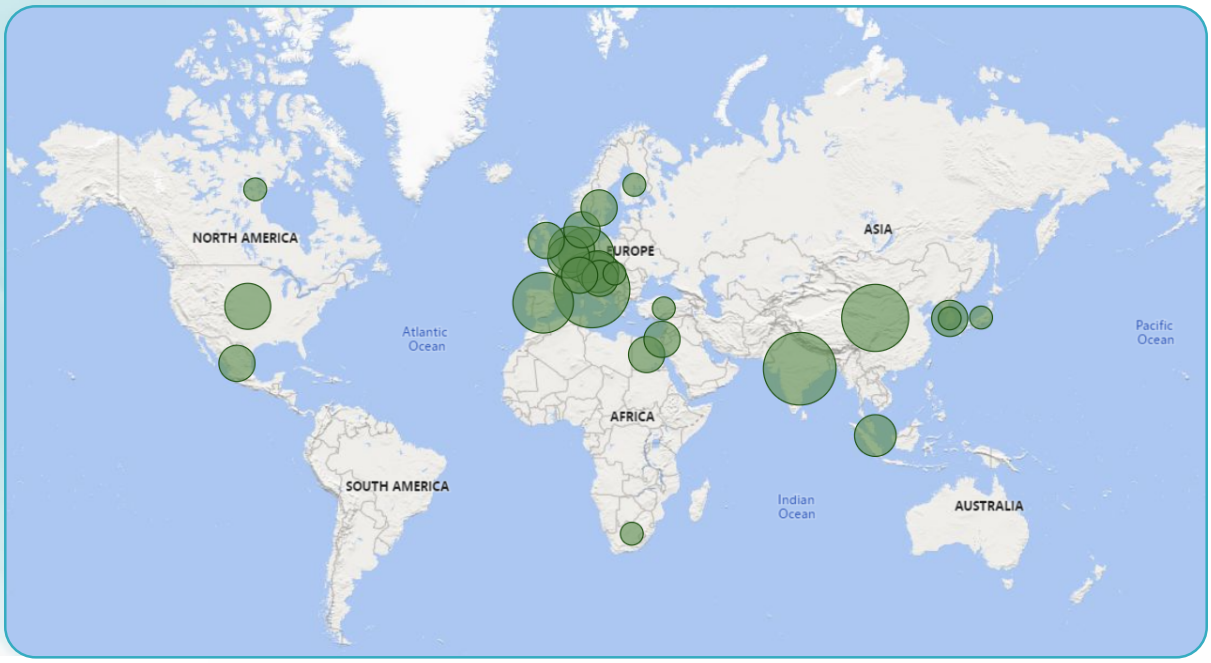

***Figure 7**: The map shows the spatial distribution of the API sites in an aggregated manner for all 11 medicines.*

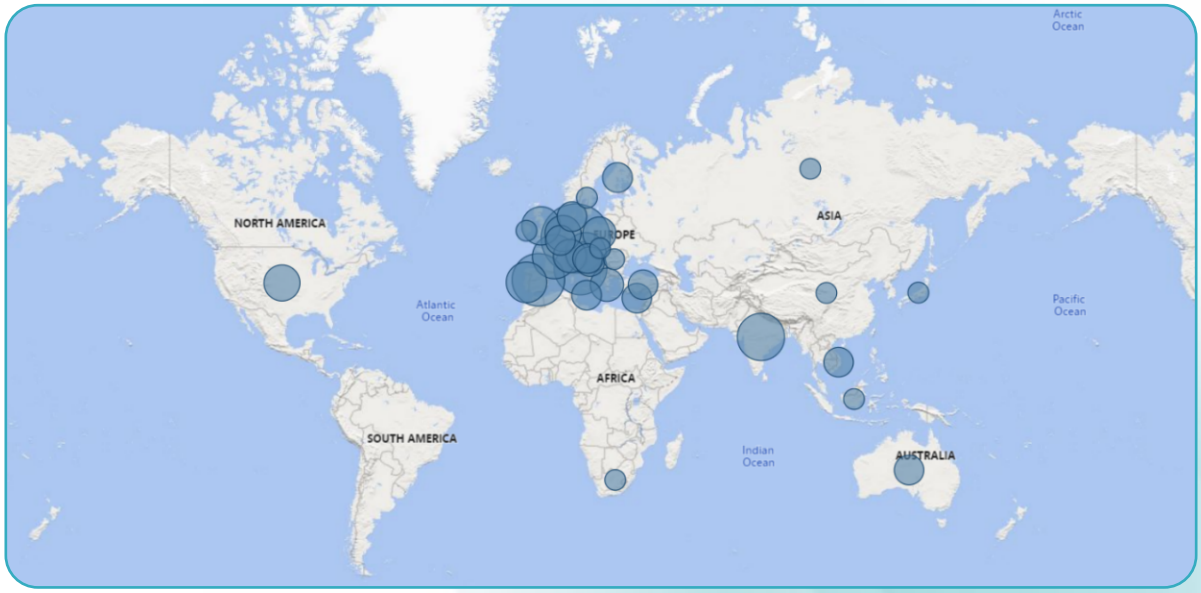

***Figure 8**: The map shows the spatial distribution of the fill and finish sites in an aggregated manner for all 11 medicines.*

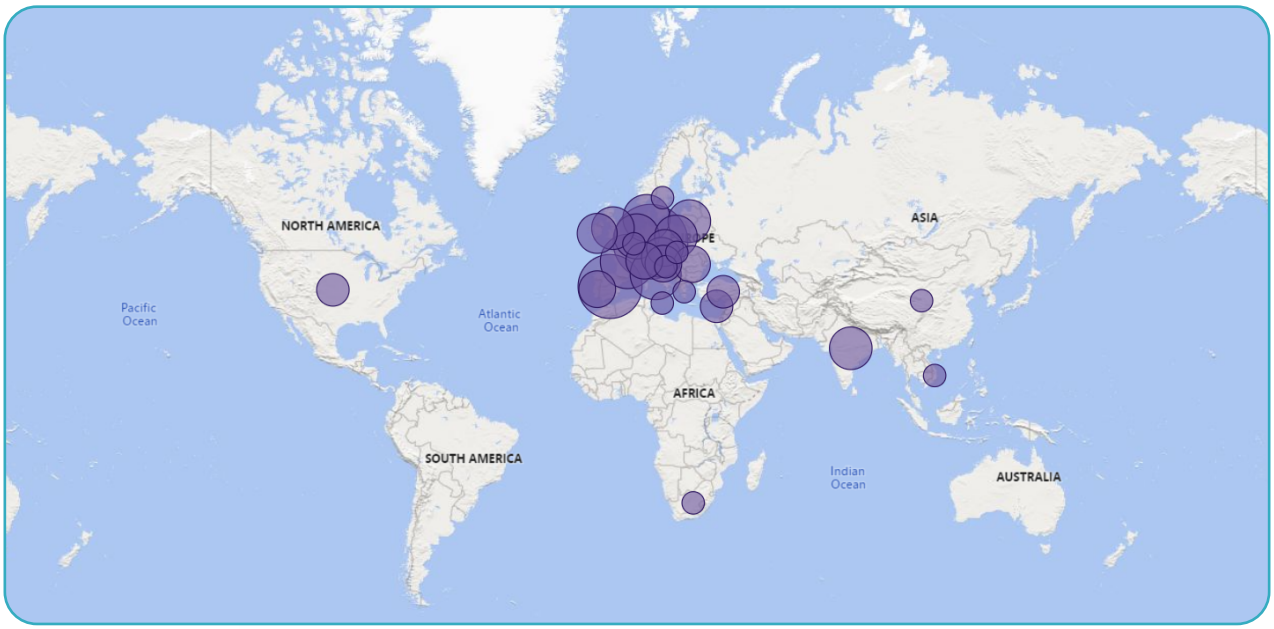

***Figure 9**: The map shows the spatial distribution of the packaging and labelling sites in an aggregated manner for all 11 medicines.*

The maps in the above figures are the result of aggregating the information received for the 11 medicines in scope. Each circle on the map represents the presence of at least one site; the bigger the circle, the higher the number of sites in that region.

As depicted on the maps, the sources of active API for the 11 medicines under consideration are widely distributed geographically. Notably, there is a considerable reliance on API providers located outside the EU. In contrast, MAHs are relatively less dependent on non-EU-located fill and finish manufacturers compared to their dependency on non-EU API sources. This observation indicates that the EU's resilience and degree of self-sufficiency are higher for this tier of the supply chain. The sites for packaging and labelling are mainly concentrated in the EU territory, showing a lower risk of dependence compared to other supply chain tiers.

2. Main root causes of shortages

The analysis of the root causes of shortages gathered from the replies to the questionnaires from Member States, as well as information provided by the EMA ([6]) based on the critical shortages single point of contact register, highlighted that the root causes of shortages vary from manufacturing issues, quality issues, and an unexpected increase in demand. It is important to note that a lot of information on shortage notifications lacked specificity regarding the root cause. The analysis of the information available revealed that shortages of critical medicines analysed at an EU/EEA level, primarily coming from manufacturing issues and unexpected increases in demand.

([6]) Data coverage from 01/01/2021 to date (i.e., Q1 2024).

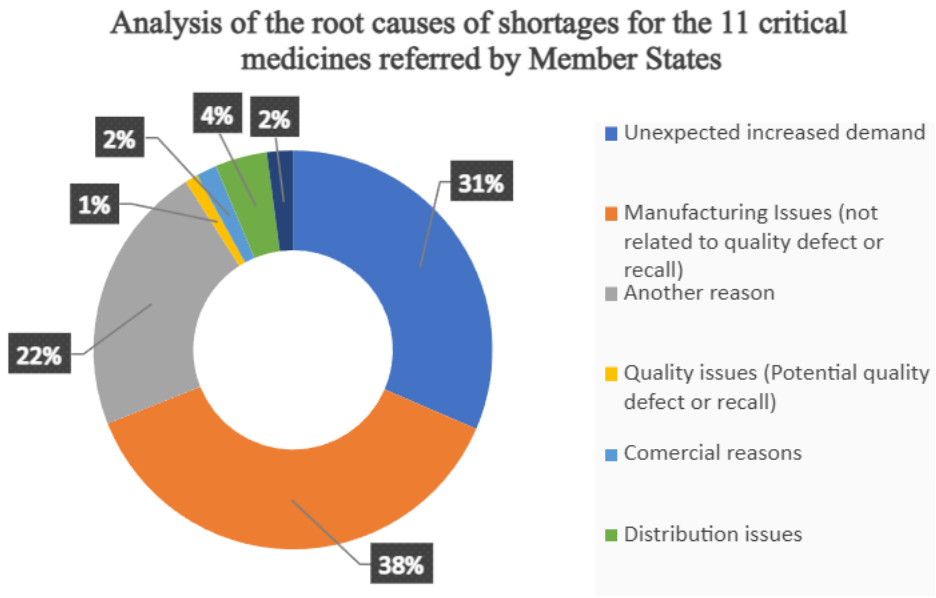

***Figure 10**: Summary of the root causes of shortages referred by Member States of the 11 critical medicines in scope from year 2021 to 2023.*

3. Member States main shortage mitigation measures

The mitigation measures employed by Member States to address the shortages for the 11 medicines in scope in the past 3 years can be categorised into: the use of regulatory flexibility, controlled distribution, alternative protocols or dose-sparing measures, communication with stakeholders, and export bans.

Notably, regulatory flexibility and controlled distribution measures were the most reported measures. Approximately 50% of Member States have reported granting approvals for exemptions, such as foreign language package allowances and unlicensed medicines.

In countries that implemented controlled distribution, this typically involved limiting prescriptions to essential indications, restricting the number of prescribed packages, or redistributing available doses among hospitals and pharmacies. Finally, some countries have reported the possibility of substituting the medicine subjected to shortages with equivalent treatments or adjusting the pharmaceutical form/dosage prescribed.

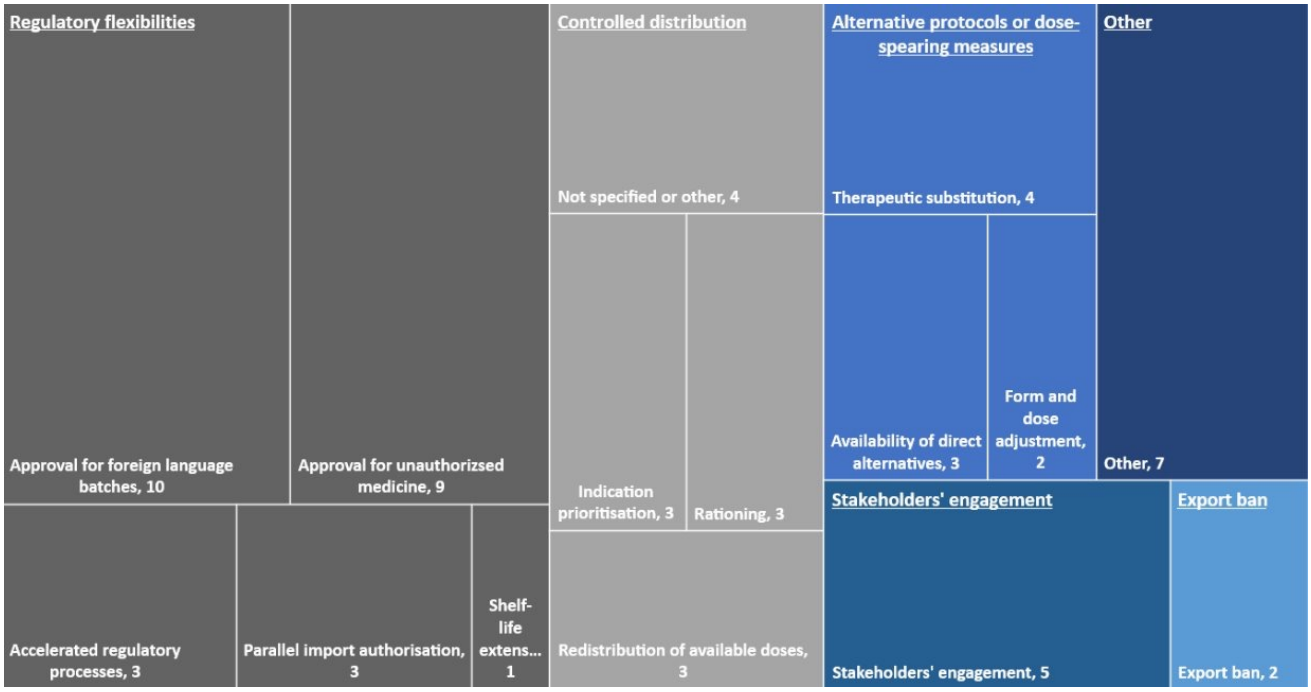

***Figure 11**: Summary of the mitigation measures strategies referred by Member States to address shortages of the 11 critical medicines in scope from year 2021 to 2023.*

OTHER FINDINGS

Information gathered from bilateral calls with Marketing Authorisation Holders

Following the data collection from MAH through the questionnaire, the Commission held bilateral calls with some MAHs, where relevant, in scope of the exercise. The bilateral calls allowed to discuss data submitted and general aspects on the supply chains (e.g. corporate supply chain risk management, methodologies for demand and supply forecasts and identified supply chain risks). In addition, the bilateral calls provided an opportunity for MAHs to share their experience in participating in this pilot exercise and to provide suggestions for improving the effectiveness of the exercise.

The main findings of these interviews confirmed that most companies have short-term (3-6 months), mid-term (2-3 years) and long-term (5-10 years) manufacturing capacity and production planning for which they use different methods, including Artificial Intelligence, to estimate the demand. For short-term production planning of generic medicines, MAHs appear to commonly use current sales rates for estimating the demand. However, this approach was perceived to have some serious limitations in case of unexpected significant demand fluctuations, such as those observed during the pandemic and the post-pandemic period.

In performing supply chain risk assessments, MAHs indicated that they use different methods, systems, and software solutions. According to the feedback we received, the most common mitigation measure to avoid shortages of generic medicines was maintaining safety stocks of finished products, APIs, and

other critical materials, as well as having more than one supplier for APIs or other critical materials.

MAHs regard manufacturing and logistical issues as the main reasons for supply chain discontinuities, and in few instances, regulatory issues. Manufacturing issues are related to the complexity of production processes and the fact that investing into new or modified production lines with a higher/more stable production volume is economically risky and takes time to get regulatory approval. The incentive for modernising the production process seems to be confronted with a number of obstacles.

In addition, with regards to the pilot exercise, almost all suppliers raised concerns about the amount of data requested in the exercise. Generating this data required a lot of time and resources on the MAHs side. They made clear that there is a need for a streamlined data submission process.

CONCLUSIONS

Significant dependences on non-EU API suppliers

The high vulnerability of 4 out of 11 substances due to reliance on API sources outside the EU highlights a substantial risk. This dependence indicates a potential disruption risk in the supply chain if these non-EU suppliers face production issues.

Risk from market concentration

The fact that all 11 products have over 30% of their supply coming from a single country or manufacturer underscores a risk of vulnerability. This concentration increases the risk of supply chain disruption due to geopolitical issues, trade restrictions, or production problems.

Variable production resilience

The mixed results in the diversification of manufacturing sites reveal that while some supply chains may be robust, others lack the necessary resilience. This variable resilience suggests a need for targeted strategies to diversify production sites to mitigate risks associated with localized disruptions.

Market dynamics uncertainty

The complex landscape of unpredictable demand for these substances indicates vulnerability to rapid changes in market conditions, which can complicate supply chain planning and response strategies. This uncertainty may require more flexible and responsive supply chain systems to adapt quickly to changing market demands.

Economic viability concerns

Economic viability challenges affecting 4 of the substances (according to MAHs) point to vulnerabilities that could compromise their long-term sustainability and profitability. Addressing these economic challenges is crucial to maintaining the health and viability of these supply chains.

There is need for strategic interventions to enhance resilience, such as diversifying supply sources, enhancing production capacity flexibility, and developing robust risk management frameworks to handle economic and market variability effectively. Shortages of critical medicines primarily stem from manufacturing issues and unexpected increase in demand.

This pilot reflected significant engagement and interest from all stakeholders: their contribution within the limited timeframe shows a collective commitment to building a resilient supply chain for critical medicines.

Considering the overall data coverage and quality, the outcomes from this pilot exercise shows some real limitations:

- **Lack of legal basis** on the data collection and the information sharing
- **Absence of harmonized data format** and standards leading to interoperability issues
- **Hesitancy of MAHs** to share highly sensitive commercial data.

It is recommended to undertake a comprehensive revision of the current methodology and indicators to establish a robust vulnerability signalling system. This system should be capable of:

- **Anticipating** vulnerabilities in the supply chain of critical medicines from the Union list.
- **Facilitate** focused monitoring of supply chain vulnerability.
- **Prioritisation/ Implementation** of mitigation measures on risk-based approach.
- **Better alignment** between the notification time of a shortage being identified as possible and the lead times of critical medicine manufacturing processes.

Refinement and extension of the methodology beyond its pilot phase is challenging within the limitations of the present legal framework and the constraints imposed by the existing data collection tools and formats.

LESSONS LEARNT

REFLECTIONS ON DATA MANAGEMENT

The reliance on past market sales data (public commercial database 2022 sales) lead to uncertainty in depicting current market dynamics.

Availability and access to up-to-date information of the market coverage of marketing authorisation holders of critical medicines is pivotal to obtain reliable results considering that the market can change significantly in a short period of time.

1

Despite the instructions provided on how to complete the questionnaire and the webinar sessions organised for stakeholders in scope of this pilot, there were variations in how specific questions were interpreted. This led to non-standardised and inconsistent responses, making comparison and aggregation of the information gathered via the questionnaires challenging. As an example, some company reported precise numbers for volumes of production others provided relative shares, and some MAHs opted to not disclose their production volumes.

2

In order to derive reliable and coherent results, it is essential to define and apply common terminology and standards across stakeholders.

The response rate obtained was of circa 50% for MAHs and circa 64% for Member States. These response rates were obtained the exercise was carried out in a framework where there is a lack of legal basis and an operative standardised platform for data collection. The outreach to participants and relevant stakeholders prior to the launch of the questionnaire raised awareness of the importance of participation in this pilot exercise and encouraged participation. Some participants indicated that the limited time to prepare the answers had conditioned their participation in the study. Further actions will benefit from longer timelines for data collection.

3

Data coverage could be significantly facilitated if adequate legal basis and an operative standardised platform are in place.

The data received did not adhere to any coherent validation process and, in some cases, were based on self-reported measures.

4

The lack of harmonisation in format, definitions, and quality standards can result in potential reliability issues, leading to biased outcomes and skewed conclusions.

5

Overall, refinement and extension of this exercise beyond its pilot phase is challenging within the limitations of the present legal framework and the constraints imposed by the existing data collection tools and formats.

REFLECTIONS ON METHODOLOGY

The thresholds of the indicators are not based on (historical) data analysis and/or expert opinions; hence they may fail to accurately reflect the true levels of risk, leading to either overestimation or underestimation of potential supply chain issues.

Furthermore, the original thesis that the chosen indicators are capturing adequately the root causes of shortages can only partially be confirmed with the pilot. MSs and participating MAHs indicated that there is a broad spectrum of root causes for shortages and current indicators are unable to anticipate and depict them.

6

The design of the indicators should be critically discussed and modified to adopt or develop possibly new indicators and thresholds.

The current method envisages the collection of aggregated response per INN by MAHs that has resulted in a loss of critical information, hindering our ability to effectively trace specific problems to different steps of the supply chain and lack of vulnerabilities associated with specific steps within each tier (i.e., API, FF, PL).

7

To conduct vulnerability assessment in future, a more detailed and granular level of information may be considered when enhancing the methodology. The revision of the current method with inclusion of additional data request should guarantee workable and sustainable approach (i.e., regarding volume of information to be requested by the stakeholders and resources needed for its provision by the MAHs).

Experts and insights from the various fora (e.g., MSSG, Joint industrial cooperation forum of HERA and the Critical Medicines Alliance) should refine the vulnerability analysis methodology. This consultation among stakeholders aim at pinpointing priority actions and devise solutions for strengthening the supply of critical medicines in the EU. By integrating the collective knowledge into our analysis approach, we aim to offer a comprehensive understanding of the factors contributing to supply chain vulnerability, ultimately informing the development of targeted, effective strategies to mitigate potential shortages.

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A comprehensive revision of the current methodology and indicators to establish a robust vulnerability signalling system is necessary. This system should be capable of:

Anticipating vulnerabilities in the supply chain of critical medicines from the Union list.

Facilitate focused monitoring of supply chain vulnerabilities.

Prioritisation/ Implementation of mitigation measures on risk-based approach.

REFLECTIONS ON STAKEHOLDER ENGAGEMENT & COMMUNICATION

This pilot reflected significant engagement and interest from all stakeholders: the impressive contribution within a limited timeframe shows a collective commitment to building a resilient supply chain for critical medicines.

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Supply chain reliance and robustness can only be achieved and established with engagement, cooperation, and participation from all the stakeholders.

The tight timespan (5 weeks) allocated to stakeholders for the data gathering resulted in missing data and lack of validation of reported information against available sources. In addition, the lack of harmonisation of format, definition and quality standards lead to significant efforts by HERA to normalise the received data and allow a coherent data analysis on time. Finally, the solution to manage data as well as the lack of standards proved to be overall time-consuming.

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All the involved stakeholders expressed concerns about the time and the resources required to participate in these exercises; especially if expanded to include the full EU critical medicines list. Streamlined data submission process and legal framework is pivotal to scale this exercise to the full Union critical medicines list.