EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Moving together towards better prevention of medicine shortages in the EU

Feedback from the HMA/EMA multistakeholder workshop on shortages

An agency of the European Union

Contents

Introduction

Shortages of medicines have been a public health concern in the EU and globally for many years and recent exacerbations in shortages have pushed these concerns to the top of the healthcare agenda.

In 2016, the Heads of Medicines Agency (HMA)/European Medicines Agency (EMA) Task Force on Availability of Authorised Medicines for Human and Veterinary Use (TF AAM) was set up to look for strategic and structural solutions to address disruptions in the supply of medicines and ensure their continued availability in the EU. The work of the taskforce led to a number of initiatives, including EU-wide guidance to improve the management of medicine shortages in the EU and the EU Single Points of Contact for Shortages (SPOC) network.

The COVID-19 pandemic compounded the problem of medicine shortages and EMA initiated several activities to better monitor and coordinate actions on shortages in crisis situations within the EU regulatory network. The new structures and activities, which were set up without a formal mandate during the COVID-19 pandemic, were then enshrined in legislation last year (EMA's extended mandate[1]) to ensure better management of shortages during times of crisis.

Shortages remain a key priority for the EU regulatory network and are addressed in the European Medicines Regulatory Network Strategy to 2025[2]. TF AAM's activities were put on hold during the pandemic, but operation resumed in December 2021 under a new mandate to continue work and streamline processes for better management of shortages (i.e. beyond a crisis situation scenario).

On 1 and 2 March 2023, acknowledging the important role stakeholders play in the prevention and management of shortages, the Agency convened a workshop bringing together national competent authorities (NCAs), the European Commission (EC), industry, patient and healthcare professional representatives, health technology assessment bodies, payers and academia as well as veterinary medicine representatives. During the workshop, these stakeholders discussed recent initiatives and reflected on possible actions to better and more proactively prevent, mitigate and manage medicine shortages in Europe.

The workshop provided an opportunity for stakeholders to reflect on the work of the TF AAM and to identify next steps needed to become more proactive and focus on preventative actions to better anticipate and manage emerging situations. This workshop was timely in light of the recent shortages of antibiotics which have had a significant impact on public health and have tested the existing system, highlighting its limitations and identifying the most critical/urgent areas for improvement. It provided an opportunity for stakeholders to reflect on TF AAM's work and to look ahead at the next steps needed to proactively anticipate and manage emerging situations in the future.

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[1] 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. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L:2022:020:TOC Date accessed:11 March 2023

[2] European medicines agencies network strategy to 2025 Protecting public health at a time of rapid change. https://www.ema.europa.eu/en/documents/report/european-union-medicines-agencies-network-strategy-2025-protecting-public-health-time-rapid-change_en.pdf (accessed 30 March 2023)

Session 1

Setting the scene

Moderator: Karl Broich (HMA)

Key messages:

- Many initiatives are ongoing to adapt the EU regulatory system to better respond to shortages. These include legislative changes, such as EMA's extended mandate providing new tools to manage shortages in crisis situations, and the upcoming revision of the pharmaceutical legislation that is expected to strengthen existing obligations to address medicine shortages and withdrawals from the market.
- There are differences between managing shortages during and outside of crisis situations. However, regardless of the circumstances, collaboration between the national agencies, EMA and the EC is essential for effective shortage management.
- TF AAM has a key role in the management of shortages in normal circumstances, where it provides structural support for policy and guideline development.

The political landscape has changed dramatically over the last few years and there are many ongoing initiatives at national and EU level to address shortages of medicines in the EU. The pandemic saw an escalation of medicine shortages linked to lockdowns and supply chain disruptions as well as increases in demand. Learnings from handling the pandemic have led to new legislation (**EMA's extended mandate**[1]), which has provided EMA with a stronger capacity to deal with shortages and created new processes to manage shortages in crisis situations.

In addition, further legislative and non-legislative changes are being made at EU level. The EC study on shortages[3] and its resulting recommendations, together with the EC's **pharmaceutical strategy for Europe**[4] that seeks to make the European pharmaceutical system more patient-centred, future-proof and crisis-resistant, have paved the way for the **revision of the pharmaceutical legislation**, for which a proposal is expected in April 2023. The revised legislation is expected to include stronger obligations for supply of medicines and transparency, earlier notifications of shortages and withdrawals, and enhanced transparency of the supply chain.

The proposal is based on extensive input from stakeholders and takes into account results from the EC-led **structured dialogue on security of supply of medicines**[5]. This initiative was set up in 2021 with a mandate set out in the pharmaceutical strategy to identify vulnerabilities in the supply chain and to find solutions to ensure the security of supply and availability of medicines. It did so by involving all actors in the supply chain, public authorities, patient and healthcare professional organisations and the research community.

The EC-led **structured dialogue** also led to the proposal for an EU list of critical medicines. This list should set out medicines with a significant impact on public health for which measures should be taken to improve security of supply. This EU list will be developed by TF AAM. The list applies outside of public health emergencies and should not be confused with the list of critical medicines for established public health emergencies. The latter defines critical medicines

[3] European Commission, Directorate-General for Health and Food Safety, Jongh, T., Becker, D., Boulestreau, M., et al., Future-proofing pharmaceutical legislation : study on medicine shortages : final report (revised), Publications Office of the European Union, 2021, https://op.europa.eu/en/publication-detail/-/publication/1f8185d5-5325-11ec-91ac-01aa75ed71a1/language-en

[4] The pharmaceutical Strategy for Europe. https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe_en

[5] Structured dialogue on security of medicines supply. https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe_en

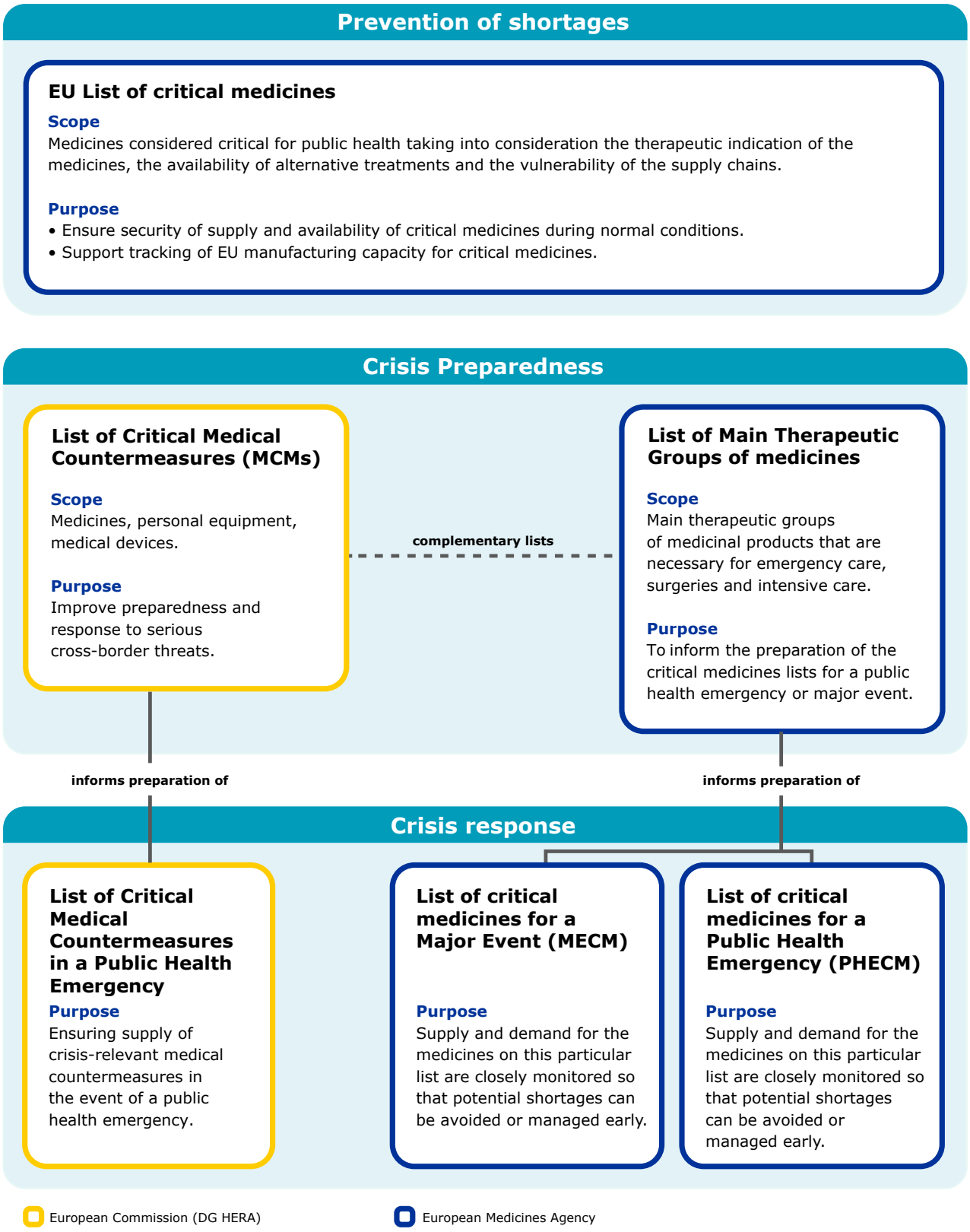

Figure 1: Lists of critical medicines and critical medical countermeasures

authorised for the management of public health emergencies (e.g. COVID-19 or Mpox) for which the supply and demand should be closely monitored to identify and manage potential or actual shortages (Figure 1).

More recently, the **EU initiative Joint Action CHESSMEN**[6] (Coordination and Harmonisation of the Existing Systems against Shortages of Medicines) was set up as an EU-wide project involving organisations representing 22 EU Member States. It aims to strengthen the existing harmonisation efforts of the EU network in the area of shortages and provides financial support to build national capacity and infrastructure in managing shortages.

Shortages of medicines are a key challenge for the longer-term development and sustainability of the regulatory network. To better tackle medicine shortages, developments are seeking to optimise the current structures of the EU regulatory network. While Member States are at the core of medicine shortage management, shortages have multiple interdependencies and cannot be managed in isolation but require collaboration with stakeholders: collaboration with patients and healthcare professionals, between authorities (such as the EU NCAs, EMA, the EC including the Health Emergency Preparedness and Response Authority [HERA]) and at an international level is essential to ensure that shortages can be effectively managed for the benefit of patients.

Availability and accessibility of medicines are therefore described as a strategic focus area in the **European medicines agencies network strategy (EMANS)** to 2025[6], which outlines priority focus areas for the network reflected in EC's pharmaceutical strategy for Europe. For availability and accessibility of medicines, EMANS highlights three key areas: investigation of factors causing medicine shortages, development of strategies for shortage prevention and management, and improvement in the coordination of activities and communication. Work in these areas will give further opportunities for national and European legislation proposals.

The introductory session of the workshop differentiated between the handling of shortages during crisis situations and under normal circumstances.

For shortages in crisis situations, the extended mandate has provided EMA with new governance structures and tools:

- EMA's Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG), which is an executive body that coordinates urgent actions within the EU to manage medicine supply issues in a public health emergency or major event and in preparation of a crisis;
- Its working party, the Medicines Shortages Single Point of Contact working party (SPOC WP), which is responsible for monitoring and gathering intelligence that will inform the actions of the MSSG. In a crisis situation, the SPOC WP is responsible for identifying critical medicines which require close supply and demand monitoring. The SPOC WP consists of experts dealing with supply issues at national medicines agencies in EU/EEA Member States and is therefore closely linked to the supply chain actors in the Member States including distributors and healthcare systems;
- During times of crisis, EMA's crisis activities, coordinated through MSSG and SPOC WP, are complemented by activities managed by HERA to ensure availability of, and access to, key medical countermeasures (medicines and medical supplies that can be used to diagnose, prevent, or treat diseases related to such threats). These will contribute to the global health emergency response by activating mechanisms for monitoring, development, procurement and joint purchase of medical countermeasures.

Further milestones of the extended mandate still lie ahead, with the establishment of a similar infrastructure for the monitoring of medical devices in crisis situations, as well as the introduction of the European Shortages Monitoring Platform (ESMP). Once initiated, pharmaceutical companies and the Member States will use this platform to report shortages and provide relevant supply and demand data for critical medicines during crisis situations, as well as to report

[6] Joint Action CHESSMEN – Coordination and Harmonisation of the Existing Systems against Shortages of Medicines, European Network. https://www.aifa.gov.it/en/-/meeting_apertura_progetto_europeo_chessmen (accessed 30 March 2023)

potential supply issues that may lead to such crises. After it comes into operation in February 2025, the ESMP will lead to more effective monitoring and prevention of shortages in the EU and improved coordination of these activities.

For shortages outside crisis situations, important monitoring work continues. The SPOC WP continuously monitors critical shortages, i.e. actual or potential shortages of medicines likely to lead to a major event or a public health emergency, and shares information on availability of alternative medicines. In parallel, HERA contributes to the global health emergency preparedness by carrying out important work for key priority threats (pathogens with pandemic potential, antimicrobial resistance, and chemical, biological, radiological and nuclear threats) (also see figure 1).. For these areas, HERA identifies relevant medical countermeasures and monitors vulnerabilities and strategic dependencies related to the development, production, procurement, timing and distribution of these countermeasures.

Whereas the MSSG acts as an executive group for preparing for and managing crisis situations, TF AAM is a central "hub" providing structural support for policy and guideline development for the management of shortages and availability issues outside crisis situations. TF AAM's new mandate, together with its renewed structure and composition, builds on the objectives described in EMANS to streamline processes, foster synergies and avoid duplication of work within the network. The taskforce has also become an important hub to track other related activities in the area of medicines availability. Since its inception, TF AAM has led to a number of important deliverables that define the way shortages are currently monitored, managed and communicated on. A key outcome of TF AAM under its previous mandate was the establishment of the SPOC network to improve information sharing between Member States, EMA and the EC on important human and veterinary medicine shortages and to coordinate actions to help prevent and manage shortages. The SPOC network was strengthened under EMA's extended mandate and renamed the SPOC Working Party (SPOC WP). The SPOC WP is the engine for today's monitoring activities of shortages within the network, fundamental to both the MSSG and TF AAM in crisis situations and during normal circumstances (Figure 2).

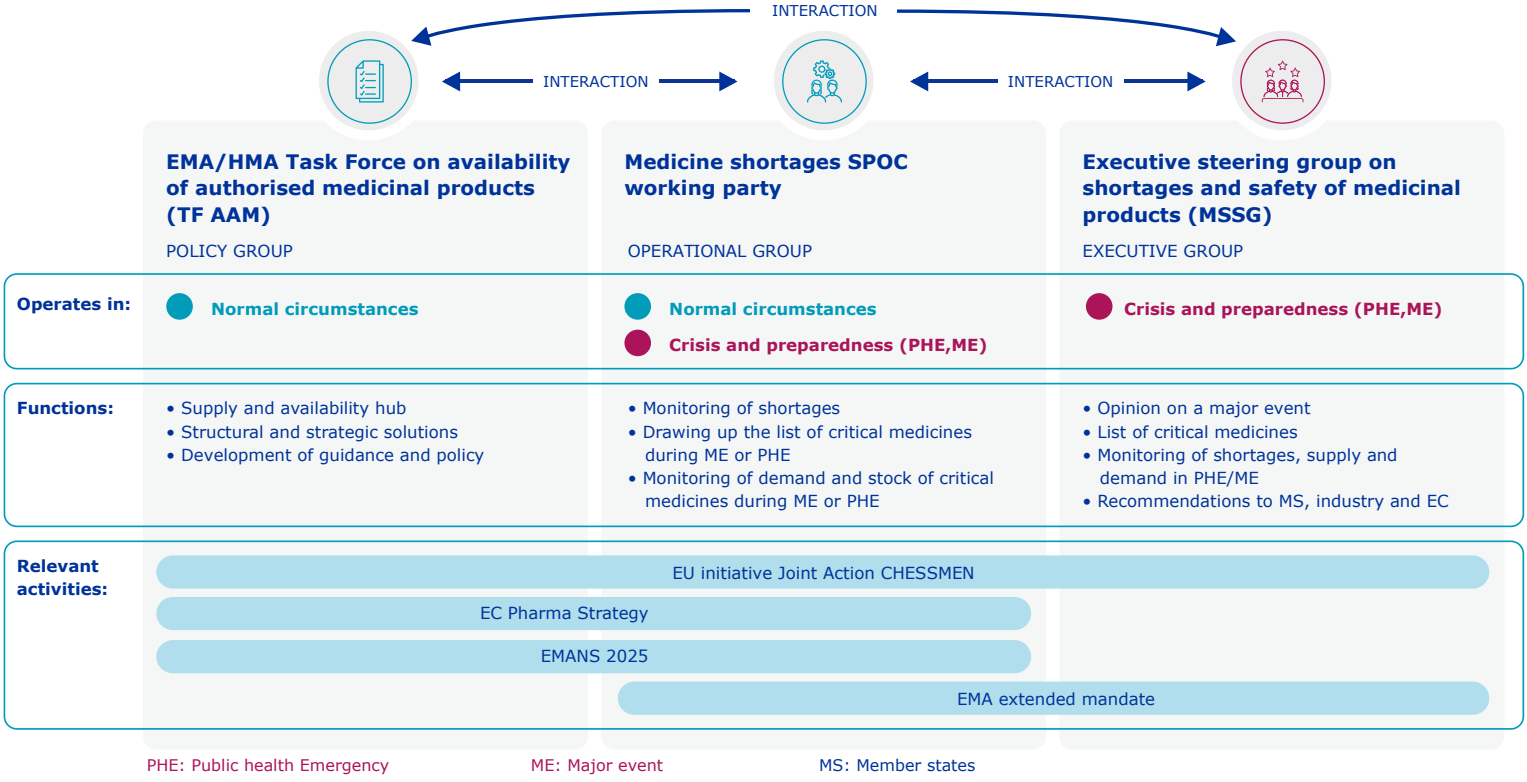

Figure 2: Monitoring and prevention of shortages in crisis situations and under normal circumstances

Session 2

Feedback from parallel breakout sessions

The workshop included three parallel sessions on topics requested by stakeholders:

- Supply and availability of immunoglobulins
- Biosimilar medicines
- Veterinary medicines

Supply and availability of immunoglobulins

Facilitators: María Jesús Lamas (HMA)
Rapporteur: Emilija Matelytė (EMA)

This session's aim was to better understand the complexity of the immunoglobulin supply chain and identify potential solutions to improve the availability of human immunoglobulins.

Two legislative frameworks are applicable in relation to the supply and availability of immunoglobulins. The steps of collection, processing, testing, storage and distribution of plasma are covered under the EU legislation on blood, tissues and cells[7], and the steps of transportation, storage, testing, processing/ pooling and manufacturing of immunoglobulins are covered under the EU Pharmaceutical legislation.

Various initiatives are ongoing at EU level to improve current availability issues. The SPOC WP is monitoring the supply of immunoglobulins and interacts with stakeholders to analyse the supply and availability situation. Under the blood framework further initiatives aim to increase plasma collection capacity in national blood services, and a new EU legal proposal (Regulation on standards of quality and safety for substances of human origin (SoHO)[8] intended for human application) includes measures to monitor supply and ensure donors are well protected and motivated.

Current availability issues can lead to inadequate treatment (i.e. reduction in treatment frequency or dose) with adverse outcomes for patients. Stakeholders therefore noted the need for harmonised clinical recommendations and scientific guidelines that prioritise use based on disease severity, the need for monitoring of adherence to such recommendations and the need to have available treatment alternatives.

Key areas of concern were the imbalance between the supply and demand of immunoglobulins, as well as the imbalance between plasmapheresis and whole blood collection procedures, with participants noting the need to consider increasing plasma collection through the increase of plasmapheresis procedures. An EU-funded initiative, strengthening voluntary non-remunerated plasma collection capacity in Europe (SUPPLY)[9], is building and transferring expertise on how public services can develop more plasmapheresis activities and how the collected plasma should be tendered to ensure supply of plasma-derived medicinal products (PDMPs). Stakeholders highlighted the existence of different national policies, which limits the supply of plasma and PDMPs at Member State level.

Given the rapid increase in demand, timely and accurate supply forecasting data from industry and other stakeholders was highlighted as a key requirement for regulators to understand the supply situation and plan measures to prevent or mitigate actual or potential shortages. In addition

[7] Directive 2002/98/EC – quality and safety standards for the collection, testing, processing, storage and distribution of human blood and blood components: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32002L0098 (accessed 17 April 2023)

[8] Proposal for a Regulation of the European Parliament and of the Council on standards of quality and safety for substances of human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52022PC0338 (accessed 17 April 2023)

[9] Strengthening voluntary non-remunerated plasma collection capacity in Europe (SUPPLY) https://supply-project.eu/ (accessed 17 April 2023)

to improving supply forecasting, participants emphasised the need to consider harmonisation and streamlining of production efficiency to increase the yields of plasma-derived medicines. Stakeholders also stressed the need for more in-depth analysis of the root causes of shortages and of the role that pricing plays in the supply of PDMPs.

Stakeholders noted the following additional possible actions:

- Financial support from the EC to Member States and coordinated plans for increasing plasma collection. Investments in the public (donor recruitment) and private sector (novel technologies to increase the yield) to improve plasma collection, production and product development.
- Need for harmonisation in donor eligibility criteria, such as donor deferrals. Need for increased awareness on donating whole blood or plasma and new plasma collection centres.
- Regulatory flexibilities for plasma master files, a mutual recognition agreement for GMP inspections.
- Closer collaboration between all stakeholders to ensure coordinated actions across the complex supply chain and improve availability of immunoglobulins for EU citizens.

Although some of the issues presented above are not within the scope of EMA's mandate, its important role as a central EU authority was acknowledged.

Biosimilar medicines

Facilitator: Steffen Thirstrup (EMA); Rapporteur: Rosa Gonzalez-Quevedo (EMA)

This session's aim was to better understand availability issues of biological medicines, discuss their interchangeability and get stakeholders' views on whether the use of biosimilars could prevent shortages of biologicals. Biosimilar experts provided an overview of the extensive scientific and clinical experience with biosimilars, including safety and prescriber-led switching. The work of the HMA/EMA working group on biosimilars was also presented, as well as EMA's scientific position on interchangeability[10].

A survey carried out by session participants before the meeting showed the need for more information on interchangeability of biosimilars. Overall, 50% of respondents had experienced shortages of biological or biosimilar medicines and most respondents trusted interchangeability and considered biosimilars as useful alternatives to prevent shortages of biological medicines.

As for all shortages, those affecting biological medicines are multifactorial, linked to procurement policies for these medicines, market forces and patent issues. Stakeholders agreed that the use of biosimilar medicines can address shortages of biological medicines, but there are hurdles that need to be overcome. Stakeholders pointed out that biosimilar development needs to become more sustainable. Payers identified issues when switching among biological products that use different delivery devices and indicated there may be a need for studies investigating compatibility of these devices. In addition, it was acknowledged that it is important to address any concern that may arise in clinical practice, such as interchangeability when the biosimilar medicine is used for a condition authorised for the reference but not the biosimilar medicine (i.e. off label use) or vice versa. Another aspect discussed was patient consent to switching.

Communication was a key issue highlighted by stakeholders to increase the uptake of biosimilars. This includes timelier communication on the regulatory science underpinning biosimilars and consistent messaging for all stakeholders in the healthcare system.

Veterinary medicines

Facilitators: Ivo Claassen (EMA) and Constance McDaniel (HMA); Rapporteur: Janos Kovacs (EMA)

The session was the first multistakeholder discussion on shortages of veterinary medicines. Its aim was to differentiate availability issues from

[10] Statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU (europa.eu): https://www.ema.europa.eu/en/documents/public-statement/statement-scientific-rationale-supporting-interchangeability-biosimilar-medicines-eu_en.pdf (accessed 30 March 2023)

shortages, identify their root causes, see the role of Regulation (EU) 2019/6[11] in supporting availability of veterinary medicines and identify actions that are needed and actions to be avoided.

Therapeutic gaps, i.e. lack of authorised medicines for a certain disease/species were out of the scope of the session, but it was agreed that this problem needs to be discussed.

There are important differences between shortages of medicines for human use and shortages of veterinary medicines. Actions taken on the human side cannot be automatically applied on the veterinary side. It seems that market availability issues (lack of products that are authorised but not or no longer marketed) are a bigger problem than medicine shortages (supply chain disruptions directly preventing the availability of authorised and marketed products).

Regulation (EU) 2019/6 provides support for supply continuity and requires the recording in the Union Product Database of the annual volume of sales and information on the availability for each veterinary medicinal product. The Union Product Database could be developed further for the monitoring of shortages of veterinary medicinal products.

Regulation (EU) 2019/6 provides no legal basis for reporting shortages. The extent and severity of shortages in the veterinary sector are currently unknown in many EU Member States. Further investigation at multi-stakeholder level is needed to gather the missing (quantitative) data and identify root causes of shortages. Veterinary stakeholders agreed on the benefits of having a list of critical veterinary medicinal products even if the situation amongst Member States is different. Veterinary medicines should be considered as essential goods in line with human medicines and should receive the same regulatory flexibilities. Although guidance similar to the one developed for human medicines was not considered necessary for the time being this should be reviewed when the full size of the problem of shortages for the veterinary sector is known. Any development in this area should be proportionate to the extent of the problem to minimise any administrative burden.

[11] Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC: https://eur-lex.europa.eu/eli/reg/2019/6/oj (accessed 30 March 2023)

Session 3

Prevention of shortages

Moderator: Darren Scully (HMA)

Key messages:

- Medicine shortages have a negative impact on patients, consumers and healthcare professionals, and the situation has recently worsened.
- More efforts need to be put into preventing shortages.
- Prevention of shortages is a shared responsibility involving all stakeholders. Key recommendations for prevention centre around shortage prevention plans, adequate forecasting of demand, early monitoring and reporting systems that can be accessed by healthcare professionals and patients.

Prevention is an important aspect of shortage management and the work of TF AAM focuses on ways to become more proactive and preventative whilst trying to better anticipate and manage emerging situations.

Shortages have an important impact on patients and healthcare professionals alike. Surveys carried out in 2020 by consumer groups in five European countries[12] showed that 90% of shortages concerned prescription medicines and led to problems, such as adverse events and medication errors as well as increased out-of-pocket expenditures for patients. Shortages also have a significant impact on healthcare professionals. Surveys carried out amongst community pharmacists[13] showed that the incidence of medicine shortages worsened in 2022 compared to 2021 in the majority of EU countries, increasing the average time spent by pharmacists on dealing with shortages.

A. Santos (BEUC, European Consumer's Organisation) highlighted that the recent shortages of antibiotics illustrated the need for better policies and preventative measures. The planned legislative changes should address requirements, such as shortage prevention plans, industry obligations to hold safety stocks for medicines of major therapeutic interest, stock monitoring systems by competent authorities, earlier shortage notifications and dissuasive financial sanctions. J. Batista (PGEU, The Pharmaceutical Group of the European Union) highlighted systems for reporting disruptions that are in place in a number of countries involving pharmacists, as well as twinning CISMED, a pharmacy-based pilot system to exchange comparable information on medicine shortages within 4 countries and thereby facilitating international cooperation. Early reporting of signals by healthcare professionals plays an important part in shortage prevention but further improvements are needed. One of the areas highlighted was to broaden the competency of pharmacists to better manage patient care and to guarantee continuity of treatment during shortages.

S. Roenninger (on behalf of industry associations) highlighted a number of industry initiatives on prevention of shortages, such as diversification of global supply chains and the establishment of drug shortage prevention plans using a risk-based approach.[14] Best practice tools are available and maintained. However, there is not one solution to address all issues. Each stakeholder group, including media, must realise their influence. Best practices should be adapted based on specific characteristics such as the target patient population size, product modality, and stage in the supply chain and life-cycle of the product.

Harmonised criteria for critical shortages are needed to allow prioritising preventative actions. Marketing authorisation holders do not have the full oversight of the supply chain and prevention of shortages is therefore a shared responsibility involving all stakeholders. Appropriate strategies to forecast demand are needed and regulatory processes should be streamlined and made more flexible and agile.

In the veterinary sector, the market for medicines is very small when compared to the market for human medicines and multiple species have to be considered within this market. In many countries there is no legal obligation for marketing authorisation holders to report shortages of veterinary medicines. N. de Briyne (FVE, the Federation of Veterinarians of Europe) explained that the biggest challenge for the veterinary sector is the fact that there are insufficient veterinary medicines coming to the market and too many medicines being withdrawn. This lack of availability is one of the key areas of focus of Regulation (EU) 2019/6. A survey amongst FVE members showed that shortages affected vaccines as well as narrow-spectrum antibiotics with potential consequences on antibiotic resistance. As for human medicines, shortages of veterinary medicines can only be prevented through better collaboration and communication, facilitating the

[12] Surveys show medicine shortages hit consumers hard across Europe – BEUC (01/02/2022) https://www.beuc.eu/news/surveys-show-medicine-shortages-hit-consumers-hard-across-europe (accessed 30 March 2023)

[13] Medicine Shortages - PGEU Survey 2022 Results: https://www.pgeu.eu/wp-content/uploads/2023/01/Medicine-Shortages-PGEU-Survey-2022-Results-2.pdf (accessed 30 March 2023)

[14] E. Ramnarine, M. Jornitz, M. A. Long, K. O'Donnell, S. Rönninger, C. Smalley, A. Vinther, Risk based approach for prevention and management of drug shortages, PDA Technical Report, 68, 2014, 1-45. https://www.pda.org/scientific-and-regulatory-affairs/regulatory-resources/drug-shortage (accessed 30 March 2023)

single market and empowering the Union Product Database.

M. Alcaraz (EMA) highlighted the current work of TF AAM, with a focus on the good practice guidance for prevention of shortages. The guidance contains two parts, one, already published, which gives recommendations to patients and healthcare professional organisations, and a second providing recommendations to industry to optimise current systems of notification to increase transparency and accuracy. Key recommendations also centre around shortage prevention and management plans and communication within the supply chain. The guidance has been consolidated to include comments from industry stakeholders and will be finalised shortly.

Session 4

Permanent withdrawals from the market

Moderator: Momir Radulovic (HMA)

- Withdrawals from the market have a significant impact on healthcare systems, resulting in a significant impact on patients.
- Many marketing cessations are due to commercial reasons. This could be improved by changing public procurement practices to focus on security and continuity of supply.
- Earlier notification (at least 12 months in advance) of withdrawals from the market and better communication are key for public bodies (e.g. regulators and payers), patients and healthcare professionals.

Withdrawals from the market occur when a marketing authorisation holder intends, either temporarily or permanently, to stop supplying a medicine (Directive 2001/83/EC). When marketing authorisation holders intend to stop marketing a product, either temporarily or permanently, they are required to inform the regulatory authority no less than 2 months before the marketing cessation (per article 13(4) of regulation (EC) No 726/2004 and article 23a of Directive 2001/83/EC)).

Withdrawals often concern old, and well-established medicines but can also affect innovative medicines. The causes are varied but are mostly due to commercial reasons (i.e. small market size, pricing and reimbursement issues) or reduced manufacturing capacity. Despite the introduction of new medicines on the market, these often do not replace the medicines that are discontinued. M. Marc (JAZMP, the Agency for Medicinal Products and Medical Devices of the Republic of Slovenia) highlighted that withdrawal notifications are usually received when the companies have already made their decision to cease market supply of a product and regulatory authorities therefore have limited tools to negotiate with marketing authorisation holders. In cases where no authorised alternatives are available, regulatory authorities may have to issue special licences to import unlicensed medicines.

Several examples of high-profile withdrawals were highlighted by the speakers. C. Roffiaen (EPHA, European Public Health Alliance) highlighted the withdrawals of the well-established medicine mitomycin and of intravesical BCG immunotherapy, which were withdrawn in 2016 and 2019, respectively, as well as the withdrawal of the innovative medicine ibalizumab which left patients without treatment alternatives. Such withdrawals can lead to interruption of treatment or to potential adverse events and medication errors associated with the use of alternatives. M. Ermisch highlighted the example of alemtuzumab,

which was withdrawn for commercial reasons in its approved indication to be marketed at a higher price for another indication.

When looking at the causes of withdrawals, A. van der Hoeven (on behalf of the industry) highlighted that tendering practices which focused solely on pricing constitute a risk factor for shortages and withdrawals from the market. In his view, procurement practices should be reviewed, and include criteria such as security and continuity of supply, to prevent shortages and withdrawals. This was also echoed by M. Marc.

In terms of solutions, the need for prolonging the notice period was highlighted by several speakers. More transparency and guidance to prescribers on switching and using alternatives was highlighted by M. McCarthy (UEMO, European Union of General Practitioners). This would give healthcare professionals and patients more time to find alternative treatments and to switch patients in time. Earlier notification deadlines (at least 12 months in advance) would also allow regulators to liaise with potential alternative producers to take over production.

A discussion around pricing strategies and their impact on shortages and withdrawals led to diverging positions between industry representatives and payers.

Network priorities to 2025: TF AAM workplan

J. Ferreira and M. Berntgen (EMA) highlighted the actions of TF AAM in the field of withdrawals from the market. A survey in 2019 collected practices of NCAs on how they handle marketing cessations nationally:

- Dialogue with marketing authorisation holders to manage existing stocks and anticipate future supplies.
- Dialogue with clinical experts on guidance and protocols for therapeutic alternatives.
- The possibility of fast-tracking regulatory procedures for the approval of potential alternative medicines.
- Working with parallel importers to obtain unauthorised medicines through national permission schemes.

A panel discussion followed on the need for future actions in this area. This highlighted the need for a mechanism for industry and Member States to discuss withdrawals from the market at an early stage. Often patients are informed of a withdrawal late or not informed at all. Transparent publication, early availability of information and involvement of patients' and healthcare professionals' organisations to assess the impact of withdrawals from the market are urgently needed. A review of tendering practices was also highlighted as an opportunity to lessen the impact of marketing cessations. Currently, there is no guidance for industry on the identification/ reporting of withdrawals from the market (contrary to the TF AAM guidance on shortages reporting published in 2019). Changes in the upcoming revision of the pharmaceuticals legislation will further inform the need for actions in this area.

Session 5

Communication and transparency

Moderator: Yngvil Knudsen (HMA)

- Information on shortages has become more accessible across the EU/European Economic Area (EEA) in recent years.
- Public catalogues of shortages are a routine tool used by many EU/EEA national medicines agencies to provide information to the public. However, further improvements are needed.
- Improvements are possible in terms of both, the timing and the level of information provided: communication should come earlier, with more information on the extent of and duration of a shortage and available alternatives.
- Communication needs to be balanced and contextualised to counter one-sided media reports and should also cover preparedness activities to foster trust and promote rational use of medicines (and prevent stockpiling behaviour).

Communication is a crucial aspect in the management of shortages. This applies to communication between the actors within the supply chain, but also to transparent communication with the target audience. Poor communication within the supply chain means that shortages cannot be appropriately prevented or managed. Lack of communication to patients and healthcare professionals can lead to treatment interruption and negative outcomes for patient.

Different stakeholder representatives provided their views on how transparency and communication is key to the functioning of the supply chain and how it can reduce the impact of shortages.

J.F. Duliere (industry) focused on transparency between all stakeholders, highlighting the need for seamless communication and dialogue between the pharmaceutical industry and regulatory bodies, with simplified and standardised procedures including interoperable databases to avoid duplication of effort.
M. Korenjak (PCWP, EMA's patient and consumer working party) provided the perspective of patients and how communication from authorities can reduce the impact of shortages. Both speakers highlighted the role of mainstream media and the need for balanced communication from authorities, not only to objectively inform but also to counterbalance media reports which can incite stockpiling behaviour. R Giuliano (HCPWP, EMA's healthcare professional working party) provided the perspective of healthcare professionals and highlighted the importance of timely communication to ensure healthcare professionals can make the necessary preparations to switch to an alternative. She also highlighted the need to select the right channel of communication to address media reports.
D. Pernas (AEMPS) used the recent shortage of amoxicillin to map the timelines of the shortage management with those of public communication from authorities and mainstream media in Spain. In this case, media attention started and continued when measures had already been taken and the situation improved. Important learnings can be taken from this case to better monitor and respond to media coverage and to communicate earlier and clearly on preparedness activities.

J. Garcia Burgos and I. Abed (EMA) provided an overview of the initiatives of the TF AAM in the area of public communication on shortages and future work that is planned within this area. In 2019, the TF AAM working group on communication published the Good Practice guidance for communication to the public on

medicines' availability issues, which laid the basis for increasing transparency to the public and aims to provide a harmonised approach in communicating shortages. The key recommendation focuses on the use of shortage catalogues to communicate shortages to the public in a balanced way. The use of shortage catalogues as a communication tool by regulatory authorities has increased since the publication of the guidance; catalogues are now used in over 80% of EU/EEA Member States. The TF AAM will further look into how communication practices can be improved, using dedicated surveys to gather feedback on recent shortage cases. Activities regarding monitoring the implementation of the guidance will be linked with activities to increase awareness. In addition, EMA is looking at increasing transparency around shortages by publishing more information from the SPOC WP and the MSSG, fully recognising that enhanced transparency not only guarantees continued patient care but is also essential to build trust amongst key stakeholders.

The discussion that followed highlighted the need for communication to be proactive, balanced and contextualised, including more information on the extent and duration of shortages and alternatives. Efforts need to be made to counteract misinformation.

Summary and take-home messages

In light of recent high-profile shortages, this workshop was timely and provided an optimal forum for stakeholders from across the EU/ EEA to reflect collectively on the processes in place to manage shortages and withdrawals from the market, and to identify what needs to be done to become more proactive and shift focus to ensure better prevention, anticipation and management of emerging situations.

The current landscape in the EU/EEA is very different to the landscape in 2018, when the last workshop took place. There have been many changes, including legislative and non-legislative policy changes, which have led to new structures equipping the network to better handle shortages of human medicines. For veterinary medicines the focus is on availability and the recently adopted Union Regulation aims at improving availability of veterinary medicines in European Member States. Although some concrete steps in legislative and non-legislative actions have already taken place, stakeholders agreed that further actions are needed. Stakeholders showed a clear commitment for more solidarity, collaboration and partnership.

Communication was highlighted throughout the workshop as being critical; stakeholders asked for communication to be more timely, focusing on relevant information needed to ensure patient care. It was also considered that enhanced communication is needed for withdrawals from the market, together with earlier notifications. In the area of prevention of shortages, prevention plans were highlighted as key, together with early monitoring and reporting systems. There was a clear commitment from all stakeholders for more collaboration and enhanced communication.

The upcoming revision of the pharmaceutical legislation is now eagerly awaited, to further shape the work of the taskforce to handle shortages and allow the network to move from having a reactive to a more proactive role in the prevention, mitigation and management of shortages.

More information

The MSSG and SPOC WP

Under its new mandate, Regulation on EMA's Reinforced Role (Regulation (EU) 2022/123), EMA has new responsibilities to monitor critical medicines shortages that might lead to a crisis situation. The Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) has been set up to ensure a robust response to medicine supply issues caused by major events or public-health emergencies. The members of the MSSG include representatives of EU Member States, one representative of the European Commission, one EMA representative, as well as an observer from EMA's Patients' and Consumers' Working Party (PCWP) and its Healthcare Professionals' Working Party (HCPWP). The MSSG is formally supported by the SPOC WP.

Shortages can be brought to the MSSG if they are considered an actual or imminent major event. This may then lead to additional reporting requirements for the marketing authorization holder, including reporting on the cause of the shortage, current supply and demand data, which will help to better allocate existing stocks and to issue recommendations on additional mitigating measures.

The SPOC WP is responsible for monitoring and reporting events that could affect the supply of medicines in the EU. It provides recommendations to EMA's Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) on all matters related to the monitoring and management of medicines shortages and other availability issues affecting human and veterinary medicines.

For more information about EMA's responsibilities for monitoring and mitigating medicine and medical device shortages under Regulation (EU) 2022/123, see https://www.ema.europa.eu/en/about-us/what-we-do/crisis-preparedness-management.

Glossary

EC
the European Commission

EMA
The European Medicnes Agency

EMANS
European Medicines Agencies Network Strategy

ESMP
European Shortages Monitoring Platform

GMP
Good Manufacturing Practice

HERA
Health Emergency Preparedness
and Response Authority

HMA
Heads of Medicines Agencies

Joint Action CHESSMEN
Coordination and Harmonisation of the Existing
Systems against Shortages of Medicines

MSSG
Executive Steering Group on Shortages and
Safety of Medicinal Products

NCA
National Competent Authorities

Plasma Master File
A compilation of all required scientific data on the
quality and safety of human plasma relevant to
medicines, medical devices and investigational
products that use human plasma
in their manufacture

SPOC WP
Medicines Shortages Single Point
of Contact Working Party

TF AAM
HMA/EMA Task Force on Availability of authorised
medicines for human and veterinary use

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5) Structured dialogue on security of medicines supply

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