

23 August 2018
EMA/565780/2018
European Medicines Agency

EU regulatory network reflection paper on the availability of authorised medicinal products for human and veterinary use

Agreement by HMA	November 2016
Agreement by the EMA Management Board	December 2016

Table of contents

1. Introduction and purpose	2
2. Scope	4
3. Planned initiatives and proposals	4
3.1. Theme 1: Marketing of authorised medicinal products.....	4
3.2. Theme 2: Supply Chain Disruption.....	5
3.3. Theme 3: Communication	7
3.3.1. Internal communication.....	8
3.3.2. External communication and transparency.....	8
4. Organisational and operational considerations	9
4.1. Governance	9
4.2. Reporting	11
5. Next steps	11
ANNEX 1	12
References	16

1. Introduction and purpose

Unavailability of medicinal products in the European Union (EU) has been a topic of considerable concern for authorities, patients and consumer groups, healthcare providers and indeed the pharmaceutical industry itself for a number of years. Unavailability may arise due to three main reasons:

1. Medicinal products are not authorised. This concerns mainly medicinal products, determined by the Member States, whose availability is important for patients, but for which the marketing authorisation application has not been presented for that Member State or the previous valid registration has been withdrawn.
2. Medicinal products are authorised, but are not marketed or no longer marketed.
3. Supply chain disruptions directly prevent the availability of authorised and marketed products (GMP manufacturing difficulties, GCP problems or other problems affecting the quality of medicinal products or resulting from a safety concern, parallel trade, and lack of continuity within the supply chain of medicinal products).

The root causes for these reasons are diverse and multi-dimensional in scope and the Network has undertaken a number of initiatives in recent years to address the problems within the scope of its responsibility.

The unavailability of medicinal products has an impact on the entire supply chain from manufacturer to dispensing pharmacist with consequential impact on health care systems, and a potentially profound impact on human and animal health.

There are multiple causes for the problems of availability of medicinal products but only one consequence: the lack of a certain medicinal product for a specific patient who needs it. The impact that the absence of a medicinal product may have ranges from mere substitution by another medicinal product without any health consequences, to serious consequences in the case of medicinal products with no therapeutic alternative, which implies a human health risk.

Similarly, the availability of an adequate range of veterinary medicinal products to treat the wide variety of animal species and diseases in the European Community has been a growing challenge over the last two decades, and in many cases it implies an animal health risk and also in some cases a human health risk.

From the veterinary perspective, shortages may also have a major impact from another viewpoint as the control of certain veterinary infectious diseases also has health and economic importance. Interest goes far beyond the individual treatment of an animal and is extended to the entire livestock. An absence of available vaccines against foot-and-mouth disease or Bluetongue, to name but a few examples, can have very serious consequences on animal health of a country and also neighbouring countries. However, whilst the problem of availability is the same as for human medicines, the underlying causes and consequent actions to address these causes may be different due to the entirely commercial nature of the veterinary market and its particular features such as the wide range of species covered.

It can also be said that the problem of availability is a global problem, regardless of whether one cause or another is able to have greater or lesser importance in the different countries and that it has been perceived as an increasingly greater problem in recent years. The lack of availability of medicinal products can affect individual Member States or it can affect multiple Member States within the European Union and given the globalised nature of pharmaceutical supply chains that are designed to optimise cost efficiencies, may have significant and wide-spread international effects.

There may be an interrelationship between the multiple causes that can explain the problems of provision, supply or availability of medicinal products, so it is therefore unlikely that acting on cause alone is able to resolve all the problems.

This lack of availability of authorised medicinal products that may never reach the market or that may become temporarily or permanently unavailable has been recognised as a significant issue in the EU Medicines Agencies Network Strategy to 2020. The lack of availability of medicinal products is considered as a priority for the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) and there is recognition that due to the globalised nature of the pharmaceutical industry the problem has to be also confronted from a global perspective.

This objective has been acknowledged and identified by the network as a priority and has been included in the work plans of the different partners as objective for the coming years.

In this line, HMA and EMA approved at the end of 2015 a joint high level strategy (HLS) for the network until 2020, the 'EU Medicines Agencies Network Strategy'. One of the objectives stated in this HLS is to ensure the availability of appropriately authorised medicinal products for both human and veterinary medicinal products.

The HMA multi-annual work plan (MAWP), approved in February 2016, sets out how the work of the HMA will be focused on delivery of the objectives stated in the HLS.

In the same way, the EMA MAWP, approved in June 2016, also reflects the structure of the Network strategy and mirrors many of the key objectives included in the HMA MAWP, including the availability of medicinal products.

The Council adopted in June 2016 conclusions recognising that further analysis to examine the current functioning of the pharmaceutical systems in the EU and its Member States would be useful, in particular in relation to the impact of certain incentives in EU pharmaceutical legislation, on innovation, availability, inter alia, supply shortages, accessibility and affordability of medicinal products, including innovative treatment solutions to common diseases that cause a heavy burden to individuals and health systems.

In view of these circumstances, it is necessary for coordinated actions to be developed at all levels and by all the stakeholders involved so as to reverse this trend and guarantee continuity of supply so that patients have access to the medicinal products they need.

This reflection paper aims to provide an oversight of initiatives, propose and explore intended actions to be considered by the network to facilitate a better prevention, identification, management and communication of shortages.

It will summarise the various initiatives that have been undertaken by the EU network to date reflecting on the initiatives that are currently planned to facilitate a better prevention, identification, management and communication of shortages. It will also reflect on how these initiatives can be drawn together into a coherent implementation plan at EU Medicines Regulatory Network level to fulfil the objectives set out in the EU Medicines Agencies Network Strategy to 2020 which can be referenced by other stakeholders within the wider institutional framework.

The reflection paper will focus on three thematic areas, marketing authorisation procedures, supply disruptions and communication.

The initiatives already taken and actions done in the EU during previous years are listed in Annex 1.

The planned initiatives and proposals for coordinated work with the aim to save resources are described in section 3 of this reflection paper.

2. Scope

The scope of this reflection paper covers the identification of measures/actions to facilitate the identification, prevention, management and resolution of shortages and supply disruptions of the following categories of medicinal products:

1. Medicinal products not authorised.
2. Medicinal products authorised but not marketed or no longer marketed.
3. Supply chain disruptions directly prevent the availability of authorised and marketed products

Although rising pricing issues are out of scope, those situations where pricing may affect availability of certain products, e.g. through parallel trade, should be within the scope and considered by the task force in its planned initiatives and proposals if these are in the regulatory competence of the Network. It may be mainly the information exchange and facilitating the cooperation as the pricing issues are mainly in the competence of Member States.

For veterinary medicinal products there are measures proposed by the European Commission in the regulation currently negotiated in Council and European Parliament that are intended to stimulate the authorisation of a wider range of products and to promote availability and retention on the market of existing medicines. Furthermore, initiatives to stimulate authorisation of a wider range of veterinary vaccines form the focus of a dedicated joint Steering Group on Availability of Veterinary Vaccines between HMA and EMA and are therefore out of scope of this reflection paper. Measures to promote and ensure the continued availability and retention on the market of existing veterinary medicinal products fall within the scope of this paper.

The scope includes medicinal products for human and veterinary use, irrespective of the licensing route (CAPs and non-CAPs) although a tailored approach will be required to take into account the specificities of human and veterinary medicinal products.

The extent to which solutions developed for the human domain are appropriate and can be applied in the veterinary domain should be carefully examined in view of the lower level of overall resources, both human and financial, that are available in this sector. A balance will need to be struck that ensures that shortages are appropriately addressed without a substantial increase in administrative burden that would itself negatively impact availability.

3. Planned initiatives and proposals

Taking into account planned actions and the additional items identified in the HMA Network Strategy it is proposed that an overall task force for the topic of unavailability be established. The task force would oversee three thematic areas with some overlapping and supportive topics, objectives and outputs and some theme specific topics, objectives and outputs. The thematic areas would seek involvement of key stakeholders (National Competent Authorities - NCAs), Coordination Groups for Mutual Recognition and Decentralised Procedures (CMDh and CMDv), Good Manufacturing and Distribution Practice Inspectors Working Group (GMDP IWG), European Surveillance Strategy Working Group (ESS WG), Industry associations, Patient and Healthcare stakeholders, EMA and where relevant the European Commission (EC).

3.1. Theme 1: Marketing of authorised medicinal products.

This theme will draw together measures that are aimed at preventing shortages through promoting the marketing of authorised products in Member States making use of the current regulatory framework

and reviewing recommendations made by The Project Group on Facilitating Supply in Small Markets. This theme may also cover economic matters that fall within the remit of national competent authorities such as use of public service obligations, and incentives to promote marketing. The activities listed below may require specific involvement of CMDh, CMDv, EMA, and the EC where relevant.

- Activities promoting the entry of generics and biosimilars work sharing and reduced timetables.
- Promotion of work sharing and reduced timetables for variations in the event of shortages and exceptional situations, such as radiopharmaceuticals in the context of high-enriched uranium (HEU)/ low-enriched uranium (LEU) conversion and in the event of the need to urgently replace reactor sources in the event of severe outages.
- Investigate proposals for the continuation of the marketing of old niche products (human and veterinary).
- Facilitating and promoting the planning and use of multilingual packages to avoid availability problems later during marketing.
- Open initiatives for specific subgroups of medicinal products as needed.
- Review of the procedure for withdrawal applications in order to assess the possibilities of covering the market with marketed alternatives (common guideline for withdrawal applications). Ensure an adequate exchange of information about withdrawals between Member States.
- Stimulate mutual recognition (MRP) and repeat use procedure to favour potential marketing authorisation holders (MAH) to enter new Member States affected by shortages.
- Promote the inclusion of alternative manufacturers in the dossiers of those medicinal products that have been identified as critical in order to promptly respond in situations where supply disruptions due to manufacturing or quality problems may arise.
- Investigate the feasibility of EU common emergency stockpiling for essential/critical medicinal products.
- Identification of essential/critical/valuable old or niche products that fulfil medical need which, although not considered innovative and without commercial interest for the industry, may have a critical relevance for the health systems and patient care and therefore require enhanced support.

3.2. Theme 2: Supply Chain Disruption

This theme will draw together measures that are aimed at preventing shortages caused by disruptions in the supply chain involving, NCAs, CMDh, CMDv, GMDP IWG, Industry Stakeholders, Patient and Healthcare stakeholders, EMA and the EC where relevant. The work done and planned by EMA and Member States in the action plan regarding supply shortages caused by GMP should also be taken into account.

- To explore whether it is possible to proceed with a proposal to amend Chapter 1 of the EU GMP Guide in order to capture the main principles of the industry inter-association shortages taskforce guidelines aimed at reducing shortages caused by quality/manufacturing problems.
- Identification of market products at risk of shortage due to any potential supply chain disruption. Further development of assessment tool and procedures.
 - Following assessment, raise awareness and ask for effective prevention plans from MAH of critical products.

- Systematically request the presentation of a supply management prevention plan in the MAH transfer of essential/critical medicinal products.
- Preparation of guidance documents for both the content and the assessment of these prevention plans.
- Development of terminology/definitions and unit of measurement.
 - Definitions should consider availability in a wider sense and then go through several items to accurately define any situation, for example, distinguishing non-availability (worldwide) from shortages where there is still product available in other Member States or outside of the EU, taking into account the duration of the supply problem¹, or the potential impact on both the patients and the clinical practice², among others.
 - To establish metrics in order to facilitate management and benchmarking across EU, i.e., monitoring number of shortages due to supply chain, manufacturing problems, or other causes.
- Preventative measures / implementation of industry best practices to minimise the risk of shortage due to potential supply chain disruption.
- Monitoring of shortages of authorised products (human and veterinary).
- Incident Management of cases of non-compliance with best practices (GCP/GMP) for human and veterinary medicinal products (IRG/IRN) where there is an identified risk of shortage due to potential supply chain disruption.
- Finalisation of CMDv Best Practice Guide (BPG).
- Industry reporting to authorities – development of a core conceptual framework for human and veterinary medicinal products, tailored to individual Member State needs.
- Potential link to mapping of supply and distribution channels.
- Defining measures directed towards minimizing the impact of shortages on patients and health care systems once they have occurred. This would be also applicable in the veterinary field.
- Explore the possibility of establishing a common EU repository of medicinal products not authorised in the EU for patients (including other MS and third countries).
- Explore the possibility of development of recommendation of use and even guidelines on magistral formulation for exceptional cases.

EMA plans to follow up with a third phase of actions to address product shortages due to manufacturing and quality problems.

The four major actions areas relate to the following:

¹ Example: a) Lack of supply, Occasional absence of a medicinal product in the entities authorised to dispense medicinal products; b) Supply problem, situation in which the available units of a medicinal product in the medicinal product channel are inferior to the needs of national or local consumption; c) Shortages, absence of units of a medicinal product in the pharmaceutical channel

² Example: a) no impact on clinical practice due to the existence of similar medicinal products in the market; b) impact on clinical practice of medicinal products that have therapeutic alternatives in the market but the change to said alternatives requires medical intervention; c) Therapeutic gap or problem of a medicinal product that has no therapeutic alternative in the market

1. Implementation of the Industry best practice guidance; Industry were of the opinion that a regulatory 'pull & push' was required to ensure all industry stakeholders focused more on supply and availability of medicinal products and implemented the industry developed guidance.
2. There is a need for harmonised definitions for shortage and meaningful supply disruption as there is no harmonised definition or approach to the management of shortages. This would be further strengthened by a unit of measure. A unit of measure facilitates reporting across the Union and allows us to assess the impact of mitigation strategies that may be implemented by Member States. Such a unit of measure is applicable to any shortage whatever the reason, GxP or economic.

A survey performed for human medicinal products by the European Medicines Agency within the EU Medicines Regulatory Network revealed that there is no harmonised definition or approach to the management of shortages. There is a lack of clarity of what, when and to whom reports of shortage / unavailability / supply chain disruption should be made. For example in some Member States a timeframe is defined for which a shortage and supply chain disruption should be reported, 96 hours in Belgium and 72 hours in France while some Member States tolerate a 6-12 month absence of a product on their market before considering it a shortage. This survey data is supported by a similar study by DeWeerd et al., identifying that there are 20 different definitions for shortages in use across the EU and concluded that obtaining 'a uniform definition for drug shortages is important as well as identifying which conditions are preferable to report drug shortages in order to facilitate international benchmarking.

Until such definitions are in place we cannot compare shortages / supply disruptions across the EU. A single definition is unlikely to fit all scenarios. The healthcare professional and patient representatives that attended the EMA workshop in October 2015 expressed a preference for a definition of shortage that was linked to the patient and also had a timeframe defined. Industry representatives wanted a distinction between shortages that impacted the patient and supply disruptions that were managed with/without regulatory involvement.

In tandem with harmonised definitions there is a need to develop a unit of measure. A unit of measure facilitates reporting across the Union and allows us to assess the impact of mitigation strategies that may be implemented by Member States. Such a unit of measure is applicable to any shortage whatever the reason, GxP or economic. Regulators will be focused on shortages related to GxP, however such a unit of measure can be utilised to measure shortages attributed to economic factors of the local market place which is of value to Ministries for Health and Procurement entities. Pauwels et al. argues that reporting of drug shortages in Europe needs to be more harmonised with increased transparency for the reason for shortage. Mandatory early notification of shortages can help to anticipate the clinical impact of shortage while the centralisation of information is likely to reduce workload for the entire supply chain.

1. Further development of appropriate communication mechanisms to include communication between regulators and between regulators and external stakeholder organisations including healthcare professionals, industry and patient groups.
2. Application of developed industry best practices to other areas of the supply chain namely those covered by good distribution practice.

3.3. Theme 3: Communication

Development of a specific communication plan and enhancing the visibility of existing tools and procedures (HMA web linked to NCAs about availability and the EMA web).

This theme will involve NCA's, EMA, HMA Working Group of Communication Professionals (WGCP), IT Directors.

3.3.1. Internal communication

The proposal to be considered by the network would be the establishment of a common information system (e.g. a secure platform, which can be part of the European Medicines Web Portal, for sharing information within the network) for the communication and management of supply problems as a common repository to easily record up to date and relevant information on supply problems. Linked to shared definitions (above) through standardisation of the minimum information required to communicate each shortage (e.g. cause, foreseen duration, real time, aspects assessed and result)

This EU repository would facilitate not only the internal communication through the network, but also the early identification of the shortages and supply disruptions having a supranational impact. Moreover it will facilitate the implementation of a common approach when necessary to solve the problem from an EU and not only national perspective.

The agreed vision for the European Medicines Web Portal is limited to human medicinal products in accordance with the applicable legal provisions. Concerning the veterinary medicinal products, the new veterinary legislation foresees the creation of a single European Database of Veterinary Medicinal products and work has started to develop the roadmap to achieve this. The legislation foresees a requirement for MHA to record in the database when their products are placed on the market. The system therefore has the potential to act as a common information system on product shortages that would allow appropriate access to the regulatory network, to MHA and to the general public including health care professionals. Further reflexions is needed to identify which information would be necessary for a good management of supply problems and if the veterinary product database will be sufficient to provide this.

A dedicated email address for availability issues will be set up within the competent authority of each Member State and EMA.

The intention would be to define a way to proceed until the EU medicines web portal is launched. Moreover to identify how to communicate internally before the info is available in the web portal.

3.3.2. External communication and transparency

The main objective should be to provide good information on all EU shortages consistently across EU Member States, timely, in a single location (European Medicines Web Portal) and which is kept up-to-date as each shortage evolves.

Aimed to identify the best way to communicate these shortage cases to the general public (and/or specific stakeholders when needed) the following measures are proposed:

1. Share and analyse best practices on communication of shortages, including consideration of communication tools already available (e.g. information on some Member States websites and EMA shortage catalogue).
2. Promote the publication of the information uploaded in the proposed common information system for the communication and management of supply problems.
3. Increase the transparency and the information about supply problems to the general public.
4. Publication of specific and standardised information on supply problems occurring in the EU territory.

5. Make available the up-to-date information on shortages uploaded by all the Member States on a common site.
6. Establish criteria for publishing common informative notes about supply problems when needed. Develop common guidelines to determine the cases in which would be useful to publish common informative notes.
7. Publish an analysis of the evolution of supply problems in the website each year.

It is also crucial that external communication (and transparency) meets the expectations of stakeholders so as to enable trust in the Regulators' actions to tackle availability issues. Aspects to be considered relate to the provision of information on HMA and EMA websites, adequate interlinking and coordination of such information and regular proactive communication with all stakeholders. This may need the drafting of a dedicated communication plan.

4. Organisational and operational considerations

This section will elaborate on the proposed operational and organisational aspects to be considered.

This will include:

4.1. Governance

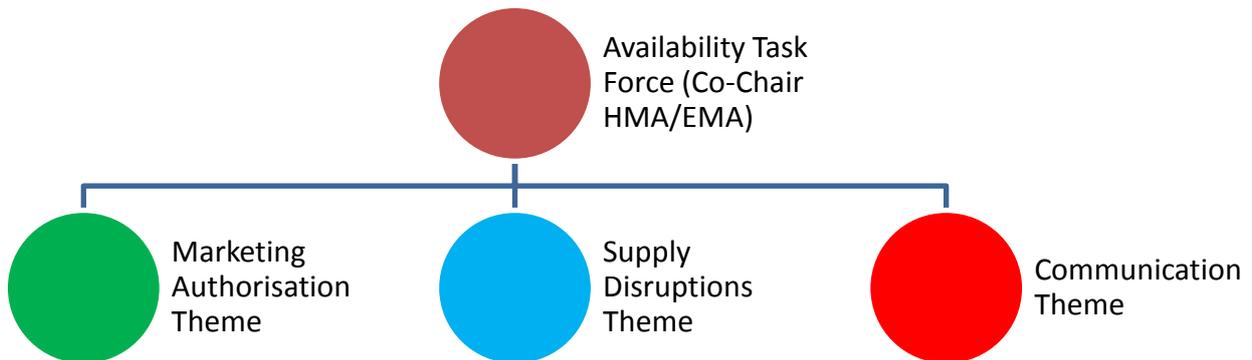
Considering the relevance of this availability problem to the network, the issue was clearly identified as a priority on the HMA and EMA MAWPs. The possibility of creating a new EMA/HMA joint taskforce to directly deal with this priority was proposed.

The taskforce provides the strategic steer and management oversight to the overall project ensuring that thematic work plans are consistent with the overall taskforce work plan and strategic objectives. The taskforce is also in charge of ensuring that any thematic work streams have specific objectives identified and progress measured while ensuring that resources are made available to support.

The taskforce would be composed of EMA, HMA and EC representatives as well as the Chairs of the CMDh and CMDv. The taskforce will be co-chaired by EMA and the HMA. The taskforce will be conducted as far as possible by means of virtual meetings, teleconferences and e-mails. The group should convene four times per year before HMA meetings or EMA Management Board (MB) meetings. The taskforce will prepare a dual report on an annual basis to the HMA and to the EMA MB.

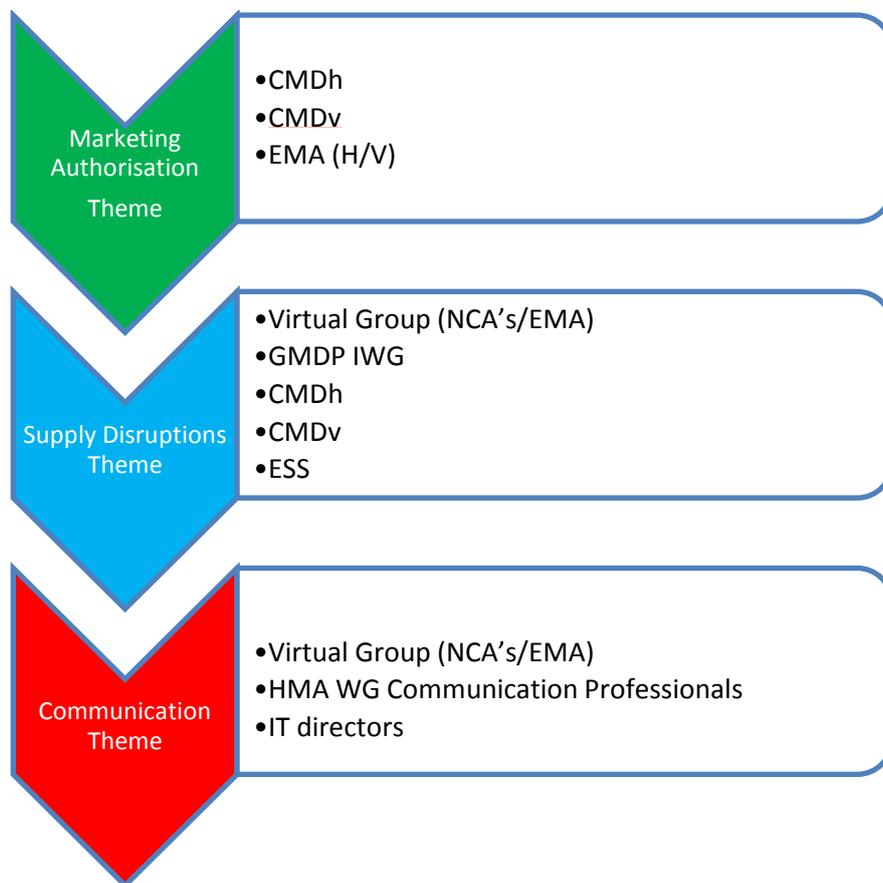
It is proposed that the taskforce establishes three thematic areas to deal with topics and objectives involving marketing, supply chain disruption and communication (Figure 1).

Figure 1 - Availability taskforce - Thematic Organisation



- The taskforce will seek to make use of existing working groups as far as possible and will ensure that specific activities related to availability of authorised medicinal products are included in work programmes of identified Committees and working groups (e.g GMDP IWG, CMDh, CMDv) who will be asked to report back to the taskforce on progress (Figure 2).

Figure 2 - Proposed Groups involved in each Thematic Area



- It is proposed that the mandate and membership of the existing operational ad hoc 'Availability Virtual Group' is reviewed and expanded and will take responsibility for activities identified within the Supply Disruptions Thematic Area and the Communications Thematic Area. As a consequence its mandate and membership will be reviewed.
- The Availability Virtual Group will continue to operate as far as possible by means of virtual meetings, teleconferences and e-mails.

The taskforce in collaboration with the various groups will develop an implementation plan with specific objectives. Progress will be measured through reporting from the various groups to the taskforce which will update HMA, EMA and where relevant the EC on a regular basis.

In addition, NCAs and EMA will each appoint a single point of contact for exchange of information on availability matters.

4.2. Reporting

The taskforce will approve a multi-annual thematic implementation plan that will set specific objectives and measures of success for each area.

The taskforce's co-chairs will report to the EMA MB and at the HMA plenary session.

5. Next steps

This reflection paper will be published once adopted/endorsed by HMA and the EMA MB as per the following steps:

- Agreement by HMA in November 2016;
- Agreement by the EMA MB in December 2016.

The next steps should be as follows:

- Adoption of multi-annual thematic action plan by the taskforce in Q1 2017 and promotion at CMDh, CMDv and GMDP IWG amongst others.
- Establishing and convening the 'Virtual group' in Q1 2017.

ANNEX 1

Initiatives on the availability

1. Heads of Medicines Agencies (HMA)

- a. Report of taskforce of HMA MG “Availability of Human Medicinal Products” 2007 followed by the Action Plan
- b. Information exchange between Member States
- c. EU Medicines Agencies Network Strategy to 2020 + HMA MAWP
- d. Publishing the information on compassionate use in Member States on its website 2016

2. European Medicines Agency (EMA)

EMA in collaboration with EU National Competent Authorities (NCAs) sought to promote a more proactive approach to shortages due to disruptions in the supply chain caused by manufacturing and quality problems. The plan had two phases, the first aimed at improving the Agency and the Network approach to assessment and decision making when dealing with these kinds of shortages and the second phase was aimed at raising industry awareness of the issue and seeking solutions from industry associations.

- a. with the objective of raising the awareness of the impact of medicinal product shortages, stimulate industry reaction and the improvement of Business Continuity Planning, a public workshop with stakeholders was held in October 2013 and EMA invited pharmaceutical industry and professional associations to propose solutions
- b. In October 2015, the Agency held a follow up workshop to look back on the results and identify areas for further work
- c. The EMA reflection paper on shortages due to manufacturing and quality problems published in 2012, completed in 2015 (in cooperation with national competent authorities, patient and consumer groups, healthcare providers and pharmaceutical associations)
- d. EMA reviewed the Incident Management Plan which deals now with all issues on veterinary medicinal products. When several Member States are concerned, the IMP is a way to manage harmonised action and coordination for shortages, quality defects and management.
- e. An implementation Plan 2012-2015 was developed within the Virtual Working Group on Product Supply Shortages under the coordination of EMA and with the participation of Italy, Spain, United Kingdom, Poland, France and the Netherlands. With the goal of a common understanding, the following documents were developed:
 - i. Criteria for classification of critical medicinal products
 - ii. Decision tree on escalation from national to European level
 - iii. Communication by the European Medicines Agency on supply shortages of medicinal products
- f. Website
- g. EU Medicines Agencies Network Strategy to 2020 + EMA MAWP 2016

- h. In 2015, the Agency decided to implement a one year pilot initiative to evaluate the effect of a fee reduction for Maltese language parallel distribution notifications on the volume of parallel distribution into Malta

3. Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)

The CMDh is currently acting as coordinating body for activities related to the management of some availability problems of medicinal products for human use. The activities of this group range from the transmission and information management (identification of supply problems and the potential therapeutic alternatives available in the different Member States) to the organisation and decision making for specific cases (i.e. identification of the essential products in Member States, management of the measures to be taken, etc.).

However, the coordination is not only limited to those shortages related to quality concerns but can be extended to any situation resulting in availability problems including, e.g. voluntary withdrawals, GCP issues (GCP CMDh WP), etc.

- a. a 'CMDh Best Practice Guidance On Collaboration Between Member States In Relation To GMP Non-Compliance Issues' aimed at facilitating the collaboration between Member States on serious GMP issues notified to the group and affecting MRP, DCP and national products including those that might have an impact on the medicinal products availability

4. Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary (CMDv)

- a. The CMDv often circulates questionnaires on availability / shortage of products at national level
- b. Special focus is made to promote the availability of vaccines
- c. In parallel there are activities to promote the registration of products for MUMS
- d. It is also working on reducing the administrative burden and for extending the multilingual label
- e. A common position paper is being discussed between Member States about veterinary autogenous vaccines with the aim to harmonise the conditions for manufacturing and use
- f. Developing a specific Best Practice Guide for on collaboration between Member States in relation to GMP non-compliance issues for veterinary medicinal products

5. Committee for Medicinal Products for Veterinary Use (CVMP)

- a. Adopted proposed criticality criteria for veterinary medicinal products that will be incorporated into the published criticality classification in the next revision of the Union Procedure on dealing with GMP non-compliance
- b. CVMP (IWP) Reflection paper on the risks that should be considered prior to the use of unauthorised vaccines in emergency situations

There are several guidelines (CVMP/IWP) about “reduced requirements” of some specific veterinary vaccines to be authorised under “exceptional circumstances”, and also about “multistrain dossiers”

6. European Surveillance Strategy (ESS)
 - a. ESS has modified the scope of its mandate to include topics related to availability and shortages by GMP and quality defects, problem of marketing as sales on internet in order to coordinate the actions at national level
 - b. Review of the Incident Management Plan for medicinal products for veterinary use
 - c. Mapping of the origin of shortages
7. Working Group of Enforcement Officers (WGEO)
8. The Good Manufacturing and Distribution Practice Inspectors Working Group (GMDP IWG)
 - a. Revised Chapters 3, 5 and 8 of the EU GMP Guide to provide better guidance to manufacturers on supply chain management and communication to authorities
 - b. Adopted a new Union Procedure on dealing with reports of serious non-compliance that incorporated the criticality criteria and the escalation decision tree to provide better guidance to authorities when dealing with GMP non-compliance
9. HMA-EMA Steering Committee on Veterinary Vaccine Availability
 - a. Initiatives to stimulate authorisation of a wider range of veterinary vaccines
10. European Commission (EC)

The EC has investigated and sought to address concerns about unavailability of medicinal products for human use in a number of ways since 2012.

- a. Matrix Report - Study on the Availability of Medicinal Products for Human Use, 2012
 - b. Proposal for a new regulation governing veterinary medicinal products in the EU
 - c. The EU Health Security Committee (HSC) are currently reflecting on taking a more strategic approach towards evaluation of possible policy interventions to mitigate the risk of vaccine shortages, with a particular focus on demand forecasting
 - d. Investigating and summarising legal tools available to National Competent Authorities when facing problems of shortages.
 - e. Establishing a European Observatory on the Supply of Medical Radioisotopes, in order to respond to the critical situation regarding the supply of radioisotopes for medicinal products.
 - f. Project group on facilitating supply in small markets that undertook a mapping exercise of supply problems and made a set of policy recommendations.
 - g. In response to the Council conclusion of June 2016, a study will be carried out on the impact of pharmaceutical incentives and rewards on innovation, availability and accessibility of medicinal products in the EU
11. World Health Organization (WHO)
 - a. 69 TH WHA resolution "Addressing the global shortage of Medicines"
 12. Industry of medicinal products
 - a. EFPIA Good Practice – Reducing Risk for Drug Products Shortages, 2013

- b. Parenteral drugs association - PDA Technical report "Risk based approach for prevention and management of drug shortages", 2014
- c. ISPE Drug Shortages Prevention Plan
- d. AESGP/EFPIA/EGA/PPTA: Industry Communication Principles to Authorities

13. Presidencies

- a. During 2016, The Dutch Presidency has tabled two Presidency notes at Council level;
- b. Council Conclusions on "Strengthening the balance in the pharmaceutical systems in the EU and its Member States" . This note reflects on legislative initiatives at Member State level and invites further co-operation at EU level. Further discussion is planned for the informal meeting of Ministers for Health in Bratislava, on 3-4 October 2016.
- c. A note on the "Security Of Supply Of Medical Radioisotopes" to the TTE (Energy) Council. This note invited the European Commission and Member States to inter alia "create a favourable regulatory environment for the licensing of radiopharmaceutical products with due consideration of their diagnostic and therapeutic potential. As part of this effort, the continuing collaboration with the European Medicines Agency (EMA) should facilitate the resolution of the regulatory issues related to the licencing of radiopharmaceuticals at EU level".
- d. A meeting of the Working Party on Public Health at Senior level on 15 July 2016 also discussed a note from the Slovak Presidency "Shortages of human medicines in the European Union" which proposed several possible actions for the EU Member States.
- e. The SK presidency has put the issue of "Shortages of Human Medicines in the European Union" for discussion at the INFORMAL MEETING OF HEALTH MINISTERS on 03 - 04 October 2016, in Bratislava
- f. The SK presidency Conference on "Shortages of Human Medicines in the European Union" on 17 – 18 November 2016.
- g. Review of the regulation of veterinary medicinal products

14. Informal Meeting of EU Directors of Pharmaceutical Policy

15. Other

- a. Common position between patients', consumers, and healthcare professionals' organisations involved in the activities of the European Medicines Agency on Supply Shortages of Medicines, 2013
- b. The memorandum of understanding for the COST action European Medicines Shortages Research Network, 2015
- c. BEUC (The European Consumer Organisation, co-funded by EU) BEUC position on access to medicines, 2016

References

International Society for Pharmacoepidemiology (ISPE): ISPE Drug Shortages Prevention Plan, <http://www.ispe.org/drug-shortages-initiative>

Parental Drug Association (PDA): Technical Report on "Risk-Based Approach for Prevention and Management of Drug Shortages", <http://www.pda.org/scientific-and-regulatory-affairs/regulatory-resources/drug-shortage>

Study on the Availability of Medicinal Products for Human Use, http://ehpta.eu/pdf/Matrix_report.pdf

Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice Compliance problems, EMA/590745/2012, London, November 2012.

EU Medicines Agencies Network Strategy to 2020, http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/12/WC500199060.pdf

Shortages of human medicines in the European Union Exchange of views, ST 10144 2016 INIT.

Security of supply of medical radioisotopes, ST 8953 2016 COR 1, http://ec.europa.eu/health/files/committee/69meeting/pharm610_shortages.pdf

Study on the Availability of Medicinal Products for Human Use, http://ehpta.eu/pdf/Matrix_report.pdf

Supply of medical radioisotopes, http://ec.europa.eu/euratom/observatory_radioisotopes.html

Project group on facilitating supply in small markets, Position Paper and Recommendations, <http://ec.europa.eu/DocsRoom/documents?locale=en&tags=Facilitating%20the%20supply%20of%20medicinal%20products%20in%20small%20markets>

Procedure for dealing with serious GMP non-compliance requiring co-ordinated measures to protect public or animal health, http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004706.pdf

General information on procedural guidance, <http://www.hma.eu/90.html>

Developing a proactive approach to the prevention of medicines shortages due to manufacturing and quality problems, Report from a stakeholder meeting at the European Medicines Agency - 9 October 2015, http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/01/WC500200281.pdf

DeWeerd E, Simoens S, Casteels M and Huys I (2015), Toward a European definition for a drug shortage: a qualitative study. *Front. Pharmacol.* 6: 253. doi: 10.3389/fphar.2015.00253

Pauwels et al. *BMC Health Services Research*, 2014, 14: 438, <http://www.biomedcentral.com/1472-6963/14/438>