How regulators are working to improve prevention and management of availability problems

Kristin Raudsepp
Director General, State Agency of Medicines, ESTONIA

Lead for Priority (Availability of appropriately authorised medicines) in the HMA MAWP

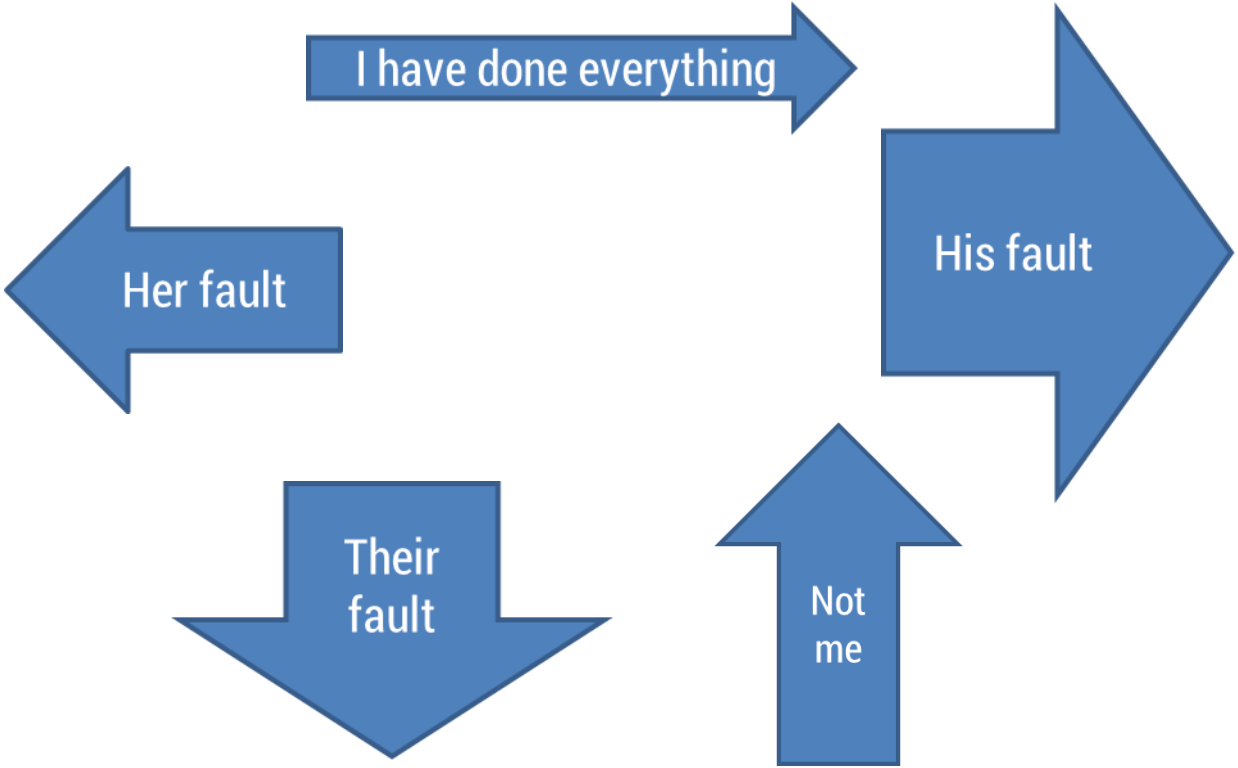
Co chair of the HMA/EMA Task Force of the availability of authorised medicines (TF AAM)

Estonian representative at the EMA MB

Availability problems are out there

- 60% of the medicines authorised (excl NAP) are not coming to the market in Estonia
- Among the medicines coming to the market we get shortage reports for approx 100 medicines per year.
- A shortage lasted an average of 93 days
- Every medicines may happen to be in shortage, we have had cases for vaccine in the national vaccination scheme, cancer treatment and lifesaving hospital medicines.
- Which means there are patients not getting the normal contemporary treatment, because the medicine is not available

Who is responsible?



Systematic management of the problem in the network

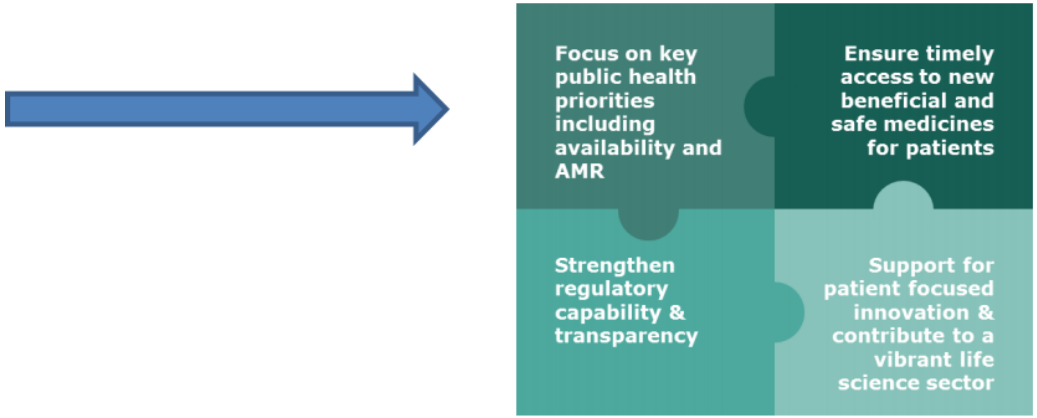
- EMA/HMA Strategy to 2020

- Multi Annual Working Plan (MAWP) of HMA + EMA working programme

- Task Force on Availability of authorised medicines

HMA/EMA Strategy 2020

Theme 1: Contributing to human health



Objective 1: Focus on key public health priorities including availability of medicines and antimicrobial resistance

The network will continue to be prepared to address public health emergencies and priorities such as antimicrobial resistance. It will also review whether there are areas that could benefit from regulatory incentives to support the development of novel products. In addition it will continue to review how to best ensure continuity of supply of good quality appropriately authorised medicines.

Availability being priority in the network

- 2016 working plans of the HMA and EMA
  - One of the selected priorities for in the HMA MAWP
- 2017 - One of the priorities for Estonian State Agency of Medicines during the Estonian Presidency of the Council of EU
- 2018 – Bulgaria, Austria

The task force has been set up by

- the European Medicines Agency (EMA)
- the Heads of Medicines Agencies (HMA)
- with representatives from the European Commission and interested national competent authorities,
- the chairs of the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) and Veterinary (CMDv),
- the GMP/GDP Inspectors Working Group,
- the Working Group of Communication Professionals (WGCP)
- and the European Surveillance Strategy Working Group (ESS WG).

Priorities of the TF AAM

- The task force will develop and coordinate actions for better prevention, identification, management of and communication on issues that can affect the availability of medicines, in order to improve continuity of supply of human and veterinary medicines across Europe.
- Key priorities of the task force include:
  - Looking at ways to minimise supply disruptions and avoid shortages by facilitating approval and marketing of medicines using the existing regulatory framework;
  - Developing strategies to improve prevention and management of shortages caused by disruptions in the supply chain;
  - Encouraging best practices within industry to prevent shortages;
  - Improving sharing of information and best practices among EU regulatory authorities to better coordinate actions across the EU;
  - Fostering collaboration with stakeholders and enhancing communication of supply problems to EU citizens.

Mandate of the Task Force

Classification of availability problems

- Medicinal products authorised, but are not marketed or no longer marketed.
- Medicinal products authorised and marketed products, but the supply chain disruptions directly prevent the availability
  - GMP manufacturing difficulties
  - GCP problems
  - other problems affecting the quality of medicinal products
  - problems resulting from a safety concern
  - parallel trade
  - lack of continuity within the supply chain of medicinal products.

Steering Committee

- **Co-Chairs**
  - Kristin Raudsepp (ET)
  - Noel Wathion (EMA)
- **HMA representatives from the MAWP lead and support NCAs**
  - Sweden - Christer Backman
  - Spain – Maria Jesus Lamas
  - France vet – Jean-Pierre Orand (Representative of Veterinary Vaccine Availability TF)
  - Netherlands – Birte Van Elk
  - Portugal – Rui Santos Ivo
- **Representatives of working groups**
  - Laura Oliveira Santamaria, CMDh Chair
  - Annette Byrholt Hansen,
  - Laetitia Le Letty, chair of the CMDv
  - Esther Martinez (EMA), GMDP IWP
  - Jean-Pierre Orand, HMA ESS WG
  - Yngvil Knudsen, HMA WGCP
  - Juan Garcias (EMA), EMA
- **Other members**
  - Agnes Mathieu-Mendes, Representative of European Commission, DHoU B4 ;
  - Ivo Claassen, Representative of Veterinary Vaccine Availability TF
  - Brendan Cuddy, EMA

Thematic Working Group 1 - Marketing Authorisation

Co-chairs:

- Laura Oliveira Santamaria, CMDh Chair
- Laetitia Le Letty, chair of the CMDv

Tasks

- To 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.
- Economic matters that fall within the remit of national competent authorities such as use of public service obligations, and incentives to promote marketing might also be covered.
- Certain activities may require specific involvement of CMDh, CMDv and EMA (H/V), and EC where relevant.

Thematic Working Group 2 - Supply Disruption

Co-chairs:

•Esther Martinez (EMA)

•Annette Byrholt Hansen (DK)

Tasks

- To 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 (H/V) and the EC where relevant. The work done and planned by EMA and MS in the action plan regarding supply shortages caused by GMP should also be taken into account

Thematic Working Group 3 – Communication

Co-chairs:

•Yngvil Knudsen, NO

•Juan Garcias EMA

Tasks

- To develop a specific communication plan and to enhance the visibility of existing tools and procedures

Work has started

- 2017

- Agreement on governance (Task Force and Thematic areas)
- Adoption of the „Composition and working methods of HMA/EMA Task Force on Availability of Authorised Medicines for Human and Veterinary Use“
- Composition of the 3 Thematic Working Groups
- Reporting lines
- Working methods were endorsed
- Adoption of Work plan

Working plan of the HMA/EMA TF AAM

- Adopted on 21 June 2017 by SG, updated 2018 in connection to the BREXIT

- Theme 1: Marketing of authorised medicinal products (12 actions)
- Theme 2 - Supply Chain Disruption (13 actions)
- Theme 3 Communication (10 actions)

Public version of the working plan published

HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 August 2018
EMA/350084/2018

Work programme of the HMA/EMA task force on availability of authorised medicines for human and veterinary use

1. Background

Unavailability of medicines in the EU, either because medicines are not marketed or due to supply disruptions, has been recognised by HMA and EMA as an area of great concern[1] affecting all stakeholder groups. Indeed, problems with the availability of medicines have an impact not only on the supply chain but ultimately on healthcare systems, resulting in a significant impact on end users. With respect to veterinary medicines, shortages may cause concern for animal health and welfare in cases where alternative medicines do not exist or are not marketed. As causes of unavailability are multifactorial the solutions require actions at different levels involving all stakeholders. An HMA-EMA task force has been set up to develop and coordinate actions that are necessary to facilitate a better prevention, identification, management and communication of shortages to ultimately ensure continuity of supply of human and veterinary medicines.

2. Scope

The work programme covers centrally and nationally authorised products, both for human and veterinary medicines, in the following cases:

- when medicines are authorised but not marketed (or no longer marketed);
- when medicines authorised and marketed are affected by supply-chain disruptions that directly affect their availability. Such disruptions may occur due to problems with good manufacturing practice (GMP), good clinical practice (GCP), good distribution practice (GDP)[2] or quality defects.

(the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) and Veterinary (CMDv)). The task force establishes links with existing working groups and ensures that any activities related to availability issues in their field will be reflected in their respective work programmes. In the context of preparing for the UK's withdrawal from the EU, the task force will provide a platform to facilitate and coordinate actions between member states, EMA and the EC. The task force is composed of a steering committee that provides strategic oversight, as well as three working groups addressing availability issues from the three critical angles: marketing authorisation, supply disruption and communication.

The groups meet mainly via teleconference and provide quarterly progress reports to the steering committee.

3.1. Details about groups and agreed actions

3.1.1. Thematic working group 1 - Marketing authorisations

This group looks at ways to minimise supply disruptions and avoid shortages by facilitating authorisation and marketing of medicines using the existing regulatory framework. Its actions were agreed in February 2017 and are as follows:

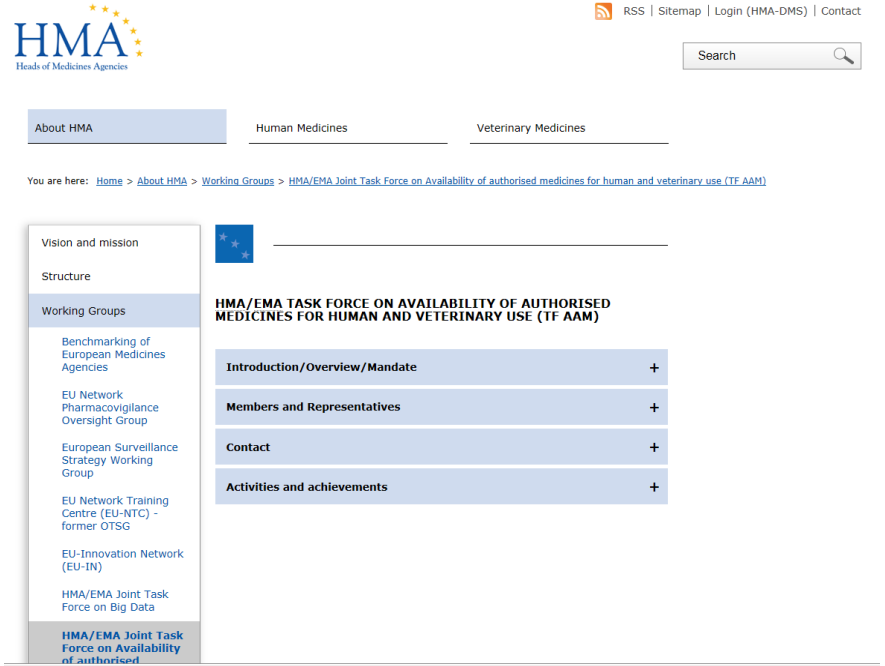
Thematic working group 1 : marketing authorisations	
Agreed actions	**Timelines**
Improve information exchange on availability issues of paediatric formulations and provide best-practice guidance to member states by establishing a dedicated paediatric task force and regular interaction with EMA's Paediatric Committee.	Q4 2020
Facilitating the approval of generics and biosimilars through joint evaluations (work sharing) and shortened timetables. This will facilitate the market entry for these medicines and help to increase users' access to medicines	Completed (Implementation of joint evaluation and shortened timetables for renewals of marketing

Actions by the HMA and EMA : Visibility and fascilitation of the access of the industry to the information

- HMA website

  http://www.hma.eu/598.html

- EMA website

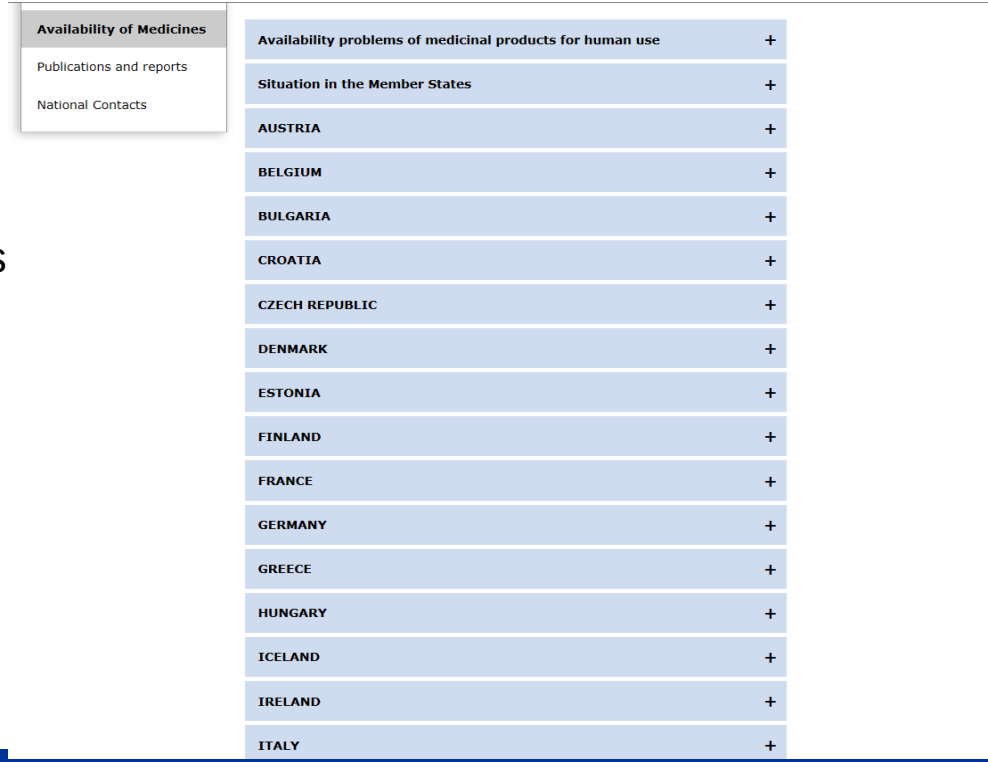


Actions by the HMA and EMA :
Visibility and fascilitation of the access of the industry to the information

dedicated analyses "EU regulatory network reflection paper on the availability of authorised medicinal products for human and veterinary use" was conducted by different Network members.

HMA initiatives to facilitate reporting www.hma.eu – information exchange

- Regarding the transparency of shortages and the information provided within the Member States, the HMA compiled an overview to share publicly the knowledge and latest updates on availability problems provided by the National Competent Authorities within Member States.
- Complete overview, incl mapping of the different solutions or best practices within each Member States can be found in a single document or per country:



HMA initiatives - www.hma.eu Stakeholders information after HMA meetings

Heads of Medicines Agencies: Highlights of the 89th meeting

The 89th meeting of the Heads of Medicines Agencies (HMA) was held from 5th to 7th of September 2017 in Tallinn. The meeting was organised by the Estonian State Agency of Medicines during the EU Presidency of Estonia.

Overall, a variety of topics (23 in total) was covered with plenty of opportunities to fruitfully discuss issues of current importance. As four of the eleven strategic priorities in the HMA Multi Annual Work Plan (MAWP) had been selected by the Estonian State Agency as key priorities to progress during its Presidency, the meeting and discussions were focused on:

- availability of appropriately authorised medicines;
- innovation and access to new medicines;
- optimisation of the regulatory operations;
- strengthen surveillance.

Availability of appropriately authorised medicines

The availability of medicines affects a large part of society. Ensuring the availability of safe, good quality and reasonably priced medicines is a challenge for many countries. Sometimes it needs a great effort to find solutions for market failure, to guarantee the sustainability of national healthcare systems and reduce influence on human or animal health.

HMA initiatives www.hma.eu – information on compassionate use

- NCAs that publish guidance on their compassionate use programs within their Member States, or other early access schemes under article 5:

NCAs that publish guidance on their compassionate use programs within their Member States, or other early access schemes under article 5:

- Austria - Austrian Medicines and Medical Devices Agency
  http://www.basg.gv.at/en/medicines/prior-to-authorisation/compassionate-use/
- Belgium- Federal Agency for Medicines and Healthcare Products (FAMHP)
  http://www.fagg-afmps.be/nl/MENSELIJK_gebruik/geneesmiddelen/geneesmiddelen/onderzoek_ontwikkeling/gebruik_in_schrijnende_gevallen_medische_noodprogrammas/
- Czech Republic – State Institute for Drug Control (SUKL)
  http://www.olecich.cz/encyklopedie/dostupnost-leciv-v-cr
  Information about actual use of non-authorised medicinal products is published regularly at http://www.sukl.cz/hodnoceni-neregistrovanych-lp
- Denmark -Danish Medicines Agency
  http://sundhedsstyrelsen.dk/da/medicin/regulering/udleveringstilladelser
- Estonia – Ravimiamet agency
  http://www.ravimiamet.ee/en/compassionate-use-programs-under-estonian-legislation
- Germany - Paul-Ehrlich-Institut (PEI)
  http://www.pei.de/EN/information/license-applicants/clinical-trial-authorisation/compassionate-use/compassionate-use-node.html
- Ireland – Health Products Regulatory Authority (HPRA)
  https://www.hpra.ie/homepage/medicines/regulatory-information/medicines-authorisation/access-to-medicines-prior-to-authorisation
- Italy – Italian Medicines Agency (AIFA)
  http://www.agenziafarmaco.gov.it/it/content/normativa-di-riferimento-sperimentazione-clinica
- Latvia - State Agency of Medicines of Latvia (ZVA)
  http://likumi.lv/doc.php?id=159645
- Liechtenstein – Amt für Gesundheit (AG), direct link to Swissmedic
  https://www.swissmedic.ch/bewilligungen/00349/index.html?lang=de
- Norway - Norwegian Medicines Agency (NOMA)
  http://www.legemiddelverket.no/Godkjenning_og_regelverk/Klinisk-utproving/Compassionate-use/Sider/default.aspx
- Romania – National Agency for Medicines and Medical Devices (NAMMD)
  http://www.anm.ro/anmdm/med_tratamente_ultima_instanta.html
- Slovenia - Agency of the Republic of Slovenia for Medicinal Products and Medical Devices (JAZMP)
  http://www.jazmp.si/zdravila_za_uporabo_humani_medicini/uvozvnos_zdravil_ki_nimajo_dovoljenja_za_promet_in_riz_zdravil/
- Spain - Spanish Agency of Medicines and Medical Devices (AEMPS)

Multilingual packages

- Encouraged
- CMD h website
- Baltic package, other combinations

e-PIL

- report published by the European Commission in March 2017
- At the moment - electronic PL formats should be complementary to paper PLs that are required by the legislation and should not replace them at this stage in order to ensure availability of the information for all patients.
- EMA initiatives together with MS and all stakeholders followed by the Collaboration with the European Commission on any follow-up actions.
- HMA working groups (Better use of medicines, IT directors)
- MS own initiatives

Common database for shortages – possible solutions

- Product Management System PMS (under SPOR project)
  - ongoing
  - H+V
  - MAH has the opportunity to add „Risk of supply shortages“
  - Definition of the shortage not yet agreed at the moment
  - Public part available through EU web-portal (EUWP *)
  - Connection to FMD repository
  - Data from art 57 and art 51 databases (H+V)

*EU Medicines Web-Portal (EUWP) project is currently on hold due to the Brexit BCP

Discussions going on

= A public list on (centrally) authorised products together with Member States where marketed

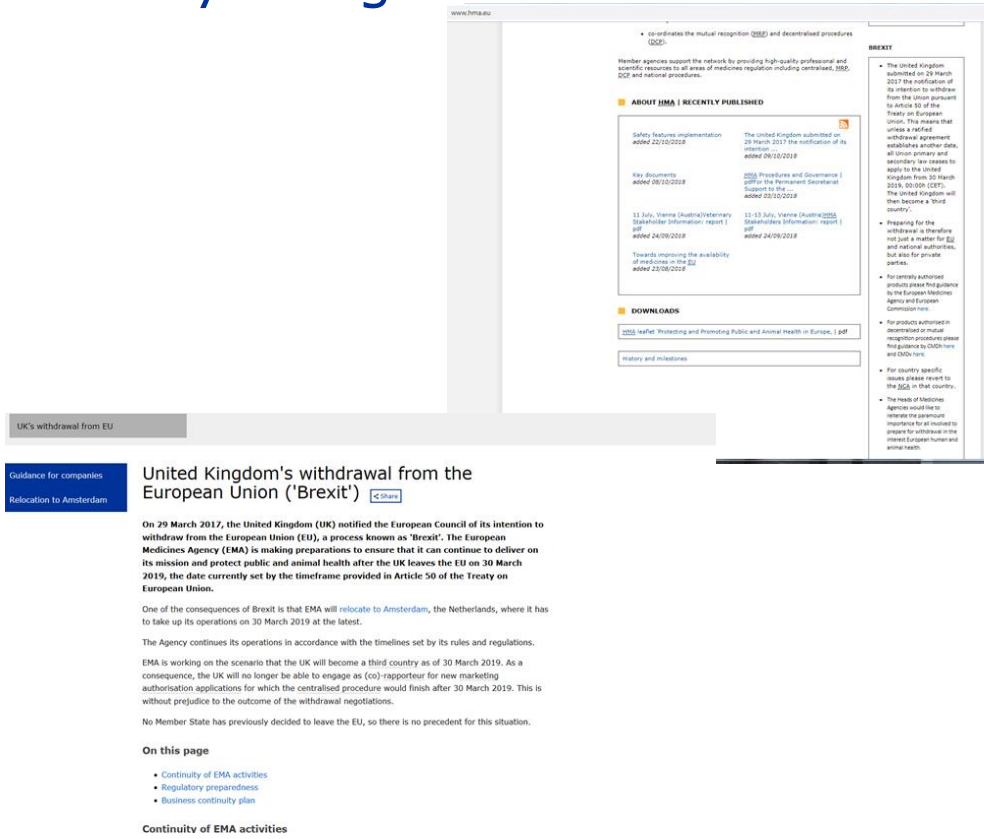
= Posibilities of the „sunset clause“

Upcoming issues and possible availability problems

- BREXIT
  - The horizon has changed
  - Resource planning in the network
- FMD

BREXIT and the availability – regulators

- The European Medicines Agency (EMA), the European Commission and EU national competent authorities are working together to ensure that the United Kingdom's (UK's) withdrawal from the EU does not disrupt the supply of medicines. This includes medicines for human and veterinary use that are either on the market or in use as investigational medicinal products, and which currently benefit over 500 million EU citizens.



BREXIT and the availability – industry

- The pharmaceutical industry has primary responsibility for continuity of supply of medicines. Thus, regulators would like to remind industry to plan for any regulatory steps required for their medicines to remain on the EU market post-Brexit, in order to minimise disruption to medicines supply and avoid shortages.
- The UK has informed the European Council of its intention to leave the EU on 30 March 2019, thus becoming a ‘third country’ after withdrawal. As a result there are important legal consequences for current supply chains.
  - According to EU legislation, the marketing authorisation holders of medicines must be located within the EU.
  - For medicines authorised via decentralised or mutual recognition procedures, the Reference Member States must be an EU member.
  - In the absence of any international trade agreement such as a mutual recognition agreement (MRA), medicines manufactured in a third country must be imported by a manufacturer located within the EU, undergo re-testing upon importation and be released onto the market by an EU Qualified Person (QP).
- no political agreement has been reached yet, and so changes to supply chains should be planned now, in order to prevent interruptions to the future supply of medicines.

FMD – Feb 2019

- Do the new requirements harm the availability of medicines?
  - in connection to the deadline?
  - in connection to the cost of the new system?
  - in connection to some unexpected IT problem?
  - in connection to the disharmony between stakeholders?

Conclusions

- HMA MAWP started 2016 as planned
- BREXIT making its corrections, some slowdown and changes inevitable
- Availability being HMA priority also in 2018 from EU Presidency Member States
- Cooperation with industry is important to prevent and mitigate the problems

Thank you

Thanks to TF AAM members, colleagues form HMA and EMA

Kristin Raudsepp

Kristin.Raudsepp@ravimiamet.ee

Any questions?

Further information

AAMTFSecretariat@ema.europa.eu

See websites for contact details

European Medicines Agency www.ema.europa.eu

Heads of Medicines Agencies www.hma.eu

Follow us on **@EMA_News**