01 February 2022
EMA/864626/2022 Rev. 1 (interim update) [1]
Health Threats and Vaccines Strategy

EMA emerging health threats plan (interim update)

Endorsed by the Crisis Response Steering Group	12 December 2022
Endorsed by the Executive Board	01 February 2023
Endorsed by the Scientific Coordination Board	01 February 2023

[1] Interim updates have been introduced in the plan to reflect new legal provisions introduced by Regulation (EU) 2022/123 and to refer to the new legislation on cross-border health threat (Regulation 2022/2371). The plan will be subject to a further revision, in particular to incorporate additional COVID-19 pandemic lessons-learned and based on experience with the implementation of Regulation (EU) 2022/123.

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List of abbreviations

ARs:	Assessment reports
BCP:	Business Continuity Plan
CTAG	Clinical Trials Coordination and Advisory Group
CTCG	Clinical Trials Coordination Group
CMD(h):	Coordination Group from Mutual Recognition and Decentralised Procedures – Human
CHMP:	Committee for Medicinal products for Human Use
DG SANTE:	EC DG Health and Food Safety
EC:	European Commission
ECDC:	European Centre for Disease Prevention and Control
EMA:	European Medicines Agency
EFSA:	European Food Safety Authority
ENS:	Early Notification System
EPL:	EMA Product Lead
EU:	European Union
ETF:	EMA Task Force
EWRS:	Early Warning Response System
FDA:	Food and Drug Administration
GMP:	Good Manufacturing Practice
GVP:	Good Pharmacovigilance Practice
HC:	Health Canada
HSC:	Health Security Committee
IDWP:	Infectious Diseases Working Party
IMP:	EU Incident Management Plan
IRN:	Incident Review Network
MS:	EU Member State
OMCL:	Official Medicines Control Laboratory
PDCO:	Paediatric Committee
PIP:	Paediatric investigation plan
PM:	Procedure Manager
PRAC:	Pharmacovigilance Risk Assessment Committee
PSUR(s):	Periodic Safety Update Report(s)
RMP:	Risk management plan
SAG:	Scientific Advisory Group
SAWP:	Scientific Advice Working Party
SL:	Scientific Lead
SOP:	Standard Operating Procedure
VWP:	Vaccine Working Party
US FDA:	United States Food and Drug Administration
WHO:	World Health Organisation
WP(s):	Working Party(ies)

1. Introduction

Planning for, responding to and communicating on serious health threats is foreseen in the EU Medicines Agencies Network Strategy to 2025 and is complementary to EC initiatives in this area. At EU level, the new Regulation (EU) 2022/2371 of 23 November 2022 repealing Decision 1082/2013/EU on serious cross-border threats to health provide the framework to coordinate preparedness and response planning to strengthen capacities for the monitoring, early warning, assessment and response to health emergencies. In addition, Regulation (EU) 2022/123 of 25 January 2022 sets out specific tasks for the European Medicines Agency in relation to public health emergencies. Pursuant to Regulation (EU) 2022/123 article 2(a) (see further below), the term 'public health emergency' indicates a situation of public health emergency recognised by the Commission in accordance with Article 12(1) of Decision No 1082/2013/EU, which is now replaced by article 23 of Regulation (EU) 2022/2371. For the purposes of this document, the term 'emerging health threat' refers to 'serious cross border threat to health' (as per the above Regulation 2022/2371, Article 3(1)) and means *a hazard of biological, chemical, environmental or unknown origin, as referred to in Article 2(1)* (of Regulation 2022/2371), *which spreads or entails a significant risk of spreading across the national borders of Member States (MS), and which may necessitate coordination at Union level in order to ensure a high level of human health protection*. Public health emergencies of international concern are also included as serious cross-border threats to health by the EU legislation, and are covered by this plan as well.

The European Medicines Agency is the European Union body responsible for coordinating the existing scientific resources for the evaluation, supervision and pharmacovigilance of medicinal products. This document explains the principles upon which the Agency will operate in the event of an emerging health threat to humans, and describes high level process, responsibilities and desired outcomes. It thus relates to human medicinal products; however, in case of need, interactions will take place with the Veterinary Medicines Division of the Agency.

An important role of the Agency is to provide regulatory support to public health decisions taken by MSs, and to streamline coordination of and contribute to scientific regulatory matters across the EU during a public health emergency.

The health threat plan is based on the Agency's Pandemic Plan (published in 2006) and on the experience from the 2009 influenza H1N1 pandemic, however it has been redefined in 2018 in order to be applicable to various acute hazards as per EU legislation (see above) and following experience gained in emergencies such as the Ebola outbreak in Western Africa in 2014-2016. The Agency published in 2011 lessons learnt from the 2009 H1N1 pandemic. More information related to the Agency's pandemic preparedness are published on the EMA website.

In March 2022, 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* came into force. The Regulation established the EMA Emergency Task Force (ETF) as advisory and support body separate from, and without prejudice to, the tasks of the scientific committees of the Agency as regards the authorisation, supervision and pharmacovigilance of the medicinal products targeting a public health emergency and related regulatory actions to ensure the quality, safety and efficacy of those medicinal products.

In addition a new Regulation on serious cross-border threats to health (Regulation 2022/2371) came into force in November 2022.

Therefore this document was revised in 2022 to incorporate the new legal provisions.

2. Preparedness prior to an emerging health threat

The Agency undertakes the following as part of routine preparedness activities to ensure that it will be in a state of readiness to deal with an emerging health threat:

- Regular interactions with vaccine/antimicrobials experts and the regulatory network via the EMA Emergency Task Force (ETF), the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) and Working Parties/Groups of the CHMP and CMD(h);

- Activities in relation to products in development, such as scientific advice or orphan designation of medical countermeasures;
- Regular interactions with the European Commission (DG SANTE and the Health Emergency Preparedness and Response Authority (HERA)), the Health Security Committee (HSC, a working group on health security at European level), the European Centre for Disease Control and Prevention (ECDC) and European Food Safety Authority (EFSA);
- Regular interaction with EU MSs, the Commission and the ECDC through the Early Warning and Response system (EWRS). EWRS is the informatics tool designed by the European Commission and the Member States allowing the notification and the information sharing of health measures planned or undertaken against serious cross border health threats. Regulation 2022/2371 Article 18 established EWRS as a permanent communication tool for the purpose of preparedness early warning and response, alert notification, assessing public health risks and determining the measures that may be required to protect public health;
- Regular interactions with industry;
- Regular interactions with international partners such as WHO, FDA and Health Canada.

3. The EMA health threat plan

3.1. Scope

The aim of this plan is to provide internal general guidance on EMA activities in preparation for and during a public health emergency. This and associated documents are based on the experience gathered from what may be viewed as the most likely cause of an emerging health threat, i.e. a biological health threat and in particular a respiratory virus with pandemic potential, and as such incorporates any existing systems/processes which might be utilized during such a crisis. However the overall plan has been redefined in order to be applicable to various acute hazards including threats of chemical, environmental and unknown origin.

The health threat plan is not intended to be triggered by product related issues, which should be handled through the EU Incident Management Plan (IMP) and the operations of the Incident Review Network (IRN) that deal with product specific incidents, and if necessary through the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG), see also section 4.1.

3.2. Main objectives

Overall the aim of the health threat plan is to meet the following key objectives, which may or may not be all immediately applicable, based on different scenarios (see also sections 3.3 and 4.3):

- Initiate and coordinate scientific and regulatory activities by involving all interested parties within the EMA and the European Medicines Regulatory network (i.e. EMA experts groups, National competent authorities and European Commission), including ECDC and OMCLs as relevant.
- Manage and coordinate the discussions on development, authorisation and surveillance of relevant medicinal products (e.g. vaccines and antivirals for a biological health threat), which are under the remit of EMA, and post-authorisation follow-up of all relevant EU authorised medicinal products to be used to address the health threat.
- Provide to the European Commission, the National Competent Authorities, Public Health Authorities of the Member States including through the Health Security Committee (HSC), and ECDC the outcome of the review of dossiers (e.g. pandemic influenza vaccines and influenza antivirals in case of pandemic influenza) and appropriate support on any regulatory aspect as needed (e.g. scientific opinion to support possible national decisions on emergency use or compassionate use across the EU or information regarding medicinal products that the ETF considers to have the potential to address public health emergencies).

- Effectively communicate relevant information to healthcare professionals, patients and regulatory partners. Communication to these parties is also foreseen during the review process.
- As required, provide support to international partners, stakeholders involved in the research and development of medicinal products and public health authorities outside of Europe, e.g. WHO.
- All of these activities should be undertaken in line with this plan and associated work instructions (see section 6).

3.3. Triggers and emergency levels

Three levels of emergency are foreseen in the health threat plan: emerging health threat, declared emergency, and crisis (see table 1), which will translate into different types and/or levels of EMA activities and consequent staff involvement in handling the public health emergency (refer also to the role of different teams in section 4 and section 4.3).

Any emerging health threat will be followed up by the Agency since its inception, regardless of whether it will lead to formal emergency declarations by official bodies. The trigger to initiate this type of activities is on the outcome of the scientific evaluation of (re)emerging or ongoing outbreaks, and the responsibility of this trigger lies with the Head of Office of Health Threats and Vaccine Strategy Office (AF-HTV), who is thus nominated the Scientific Lead for the activities related to the health threat. In this type of situation, defined as emerging health threat in Table 1, it is not mandatory to have a formal ED/DED decision to activate the plan, since the role and mandate of the Agency and of the ETF is now established by the new Regulation (EU) 2022/123.

Triggers for the 2 subsequent levels of emergency of the Health Threat Plan (declared emergency and crisis) are represented by the following actions:

- Determination of a Public Health Emergency (PHE) by the WHO or the European Commission as per art. 23 of Regulation 2022/2371.
- Declaration of a pandemic by the WHO or the European Commission during the period of spread of human influenza caused by a new subtype or any other pathogen as applicable (e.g. SARS-CoV-2).
- Activation of the EMA Business Continuity Plan by the EMA (D)ED in association with a PHE or pandemic declaration, leading to a health crisis status.

Once an emergency is declared, involvement of resources and activation of the various groups will be evaluated by the EMA Executive Director (ED) or the Deputy ED (DED) in consultation with the Scientific Lead and therapeutic area concerned. More information related to the activation of BCP is included in section 3.3.1.

The Head of Office of the Advisory Function on Health Threat and Vaccines Strategy (AF-HTV) should normally be considered the Scientific Lead (SL) and focal point of contact for any emerging health threat until a status of declared public health emergency is confirmed. The Scientific Lead should always be contacted at the start of the health threat plan activities (see section 4.2) and his/her team may be sufficient to handle the necessary activities at this stage. This represents the minimum level of activation of the plan (see table 1). The scientific lead will work in close collaboration and consultation with the heads of relevant therapeutic area offices (e.g. Office of vaccines and therapies for infectious diseases in case of biological health threats, or Office of Oncology and haematology for a radiological or nuclear event). As the health threat emerges and evolves, the EMA Emergency Task Force (ETF, see section 4.4) will be kept informed by the Scientific Lead of the main activities as considered relevant along the lines indicated in table 1. The scientific lead is normally also the EMA co-chair of the ETF. (S)he will also keep informed the EMA scientific Committees and EU experts' network at regular intervals where relevant. The ETF and the Committees will discuss products development plans and regulatory actions. For emergencies due to non-biological health threats, a Scientific Lead may be nominated by the ED or DED from outside of the Health Threats and Vaccines Strategy Advisory Function; in this case a close collaboration between the SL, the Head of Health Threats and Vaccines Strategy and the ETF co-chairs is essential for handling the public health emergency.

The maximum level of activation of the plan represents a status of health crisis (see table 1, CRISIS), because in this situation it is expected that the Business Continuity Plan (BCP) is activated in addition to and as a consequence of the health threat

emergency. Upon confirmation of a crisis (and as necessary regardless of BCP status), the Crisis Coordination Officer (CCO, see section 4.3) will take over the overall coordinating responsibility within the EMA and the SL will continue to lead the scientific activities as co-chair of the ETF.

Table 1 presents a schematic overview of likely examples of health threat scenarios and consequent levels of emergency in the EMA health threat plan.

Table 1. Different emergency levels and associated scenarios

Emergency level	Teams involved*	Staff/Experts	Activities
EMERGING HEALTH THREAT *Health Threat identified* description: outbreaks reported but no emergency yet declared (MERS-like scenario)	Scientific Lead (SL) and AF-HTV, CCO EMA Emergency Task Force (ETF)	Head and staff of AF-HTV office ETF co-chair(s) and few members	Outbreak monitoring and horizon scanning for medicines in development or authorised, SL takes the lead. ETF , CCO and Responsive Team kept informed by SL
DECLARED EMERGENCY *PHE or pandemic declared by WHO or the EC* description: There could be limited or moderate/high impact on the EU public health and EMA comms (ZIKA/Ebola-like scenario or H1N1v/Monkeypox-like scenario respectively)	Crisis Response Steering Group Responsive team, AF-HTV and Therapeutic Area Offices ETF and SAGs MSSG**	ED/DED, EMA Crisis Manager and EMA senior management SL, CCO, Head of Communication, Head of EMA International Operational staff as needed, ETF composition may need to be tailored or further enriched SAGs experts MSSG members	As for level 1 plus media alerts and increased liaison with other (non)EU Institutions, or more intense with ongoing fast approval procedures for medicinal products based on need and rapid scientific advice ETF review of available evidence, provision of advice to Committees and EU MSs MSSG activation
CRISIS *PHE or Pandemic declared* by WHO or the EC, and EMA BCP activated description: Public health in the EU severely impacted, remote working and lockdown measures in place (COVID-19-like scenario)	Crisis Response Steering Group and Responsive team, AF-HTV and Therapeutic Area Office BCP structures activated EMA scientific Committees ETF plus SAGs MSSG**	All of the above plus reallocation of resources CHMP and PRAC (co)-Rapporteurs and assessors regularly involved in ETF activities SAG experts MSSG experts	Rolling reviews and accelerated authorisation of medicines, rapid scientific advices and PIP decisions, weekly ETF meetings and ad hoc Committee meetings, monitoring of critical medicines and shortages by MSSG; Agency activities reprioritised to focus on crisis

ABBREVIATIONS: SL (Scientific Lead); CCO (Crisis Coordination Officer); Comms (Communications); EU (European Union); BCP (Business Continuity Plan); MSSG: Executive Steering Group on Shortages and Safety of Medicinal Products; AF-HTV: Advisory Function Health Threats and Vaccine Strategy

NOTES: *for a definition of the different teams see section 4; PHE (Public Health Emergency)

**The ETF will liaise with the MSSG on matters related to safety and efficacy of critical medicines, which includes contributing to the review of the list of critical medicines in accordance with Article 6(3) of Regulation (EU) 2022/123.

3.3.1. BCP activities during a health crisis

An ongoing reassessment of the need to activate the BCP is being run as a PHE or pandemic is declared. Depending on the need and in line with national or international recommendations, the ED or DED may decide to activate the BCP leading to a status of crisis. The BCP Gold Group Directorate will subsequently be activated in order to make way for any immediate, Agency-wide, strategic decisions. The BCP Gold Group Directorate is defined in the Agency's BCP and was created in order to speed up the decision-making process in specific non-scientific areas in the event of a BC situation. The BCP Gold Group Directorate is a subset of the Gold Group and comprises the ED, the DED and the Head of Stakeholders and Communications.

In the case of a health crisis, BCP Groups are involved in non-scientific activities; therefore the Health Threats Plan will run in parallel to BCP activities and will continue to oversee the scientific, regulatory and communication activities of the health crisis.

In case of a complex crisis situation it may be decided to adjust the structures for rapid decision making, which at Gold level is supported also by the Steering Group on Crisis Response.

BCP activities as currently established remain valid and are not described in this plan.

3.4. Post emergency review

Following closure of the emergency it is important to conduct a "lessons learned" exercise. This should cover aspects that were not handled well and may need to be changed, but should also describe what was done well and does not need to be changed or may even be applied outside crisis situations. The Steering Group for Crisis Response serves as the central forum to discuss these matters and identify ways of improving the emerging health threat plan. The activities linked to the lessons learned exercise are coordinated by the CCO with involvement of the Responsive team.

4. Roles and Responsibilities

The following EMA designated teams and expert groups from the Committees and relevant Working Parties will deal with the health threat/crisis:

4.1. Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG)

Regulation (EU) 2022/123 foresees a reinforced role for EMA in crisis preparedness and management for medicinal products and medical devices. One of the objectives of the Regulation is to monitor and mitigate potential and actual shortages of medicinal products considered critical in order to address a given public health emergency or other major event(s) which may have a serious impact on public health. For this purpose, an executive steering group, the MSSG, which is formed by representatives of EU MSs, EC and EMA, is established within the Agency to ensure a robust response to major events and/or public health emergencies, and to coordinate urgent actions within the Union in relation to the supply of medicinal products or issues related to the quality, safety and efficacy of medicinal products.

The operational phase of the work of the MSSG provided for in this Regulation will be triggered by the recognition of a public health emergency or the recognition of a major event. Details of the MSSG activities are reflected the MSSG Rules of Procedures.

The monitoring of the safety, quality and efficacy issues will be carried out using the Quality Defect Rapid Alert System (RAS), the Pharmacovigilance Rapid Alert (RA) and Non-Urgent Information (NUI) Systems that are in place in the context of the Incident Review Network (IRN) for medicines for human use. These systems are not part of this plan and are described separately. Notwithstanding, during major events and/or public health emergencies the MSSG is kept informed by the SL/co-

chair of the ETF of the response taken to the health threats, including activities of the ETF, and they may in turn consult the EMA scientific Committees, their working parties, other expert groups including the Emergency Task Force (ETF) and/or the CMDh on specific matters.

4.2. Crisis Response Steering Group (Gold level)

The Crisis Response Steering Group is composed of the Executive Director (ED), the Deputy ED (DED) and EMA senior management and is chaired by the EMA Crisis Manager. The Steering Group is involved from the onset of a public health emergency that is expected to lead to a declared emergency but it has no role in day-to-day activities. The Steering Group gives consideration to and gives guidance on the major scientific, regulatory and communication aspects. Other aspects of their role will be covered in the BCP, if activated.

The Crisis Response Steering Group is to be assisted by the CCO, the Scientific Lead, or the Responsive team, and as needed also by the operational staff (technical support) taking into account the level of the emergency as depicted in section 3.3.

In case of declared emergencies with BCP activated (crisis) when a rapid response is required, the ED together with the DED might have to take executive decisions in the interest of EU public health with the support of the Responsive team.

4.3. Health threats Responsive team (Silver level)

The Responsive team is composed of the following functions: the Scientific Lead (see section 3.3), the Crisis Coordination Officer (CCO), a representative of the International Affairs Team, the Head of Office of Communication and staff from AF-HTV nominated by the Scientific Lead.

In case of a complex crisis situation it may be decided to amend the composition and naming of Responsive Team (e.g. if several silver level groups have to be established separately for public health response and other aspects of the crisis).

In very early phases of any emerging threat, e.g. before formal declarations are released by official bodies, the Scientific Lead should be the initial point of contact for interactions with external stakeholders and coordination within the Agency and the network(see table 1). In such cases, the Scientific Lead ensures that other members of the Responsive team are kept informed in a timely manner by circulating a brief summary of the situation by email or a high level status report. The SL will work in close liaison with the experts of the EU network represented in the ETF (see section 4.4) and with the Committees of the EMA (CHMP, PRAC, PDCO as needed). In case it has been identified that the emerging threat has a high potential to develop into a crisis, the Core Leadership Group for Crisis Preparedness should be informed (this group of EMA senior managers monitors events of various nature that have a potential to develop into a crisis situation and considers any additional preparatory actions that might be required).

In case of declared public health emergency, the AF-HTV and the Responsive team will be regularly involved in the management of the activities related to the health threat. Within the Responsive team, scientific activities are coordinated by the Scientific Lead whereas the CCO takes the overall lead coordinating role. Thus the CCO should be kept informed of all international, institutional and scientific developments relating to the emerging health threat, as (s)he keeps a high level status report of the activities. The Scientific Lead maintains oversight of the scientific support activities throughout the duration of the public health emergency including scientific interaction with stakeholders and partners. Specific expertise from other offices will be identified and involved as required.

The EU Institutional Liaison Team (part of Institutional and Policy Department) will be involved in the activities of the Responsive team as needed based on the extent of cooperation and interaction with EU institutions.

During a declared emergency or a crisis and depending on the need identified, additional staff members may attend meetings held by AF-HTV and the Responsive team or may provide scientific/regulatory support to facilitate the team's operations; such additional staff may more likely include the Heads of Service/Office of: Pharmaceutical Quality, Regulatory Affairs, Paediatric medicines and Scientific Advice. Other ad hoc members can be directly or indirectly involved at any time in the activities of the Responsive team depending on the nature of the health threat.

The main role of the Responsive team is to ensure that the health threat plan and strategic decision taken by the ED and Steering Group for Crisis Response are followed and that the operational activities during the health emergency are conducted, e.g. stakeholder liaison, implementing communication strategy, workload management, representing the Agency at external and internal meetings as relevant. The Responsive team reports to the Crisis Response Steering Group as needed.

Once operational responsibilities and relative resources are assigned at the beginning of a health emergency, the Responsive team in principle meets if issues cannot be resolved within one operational entity or if interdisciplinary discussion is needed.

4.4. Operational staff involved in health threats activities

At the onset of a health threat, the need to involve operational entities outside of the AF-HTV function is evaluated by the SL on a case by case basis. Depending on the need, colleagues may be involved based on specific needs, e.g. scientific administrators from the Vaccines and therapies for infectious diseases, Methodology, or Pharmaceutical Quality Offices. The Office of Supply and Availability of Medicines and Devices are kept informed if a considerable impact on supply or demand of medicines in the EU is anticipated at this early stage.

Once a public health emergency is declared by WHO or the EC, key operational staff involved besides the SL, CCO and AF-HTV may include scientific officers from relevant therapeutic areas on a more regular basis. They work in close collaborations with AF-HTV and the Responsive team by implementing their decisions and ensuring information flows to PL/other product team members, Committees and Working Parties, i.e. undertaking EMA emergency activities. The main activities of the CCO vs. the AF-HTV and the PLs during a declared emergency or a crisis are summarised in table 2, but could be readjusted based on the need.

Table 2. Activities by the Coordination Officers

Crisis Coordination Officer	AF-HTV	Product Leads from therapeutic areas
Organises meetings of the Crisis Response Steering Group, the Responsive team and Core Leadership Group for Crisis Preparedness	Organises ETF meetings Organises interactions with internal and external stakeholders such as industry outside of specific procedures	Organises procedure-related interactions with internal and external stakeholders such as industry, SAGs and Rapporteurs for evaluation activities
Coordinates adequate Agency input / drafting of briefings and summaries of outcomes from the meeting of Crisis Response Steering Group and Core Leadership Group for Crisis Preparedness	Drafts content of briefings (scientific outcomes, ETF minutes, review of CHMP ARs where required) Ensures adequate information flow through experts groups and relevant WPs, if needed in addition to the ETF	Manages all evaluation procedures (rolling reviews and standard) Ensures adequate information flow through committees
Maps requests for Agency representation at relevant external meetings, and at international*/EC & ECDC level	Ensures periodic briefing of MLT (Scientific issues)	
Tracks resources needs for the crisis to make sure these are addressed by management	Ensures adequate review of disease progression and internal dissemination of information using information from ECDC/WHO etc.	

*International activities handled by EMA international Office

Other staff members to be regularly involved in operational support may include scientific administrators from the Pharmaceutical Quality, Paediatric medicines, Data Analytics and Methods, Stakeholders and Communications and Scientific

Advice functions. The Office of Supply and Availability of Medicines and Devices has a role in handling shortages of medicines and devices in case of public health emergencies and as a secretariat of the MSSG, thus liaison will occur with the HTV Office in these areas of work.

In addition, depending on the nature of the emergency, *ad hoc* staff can also be involved/consulted: scientific administrators from Regulatory Affairs, Inspections, Pharmacovigilance, Patients & Healthcare Professionals liaison, Methodology, Translational Sciences, Orphan medicines, Labelling Offices and the Legal department.

If a crisis is confirmed, a greater number of staff may need to be involved based on expertise specific to the particular health crisis, including EMA Product Leads (PLs) and additional scientific administrators from other departments. The additional staff will provide further resources to help with necessary product team related activities and ensure that adequate feedback is channelled to the SL and the CCO for coordination.

It is foreseen that in a crisis at least one or preferably two members of staff from each of the following Offices should be dedicated to the crisis: Pharmaceutical Quality, Vaccines and therapies for infectious diseases and Regulatory Affairs. At least 2 staff members should be mobilised from each of the following Offices based on need: Paediatric medicines, Inspections, Pharmacovigilance, Patients & healthcare professionals liaison, Communications, Labelling, Data Analytics and Methods, Legal department. In other types of health threat scenarios, this should be decided on a case by case basis.

4.5. Experts groups

The key experts group dealing with public health emergencies as well as preparedness is the EMA Emergency Task Force (ETF) established by article 15 of Regulation (EU) 2022/123. Other expert groups such as the Scientific Advisory Groups (SAGs) may be convened to further assist the ETF, CHMP, PRAC and PDCO. As per Regulation (EU) 2022/123, the ETF is mandated to:

- provide scientific advice to manufacturers on developing medicinal products, e.g. vaccines/ antimicrobials, against the emerging health threat;
- contribute to product-related assessment and post-authorisation surveillance activities;
- provide scientific support to facilitate relevant clinical trials conduct;
- review available evidence and prepare specific positions / input and recommendations with regard to the use of medicinal products which have the potential to address public health emergencies (including jointly with ECDC);
- interact with stakeholders;
- maintain European and International cooperation.

A full list of activities of the ETF is included in the Rules of the Procedure for this group.

The Scientific Coordination Board, which brings together the chairs of all the EMA scientific Committees, is also available as a platform for discussion and can be considered to facilitate regulatory decisions in times of emergency.

One of the main activities of the ETF is to provide product-specific scientific advice to manufacturers on behalf of the CHMP. At the onset of an health threat, initial interactions with product developers and clinical trials sponsors will likely be led by AF-HTV and occur in an informal setting, i.e. teleconferences with the SL/AF-HTV and few members of the ETF. At subsequent levels of emergency, and as products approach clinical development phases, the SL will decide when to involve the ETF regularly.

SAGs will retain their role of external expert advisory group to the ETF and the CHMP on specific questions, as per SAG mandate in non-emergency situation. Full mandates and objectives of SAGs (SAG Vaccine; SAG Infectious Diseases) and ETF in the context of the health threat plan are published.

5. Operational aspects

The following sections provide high level recommendations to be followed in key areas of emergency related activities, as identified based on the lessons learned from past health threats/crisis such as the 2009 influenza pandemic and the 2020 COVID-19 pandemic.

5.1. Facilitation on regulatory input into clinical trials

From a regulatory perspective there is the need to facilitate clinical trials design in the context of an emerging health threat by agreeing up front to key principles. Clinical trial design may differ substantially depending on the health threat and type of product. The possibility of informal early interaction/consultation with EMA and ETF, and structured procedures such as a rapid scientific advice (ETF/CHMP) is offered to both manufacturers of medicinal products and academic/investigators conducting clinical research.

The CTCG and CTAG are regularly involved in ETF activities, and the 3 groups are establishing a new working model to provide coordinated support to sponsors and developers following the entry into force of Regulation (EU) 2022/123. As per article 15(2)(c) of Regulation (EU) 2022/123 the ETF will provide to sponsors of clinical trials scientific support to study conduct to facilitate large multinational trials in collaboration with the Clinical Trial Coordination Group (CTCG). A broader involvement of clinical trial expertise involving Members of CTCG, and where relevant CTAG, will take place in declared emergencies (see above chapter 3.3).

Ongoing stakeholders' discussions and projects will be taken into account when defining this strategy further. Incentives for development are strengthened by article 16 of Regulation (EU) 2022/123 and others, such as rapid orphan designation, have been also used in previous emergency situations and may be taken into account as appropriate.

The ETF and CHMP shall provide scientific support to study conduct and scientific advice for preparedness, i.e. outside of a health threat.

5.2. Procedural aspects

In the context of an emerging health threat caused by e.g. a biological hazard, detailed procedures have been set up:

- for rapid scientific advice of products in development including on clinical trial protocols;
- for fast-track approval of medicines, e.g. involving rolling review of vaccines and antimicrobials for prophylaxis and treatment of an emerging health threat, via the centralised procedure;
- for post-authorisation follow-up of centrally authorised products, e.g. emerging data on safety and efficacy;
- to react to any safety signals arising from the use of non-centrally authorised products, e.g. from the use of bulk active substance of centrally authorised antimicrobials.

5.3. Paediatric aspects

Some aspects related to paediatric activities in times of public health emergencies have been considered and the recommendations for handling them are summarised below:

- The PDCO Chairperson or the other nominated experts participating in the ETF (follow the link for details of the ETF composition) should allow information flow between this group and the PDCO;
- An EMA/PDCO "mini-team" of 2-3 PDCO members and at least one EMA Paediatric coordinator, with relevant experience, should be set up to draft general guidance on paediatric requirements, when necessary, and manage possible PIP applications;

- Given the variety of potential health threats, a standard PIP approach is not considered feasible for most instances. Instead a flexible, informal and rapid case-by-case approach will be taken, in full respect of legislative requirements.
- PDCO opinions on relevant PIPs should be adopted via written procedure, faster than normal procedural timelines if necessary and appropriate.
- Applicants are strongly advised to consider the paediatric requirements early in development, and to contact the EMA Paediatric Medicines Office as soon as possible (paediatrics@ema.europa.eu), to prevent any possible delay in the marketing authorisation.

5.4. Pharmacovigilance aspects

Pharmacovigilance activities in the situation of an emerging health threat should be enhanced, and a number of tools and processes which could be used in these situations are in place. The main elements to be considered are summarised below:

- Activities related to signal management should be enhanced and/or accelerated during public health emergencies or mass use of new products or during mass use of previously authorised products. For authorised products, requirements for signal detection are reflected in the legislation, Guideline on good pharmacovigilance practices (GVP) and relevant EMA operating procedures. The validation and subsequent assessment of signals should be performed by the Pharmacovigilance Office in collaboration with Member States and the PRAC. A number of pharmacovigilance tools and resources which could be used in an emerging health threat situation exist. These could be targeted to medicinal products in the scope of the specific situation, and timelines could be shortened accordingly.
- Emerging Safety Issues (ESIs) are safety issues considered by a Marketing Authorisation Holder (MAH) to require urgent attention by the competent authority. The process of notification to the authorities and subsequent management is well established.
- The rapid exchange of information on pharmacovigilance issues between the EMA, MSs and the European Commission at EU level and other regulators at the international level can take place through the European Pharmacovigilance Issues Tracking Tool (EPITT). The EPITT communication channels which are in place are the Rapid Alerts (RAs) and the Non Urgent Information (NUIs). Currently resources are allocated according to current amount of EPITT notifications. Should these notifications increase, as in the situation of a crisis, it might be necessary to strengthen EPITT operation by allocating additional resources as needed.

5.5. Communication with the network, stakeholders, international partners and the public

Building on the experience with COVID-19, EMA has established transparency measures for medicines addressing a Public Health Emergency that apply to EMA's activities in relation to the development, evaluation and supervision of medicinal products addressing a public health emergency. In many cases, the measures mirror standard procedures already in place for all medicines. However, due to the high public interest expected, additional information is made available for medicines that address or have the potential to address a public health emergency, also in line with requirements of Regulation (EU) 2022/123 extending EMA's mandate with respect to public health emergencies.

Interactions with international regulators, e.g. US FDA and HC, and public health authorities, such as WHO and HERA, are expected to be on a regular basis during emergencies. Discussion on specific scientific and regulatory topics will take place as necessary in accordance with the existing framework and in compliance with the confidentiality agreements in place. The newly created Health Emergency Preparedness and Response Authority (HERA) has a key role at the EU level in preventing, detecting, and rapidly responding to health emergencies. This is achieved by facilitating development, production and distribution of medicines, vaccines and other medical countermeasures – such as gloves and masks. For this reason, EMA ensures a close and regular collaboration with HERA in preparation for and during public health emergencies for example by systematically involving HERA representatives in ETF meetings.

In addition, the International Coalition of Medicines Regulatory Agencies (ICMRA) is expected to involve Health Regulatory Authorities (HRA) in the management of global health crisis in a coordinated and consistent manner, by identifying the possibilities for international collaboration and cooperation, including on harmonisation of regulatory requirements. The EMA International Affairs Team will ensure adequate coordination of activities with ICMRA.