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HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
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European Medicines Regulatory Network COVID-19 Business Continuity Plan

1. Introduction

The COVID-19 pandemic has been affecting the whole European Medicines Regulatory Network (EMRN) (regulatory network of National Competent Authorities (NCAs) of the Member States (MSs) of the European Economic Area (EEA), the European Medicines Agency (EMA) and the European Commission (EC)), albeit to a different extent and not necessarily at the same time. Several factors have to be taken into account, such as the resources needed to respond to the pandemic as well as the unavailability of staff due to illness or the need to look after children or sick family members.

Many NCAs deal with other aspects of the pandemic than regulation of medicines, e.g. with personal protection equipment and other medical devices. Resources will be needed not only to d l with COVID-19 itself but also with the consequential effects such as shortages of medicines and mposed travel restrictions impacting for instance on the possibility to carry out inspections. The magni de of this additional work is difficult to quantify at this moment in time. The extent of th imp on the pharmaceutical industry is also unknown including whether it will result in a reduction or de y of submissions. Even if there is a reduction in submissions it might not be at the ame t me a the increase in COVID-19 related submissions and any delays might result in a cum lation of submissions at a later stage.

The impact on resources available for the handling of regulatory procedures affects centrally (CAPs) and nationally authorised products (NAPs). In this unprecedent d situation it is important that the EMRN works as a whole with a consistent approach towards b siness continuity and prioritisation of regulatory activities.

In order to address the consequences of the COVID- 9 pandemic on the regulatory activities performed by the Regulatory Authorities of the ERMN Europ an Medicines Regulatory Network COVID-19 Business Continuity Plan (EMRN CO I 19 BC has been developed. It is acknowledged that the COVID-19 pandemic is a unique sit ation a d that there are many unknown factors not least the extent of the impact and the duration. T e EMRN COVID-19 BCP will, therefore, be subject to regular review and revisions, when n d.

2. Aim of this document

The aim of this documen is to de cribe

- the agreement eache within the EMRN as to the principles for the handling of regulatory procedures in a b iness continuity context in the frame of the COVID-19 pandemic;
- how these arrangements are implemented for both CAPs and NAPs.

The arr ngem nts for CAPs and EMA procedures are provided in Annex 1, for NAPs-human medicines in Ann x 2, and for NAPs-veterinary medicines in Annex 3.

3. Priorities for the EMRN COVID-19 BCP

The first priority is to ensure that core public and animal health regulatory activities during the COVID-19 pandemic continue to be carried out in terms of the authorisation, maintenance and supervision of medicines, including those related to the treatment of COVID-19 patients and those that address potential shortages of crucial medicines used in the context of COVID-19 in particular in the intensive care units. Secondly to ensure the functioning of the EMRN as a whole through a consistent approach for all medicines irrespective of the licencing route, and through mutual support.

Mitigating measures should be put in place as needed but it is also important that work continues as usual wherever possible. Therefore, mitigating measures might not apply to all procedures at the same time. Mitigating measures should be proportionate to the issue and a stepwise approach is, therefore, undertaken.

4. Phases of the EMRN COVID-19 BCP

4.1. First phase

In phase 1 of the EMRN COVID-19 BCP the NCAs and EMA are able to cope with minim l reduc n in available work force and to continue to fulfil normal regulatory tasks for CAPs and NAPs, b th in te ms of evaluation, maintenance and monitoring tasks.

4.2. Second phase

In the second phase of the EMRN COVID-19 BCP one or more NCA(s) or the E A rep t dif culties in fulfilling normal regulatory tasks and, therefore, a first step of prioritisation nee s to be applied.

The principles for prioritisation for the EMRN are as follows:

- Under no circumstances can **COVID-19 related procedure** [1] be delayed; they should always be given 1st priority.
- **For the non-COVID-19 procedures**, any changes hat are ecessary (e.g. a change to a timetable or a change in the Lead Authority[2], if a plicab e) will be applied at the level of the concerned procedure and not at a product type o pr cedur type level.
- **For the non-COVID-19 procedures where delays re reported** the arrangements described for CAPs and EMA procedures in Annex , for NA s-human medicines in Annex 2, and for NAPs-veterinary medicines in Annex 3 apply.

4.3. Third phase

The third phase of the EMRN COVID- BCP is triggered when the majority of NCAs or the EMA are experiencing increasing fficultie in fulfilling the tasks as set out in the aforementioned phase 2 despite the level f priori sation a eady applied, and, therefore, additional mitigating measures are needed.

The need to introduce an additional mitigating measures and to move to phase 3 will be decided on by the EMRN taking into account the outcome of regular reviews.

4.4. Curren phase

As f 10 S mber 2020 the EMRN COVID-19 BCP is still in phase 2.

[1] i.e. procedures relating to treatment of COVID-19 and vaccines against COVID-19 (both new products and changes to existing products), procedures relating to products needed in the general treatment of COVID-19 patients (incl. crucial products in the intensive care unit (ICU) setting) and procedures to minimise shortages due to COVID-19

[2] Lead Authority for centralised procedures are the Rapporteur and Co-Rapporteur and for Mutual recognition and decentralised procedures the Reference Member State (RMS)

5. Specific measures relating to pharmacovigilance aspects

The following specific measures apply to pharmacovigilance aspects in the second phase of the EMRN COVID-19 BCP:

5.1. Specific measures relating to Periodic Safety Update Reports (PSURs)

The principles for prioritisation for the EMRN are as follows:

- **COVID-19 related PSUR[3] procedures** should always be given 1st priority.
- **For non-COVID-19 related PSUR procedures** the following principles apply:
  - Any changes that are necessary (e.g. a change to a timetable or a change in the Lead Authority, if applicable) will be applied at the level of the concerned proced e a d not a product or procedure type level.
  - Where delays are reported the arrangements described for CAPs and EMA pro du es in Annex 1, for NAPs-human medicines in Annex 2, and for NAPs-veterinary med ines in Annex 3 apply.

5.2. Specific measures relating to signal management

The principles for prioritisation for the EMRN are as follows:

- **Signal management of COVID-19 related active substa ces** and any important safety signals requiring urgent attention should be given first pr ority.
- **For non-COVID-19 related signals** the followin rincipl s apply:
  - Should prioritisation of signal mana emen activities for non-COVID-19 active substances become necessary, the prioritisatio will take to account the potential impact on public/animal health and/or the bene t-risk bal ce.
  - Any changes that are nece sary (e a chang to a timetable or a change in the Lead Authority, if applicable) wi be applie at the level of the concerned procedure and not at a product type or pro dure typ level.
  - Where d lays ar reported the arrangements described for CAPs and EMA procedures in Annex 1 and for N Ps-hu an me icines in Annex 2 apply.

[3] PSUR procedures for medicinal products used for the treatment of COVID-19 and for vaccines against COVID-19 (both new products and changes to existing products), products needed in the general treatment of COVID-19 patients (incl. crucial products in the ICU setting)

5.3. Specific measures relating to Post-Authorisation Safety Studies (PASS)

The principles for prioritisation for the EMRN are as follows:

- **PASS procedures for COVID-19 related medicinal products**[4] should be given 1st priority.
- **For non-COVID-19 related PASS** the following principles apply:
  - Should prioritisation of PASS activities for non-COVID-19 medicinal products become necessary, the prioritisation will take into account the potential impact on public health and/ the benefit-risk balance.
  - Any changes that are necessary (e.g. a change to a timetable or a change in the Lea Authority, if applicable) will be applied at the level of the concerned procedur nd not a product type or procedure type level.
  - Where delays are reported the arrangements described for CAPs and MA pr edur s in Annex 1 and for NAPs-human medicines in Annex 2 apply.

6. Specific measures relating to inspections

The following specific measures apply to inspections in the second phase of the EMRN COVID-19 BCP:

- For ongoing inspection requests the rapporteurs, inspectors national competent authorities and EMA, as applicable, will explore alternative solutio s an optio (remote inspections, deferred reporting, information from trusted authorities, c ock top, etc.).
- For upcoming inspection requests a risk-ba d app ach ill be introduced, as follows:
  - New triggered/preapproval inspect ns will c tinue but rapporteurs, inspectors, national competent authorities and EMA, as a plicabl , ill explore alternative solutions and options (remote inspections, deferr d re orting, form tion from trusted authorities, clock stop, etc.) on a case by case basis.
  - New requests for routine/pla ed on-site inspections are postponed if the level of safety risks is not acceptable or Insp ctors and Member States, unless an alternative solution is identified.
- New routine/p nned spectio requests will restart as soon as the level of safety risks is acceptable for In ectors d Member States or a suitable alternative solution is identified.

The Inspectors Working G ups are involved in developing alternative solutions and options such as guidance on distant assessments/remote inspections.

7. Specif c aspects of requests by applicants/Marketing Auth risation Holders (MAHs) for delays in submissions

In dd n to the principles for the handling of regulatory procedures by the Regulatory Authorities also requests for delays made by pharmaceutical companies need to be addressed.

Requests for delay in the submission of responses to questions will be handled in the following way:

[4] Medicinal products used for the treatment of COVID-19 and vaccines against COVID-19 (both new products and changes to existing products), products needed in the general treatment of COVID-19 patients (incl. crucial products in the ICU setting)

- Requests for delays in submission of COVID-19 related responses as part of a COVID-19 related procedure will not be accepted, except duly justified for short delays.
- For non-COVID-19 procedures:
  - Requests for delays in submission of responses as part of safety related changes/ applications to address quality defects will not be accepted except duly justified for short delays.
  - For any other submission of responses for any other non-COVID-19 related procedure delay will be accepted if duly justified.

Requests for delays in responding to questions in relation to PSURs will be handled as f llows:

- **For COVID-19 related PSURs** requests for delays will not be accepted.
- **For non-COVID-19 related PSURs** requests for delays will not be accepted, e cep duly ju tified for short delays *taking into account the potential impact on public health and/ r th be fit-risk balance*.

Requests for delays in responding to questions in relation to signals will be han ed as follows:

- **For COVID-19 related signals** requests for delays will not be accep d
- **For non-COVID-19 related signals** delays will not be ccepted, except duly justified for short delays taking into account the potential impact o public/animal health and/or the benefit-risk balance.

Requests for delays in responding to questions in pro edure in rela on to imposed PASS will be handled as follows:

- For PASS relating to **COVID-19 prod ct** reque or delays will not be accepted.
- For **non-COVID-19 related PASS rocedu s** requests for delays will not be accepted, except duly justified for short delays king nto ccount the potential impact on public health and/or the benefit-risk bal nce.

For any delay to submission of resp nses the revised start of the procedure will be dependent on the availability of the already a p nted L d Authority(ies) and the assessment team, and might lead to the change in Lead Auth ity(ies)

A delay in submiss n of p nned pplications might lead to a change in Lead Authority or a re-appointment of the Le d Authority(ies).

8. Regulatory guidance for applicants and MAHs

The E the Coo dination group for Mutual recognition and Decentralised procedures – human "CMDh and EMA have developed a Question and Answer document (question-and-answer (Q A) document to provide guidance to stakeholders) on adaptations to the regulatory framework to ddre challenges arising from the COVID-19 pandemic, and which was published. Subsequently, a veterinary version of the Q&A document was elaborated by the EC and the Coordination group for Mutual recognition and Decentralised procedures – veterinary ("CMDv") and EMA, and published (https://www.ema.europa.eu/en/news/regulatory-flexibility-ensure-availability-veterinary-medicines-during-covid-19-pandemic).

The Q&A document outlines areas where regulatory flexibility is possible to address some of the constraints MAHs may be faced with in the context of COVID-19. The measures introduced cover different areas of the regulation of medicines such as MA and regulatory procedures, manufacturing

and importation of active pharmaceutical ingredients (APIs) and finished products, quality variations and labelling and packaging requirements with flexibility to facilitate the movement of medicinal products within the EU. Some of the measures described are reserved for crucial medicines for use in COVID-19 patients.

The documents, both human and veterinary, will be revised to address new questions and to adjust the content thereof to the evolution of the pandemic.

9. Monitoring of the implementation

The situation will be continuously monitored at EMA Committees', CMDh and CMDv level to inform decision-making either in terms of adjustments to be introduced in phase 2 or to move to phase 3 if the situation deteriorates. Such decisions will be taken at the level of the EMRN.

10. Communication

To facilitate the streamlining of information between each NCA and EMA in case of anticipated delays in the work to be performed by the Rapporteur(s) a Single Point of Contact (SPOC) will be established within each NCA.

Transparency to stakeholders is very important and the EMRN COVID-19 BCP will be published on the websites of HMA, CMDh, CMDv and EMA. Updates and further information will be given if a new phase of the BCP is invoked or additional mitigating measures have been agreed.

Annex 1

COVID-19 BCP measures specific to the European Medicines Agency, for CAPs and EMA procedures for NAPs

1. Introduction

The European Medicines Agency (EMA) will follow the general principles as set out in the European Medicines Regulatory Network (EMRN) COVID-19 Business Continuity Plan (BCP), section 4 (Phases of the EMRN COVID-19 BCP). This annex describes how these general principles will be implemented for EMA procedures for CAPs and, as applicable, NAPs. In particular, detailed information is provided how EMA will apply the arrangements for the non-COVID-19 procedures where delays are reported as referred to in section 4.2.

2. Application of the general principles

2.1. General considerations

Translating phase 2 of the ERMN COVID-19 BCP as described in section 4.2. into the pr ct es of applications submitted in accordance with the centralised procedure results in the foll wing

- Under no circumstances can **COVID-19 related procedures**[1] be delayed they should always be given 1st priority. For authorised products this means that if the alre dy app inted Rapporteur(s) is (are) not able to perform the assessment, then (a) new Rapporteur(s) wil e appointed on a temporary basis for the particular procedure. For application for new products the appointment of (a) Rapporteur(s) will be based on the already existing crit ria such as the availability of the necessary expertise, but in addition the availability of the n cessary capacity (including at assessor level) to take on the procedure without delay is an mp rtant erequisite.
- **For the non-COVID-19 procedures**, any chan es that are necessary (e.g. a change to a timetable or a change in Rapporteur) will be applie at the level of the concerned procedure and not at a product type or procedure type evel.
- **For the non-COVID-19 procedures where de a s are reported** the following **decision tree** is followed:
  - First, use utmost flexibili within th overall timetable without extending the overall timeframe for the procedure.
  - If this is not feas le, rep ce on a temporary basis the Rapporteur with the (Co)-Rapporteur to finalise th partic lar proc dure where a delay has been reported; or in case the Co-Rapporteur norm lly n t involved in the procedure, ask the Co-Rapporteur nevertheless to take over (on c dition that the necessary assessment team is available). In case such temporary replacement is not possible, go to the next step.
  - f th emporary replacement of the Rapporteur by the Co-Rapporteur is not feasible, extend the ove ll timetable by 1-3 months on condition that the involved assessment team remains vailabl

    If this is not feasible, appoint another Rapporteur on a temporary basis for any procedure elating to the concerned authorised medicine, or permanently re-appoint the Rapporteur for planned submissions of applications for initial marketing authorisations.

[1] i.e. procedures relating to treatment of COVID-19 and vaccines against COVID-19 (both new products and changes to existing products), procedures relating to products needed in the general treatment of COVID-19 patients (incl. crucial products in the intensive care unit (ICU) setting) and procedures to minimise shortages due to COVID-19

In addition, the following should be noted:

- Requests for a delay will only be considered if the (Co-)Rapporteur provides comprehensive justifications regarding the specific and unforeseeable circumstances that prevent from respecting the procedural timelines.
- Following the receipt of a duly justified request, EMA in consultation with the affected (Co-)Rapporteur, will decide on a solution at a procedure level compatible with the criteria detailed in this annex. Such solution should not affect the quality of the scientific assessment
- If, following the decision tree, the solution is to apply a delay, 3 conditions have t be fulfi d: (1) the other mitigating measures as described in the decision tree are not successfu (2) the requested delay does not exceed 3 months, and (3) the European Commissi n (EC) can gree with the requested delay.
- Where possible, the Multinational Assessment Team (MNAT) concept w ll be a plie
- Changes to timetables, in principle, should not affect the applica t's/ma eting authorisation holder's (MAH) time frame foreseen in the legislation to answer to req s s from the Committees, unless an explicit agreement has been obtained for the modification concerned.

2.2. Initial applications, line extensions and xtensions of indications (Type II variations, 90 day procedures) with both Rapporteur and Co-Rapporteur involved in the procedure

Before the intended submission date as indicated by t applic nt/MAH, EMA will liaise with the (Co)-Rapporteurs for the procedure to enqui wh ther th y anticipate difficulties in adhering to the proposed timetable for assessment.

In case a delay is reported before the tart of roc dure the length of the delay and the procedure can give rise to three scenarios:

1. The procedure is COVID-19 rel ed.

   Since under no circumstance COVI -19 related procedures can be delayed and in certain cases may even n d to be shortene a new (Co)-Rapporteur or a MNAT for the already appointed (Co)-Rapporteur (ini l app ation only)/ another temporary (Co)-Rapporteur (line extensions and extensions of indic ions) having the capacity and expertise (including at assessor level) to take over the procedure w out delay will be appointed.

2. The ro dure is non-COVID-19 related and the length of the anticipated delays can be ac ommod ed within the timetable.

   A re sed timetable will be adopted to allow for the delay without extending the overall legal meframe.

3. Th procedure is non-COVID-19 related and the length of the anticipated delay cannot be accommodated within the timetable.

   In such exceptional cases, it may be necessary to extend the timetable beyond the overall legal timeframe or, if not feasible (length of delay more than 3 months and/or the assessment team is not available), to re-appoint (Co)-Rapporteurs or to form a MNAT for the already appointed (Co)-Rapporteur (initial applications only) or to temporarily re-assign another (Co)-Rapporteur for the procedure (line extensions and extensions of indications).

Delays being reported during the procedure that can be accommodated within the overall procedure timeframe without extending it, but would only affect the respective phase of the overall procedure, will result in a revised timetable for the affected phase of the process.

When the procedural steps foresee circulation of a joint assessment report (e.g. after Day 80 for initial applications), the unaffected (Co)-Rapporteur should take the lead in preparing the joint report, provided that the affected (Co)-Rapporteur is in a position to endorse the joint report.

Delays whereby the individual (Co)-Rapporteur's assessment report (e.g. before Day 80 for initial applications) or the Joint Rapporteurs' assessment report are not available in time to allow CxMP adoption of a List of Questions, List of Outstanding Issues or Request for Supplementa inform tion will result in a revised timetable which will extend the overall timetable beyond the legal t efram for the time strictly necessary (no more than 3 months).

In case the delay would exceed 3 months, another Rapporteur will be appointed o a tem orary basis for line extensions and extensions of indications and a Rapporteur will be re-appointe for p ned submissions of applications for initial marketing authorisations.

2.3. Initial applications, line extensions, renewals and annual re-assessments with only the Rapporteur involved in the proc dure

Before the intended submission date as indicated by the applic nt/MAH (initial applications and line extensions) or the expected submission date (renewals and an ual re-assessments), EMA will liaise with the (Co)-Rapporteur for the procedure to enquire wh her d ficulties in adhering to the proposed timetable for assessment are anticipated.

In case a delay is reported before the start of the pro dure, the length of the delay and the procedure can give rise to four scenarios:

1. The initial marketing authorisation appl ation is C VID-19 related.

   Since under no circumstances COVID 19 related pr cedures can be delayed and in certain cases may even need to be shorten a new Co)-Rapp rteur or a MNAT for the already appointed (Co)-Rapporteur (initial applications ly)/ another temporary (Co)-Rapporteur (line extensions, renewals and annual r as ssmen s) having the capacity and expertise (including at assessor level) to tak over th proced re without delay will be appointed.

2. The line extensi app ation s COVID-19 related.

   EMA will enquire wh her the Co-Rapporteur (if nominated) has the capacity (including at assessor level) to take over the procedure. If not, another temporary Rapporteur will be appointed for the line ext sion application.

3. Th procedu e is non-COVID-19 related and the length of the anticipated delays can be acco mod ted within the timetable.

   A evised timetable will be adopted to allow for the delay without extending the overall legal timeframe.

   The procedure is non-COVID-19 related and the length of the anticipated delays cannot be accommodated within the timetable.

   In such exceptional cases, it may be necessary to extend the timetable beyond the overall legal timeframe up to 3 months or, if not feasible (length of delay more than 3 months and/or the assessment team is not available), to re-appoint Rapporteurs or to form a MNAT for the already

appointed (Co)-Rapporteur (initial applications only) or to temporarily re-assign another Rapporteur to the procedure (line extensions, renewals and annual re-assessments).

Delays being reported during the procedure that can be accommodated within the overall procedure timeframe without extending it but would only affect the respective phase of the overall procedure, will result in a revised timetable for the affected phase of the process.

Delays whereby the individual (Co)-Rapporteur's assessment report (e.g. before Day 80 for initial applications) is not available in time to allow CxMP adoption of a List of Questions, List of Outstanding Issues or Request for Supplementary information will result in a revised timetable which will extend the overall timetable beyond the legal timeframe for the time strictly necessary (no more than 3 months).

In case the delay would exceed 3 months, another Rapporteur will be appointed on a temporary basis for line extensions, renewals and annual re-assessments and a Rapporteur will be re-appointed for planned submissions of applications for initial marketing authorisations.

2.4. Type II and Type IB variations with only the Rapporteur involved in the procedure

EMA is not usually informed about planned submission dates for variations (excluding extensions of indications or other changes to the authorised therapeutic indication) and is therefore not able to liaise with the Rapporteur in advance of the submission but will do so at the time of submission.

Upon receipt of the variation application EMA will liaise with the Rapporteur for the product concerned to enquire whether difficulties in adhering to the proposed timetable for assessment are anticipated.

In case a delay is anticipated, the length of the delay and the procedure can give rise to three scenarios:

1. The application is COVID-19 related.

   Since under no circumstances COVID-19 related procedures can be delayed and in certain cases may even need to be shortened EMA will enquire whether the Co-Rapporteur has the capacity (including at assessor level) to take over the procedure. If not, another temporary Rapporteur will be appointed without delay for the variation application.

2. The procedure is non COVID-19 related and the length of the anticipated delays can be accommodated within the timetable.

   A revised timetable will be adopted to allow for the delay without extending the overall legal timeframe.

3. The procedure is non-COVID-19 related and the length of the anticipated delays can not be accommodated within the timetable.

   In such exceptional cases, it may be necessary to extend the timetable beyond the overall legal timeframe or, if not feasible (length of delay more than 3 months and/or the assessment team is not available), to appoint a temporary Rapporteur for the procedure concerned.

Delays being reported during the procedure but before Day 36 (60 day procedures)/ Day 17 (30 day procedures)/ Day 20 (Type IB) that are of such a duration that it can be accommodated within the overall procedure timeframe without extending it but would only affect the respective phase of the overall procedure, will result in a revised timetable for the affected phase of the process.

Delays whereby the Rapporteur's assessment report is not available in time to allow CxMP adoption of a Request for Supplementary information or the opinion will result in a revised timetable which will extend the overall timetable beyond the legal timeframe for the time strictly necessary (no more than 3 months).

In case the delay would exceed 3 months, the Co-Rapporteur (if already nominated and available) w l be appointed on a temporary basis or if not feasible another Rapporteur will be temporarily appointed for the procedure.

2.5. Referrals

The following applies to:

- Referrals according to Article 107i of Directive 2001/83/EC or Article 78 of Dir 20 /82/EC
- Referrals according to Article 20 of Regulation (EC) 726/2004 or Article 45 of Regu ation (EC)726/2004
- Referrals according to Article 31 of Directive 2001/83/EC or Article 35 of Dir ctive 2001/82/EC
- Article 13 referrals according to Regulation (EC) No 1234/2008
- Referrals according to Article 29(4) of Directive 2001/83/EC or Article 33(4) of Directive 2001/82/EC
- Referrals according to Article 30 of Directive 2001/8 /EC or A icle 34 of Directive 2001/82/EC.

At the time of appointment of the Rapporteur(s) for refe ral EMA will enquire whether the Rapporteur(s) to be appointed anticipate difficulties in dherin to the proposed timetable for assessment. If delays are expected, then an ther Rapporteur is appointed.

Delays being reported during the procedure hat are o such a duration that it can be accommodated within the overall procedure timefram withou ext ndin it but would only affect the respective phase of the overall procedure, will result in a re ised timetable for the affected phase of the process

When the procedural steps foresee rculation of a joint assessment report, the unaffected (Co)-Rapporteur should ta e t lead preparing the joint report, provided that the affected (Co)-Rapporteur is in a p sition t endorse the joint report.

Delays whereby the ndivid al Ra porteur's assessment report is not available in time to allow adoption of a List of Questions, st of Outstanding Issues or the opinion will result in a revised timetable which will extend the overall tim table beyond the legal timeframe for the time strictly necessary (no more than 3 months).

In cas the del would exceed 3 months, another Rapporteur will be appointed for procedure.

2.6 PSURs and PSUSAs (human medicinal products)

EMA liaise with the PRAC Rapporteur or Lead Member State (LMS), as applicable for the procedure before the expected submission date to enquire whether difficulties in adhering to the proposed metable for assessment are anticipated.

In case a delay is reported before the start of the procedure, the length of the delay and the procedure can give rise to three scenarios:

1. The PSUR is COVID-19 related.

Since under no circumstances COVID-19 related procedures can be delayed the PRAC Co-Rapporteur (if available) will be assigned to the procedure or a new PRAC Rapporteur having the capacity and expertise (including at assessor level) to take over the procedure without delay will be appointed.

2. The PSUR is non-COVID-19 related and the length of the anticipated delays can be accommodated within the timetable.

   The delay will be accommodated within the timetable without extending the overall legal timeframe.

3. The PSUR is non-COVID-19 related and the length of the anticipated delays can not accommodated within the timetable.

   In such exceptional cases, it may be necessary to extend the timetable beyond the overall legal timeframe up to 3 months or, if not feasible (length of delay more than 3 months and/or assessors are not available), to assign the procedure to the PRAC Co-Rapporteur if possible (i.e. unless no PRAC Co-Rap has been appointed or the PSUSA is for NAPs only), or to temporarily appoint a new PRAC Rapporteur or LMS, as applicable, for the procedure.

Delays being reported during the procedure that can be accommodated within the overall procedure timeframe without extending it but would only affect the respective phase of the overall procedure, will be accommodated within the overall timeframe of the process

Delays whereby the PRAC Rapporteur's or LMS's assessment report is not available in time to allow the PRAC to adopt a Recommendation will result in a revised timetable which will extend the overall timetable beyond the legal timeframe for the time strictly necessary (no more than 3 months).

In case the delay would exceed 3 months, either the PRAC Co-Rapporteur (if available) or another Rapporteur or LMS, as applicable, will be appointed on a temporary basis for the procedure.

2.7 PSURs (veterinary medicinal products)

When delays in the assessment of PSURs for NAPs are anticipated or occurring, Rapporteurs and Co-Rapporteurs are asked to contact the EMA secretariat directly (VetPhV@ema.europa.eu).

Arrangements will be sought, depending on the legal time frame and an assessment of the estimated risk to animal and/or public health due to a delayed assessment of a PSUR. The signal management activity for the same product a potentially delayed PSUR is already aligned and occurs prior to the data lock point for the PSUR, and will, therefore, provide insight for assessing the potential risk of a delay.

2.8 Signal detection/validation/confirmation (human medicinal products)

If Rapporteur or a Lead MS is not able to fulfil the tasks in relation to signal detection/validation/confirmation for a product or a group of products a new temporary Lead MS (to take the lead on behalf of all MSs and perform monitoring of EudraVigilance data, validation and confirmation for the CAP) or Rapporteur (to perform confirmation for the CAP) will be appointed through a call for volunteers for the length of time that the initially appointed Lead MS or Rapporteur is unable to fulfil his tasks.

In case of no volunteer for a Lead MS, the monitoring of EudraVigilance data will have to be carried out by all MSs and validation and confirmation by the Lead MS who detected and validated a new signal.

2.9 Signal analysis and assessment (human medicinal products)

EMA will liaise with the PRAC Rapporteur for the procedure before the start of procedure to enquire whether difficulties in adhering to the proposed timetable for assessment are anticipated.

In case a delay is reported before the start of the procedure, the length of the delay and the procedure can give rise to three scenarios:

1. The signal is COVID-19 related.

   Since under no circumstances COVID-19 related procedures can be delayed the procedure will b re-assigned to a new PRAC Rapporteur having the capacity and expertise (including t asses or level) to take over the procedure without delay.

2. The signal is non-COVID-19 related and the length of the anticipated delays can b ccomm dated within the timetable.

   The delay will be accommodated within the timetable without extending the over l leg timeframe.

3. The signal is non-COVID-19 related and the length of the anticipated de ys n not be accommodated within the timetable.

   In such exceptional cases, it may be necessary to extend t e timetable beyond the overall legal timeframe up to 3 months or, if not feasible (length of del more than 3 months and/or assessors are not available), to re-appoint a new PRAC Rappo r for e procedure.

Delays being reported during the procedure that can e a commodated within the overall procedure timeframe without extending it but would only affect respe tive phase of the overall procedure, will be accommodated within the overall timefra e o he process.

Delays whereby the PRAC Rapporteur's ass ssment e ort is not available in time to allow the PRAC to adopt a Recommendation will result i revis d timetab e which will extend the overall timetable beyond the legal timeframe for the time s ictly neces ary (no more than 3 months).

In case the delay would exceed 3 m nths, another PRAC Rapporteur will be appointed on a temporary basis for the procedure.

2.10 Signal manag ment veterinary medicinal products)

Signal management cur ntly covers centrally authorised veterinary medicinal products, and the discussions are aligned with the CVMP Pharmacovigilance Working Party (PhVWP-V). When delays in the asse nt are anticipated or would occur the EMA Secretariat (VetPhV@ema.europa.eu) should be con acted. While there is no explicit legal basis at present for signal management for veterinary medici al produ ts, delays are being handled by postponing the discussion to the next meeting of the P VWP-V

2.11 mposed Post-Authorisation Safety Studies (PASS)

EMA is not usually informed about planned submission dates for imposed PASS protocols and results and is, therefore, not able to liaise with the PRAC Rapporteur in advance of the submission but will do so at the time of submission.

Upon receipt of the PASS EMA will liaise with the PRAC Rapporteur for the product concerned to enquire whether difficulties in adhering to the proposed timetable for assessment are anticipated.

In case a delay is anticipated, the length of the delay and the procedure can give rise to three scenarios:

1. The application is COVID-19 related.

   Since under no circumstances COVID-19 related procedures can be delayed and in certain cases may even need to be shortened, EMA will enquire whether the PRAC Co-Rapporteur has the capacity (including at assessor level) to take over the procedure. If not, another temporary PRAC Rapporteur will be appointed without delay for the procedure.

2. The procedure is non-COVID-19 related and the length of the anticipated delays can be accommodated within the timetable.

   A revised timetable will be adopted to allow for the delay without extending the overall le al timeframe.

3. The procedure is non-COVID-19 related and the length of the anticipated delays c n no e accommodated within the timetable.

   In such exceptional cases, it may be necessary to extend the timetable beyo d the overall legal timeframe or, if not feasible (length of delay more than 3 months and/or e ssessment team is not available), to appoint the PRAC Co-Rapporteur (if possible) or a temporary Rapporteur for the procedure concerned.

Delays being reported during the procedure that are of such a ration that it can be accommodated within the overall procedure timeframe without extend ng i but th se would only affect the respective phase of the overall procedure, will result in a revise tim table for the affected phase of the process.

Delays whereby the PRAC Rapporteur's assessm nt rep rt is ot available in time to allow the PRAC to adopt a Recommendation will result in a rev sed ti etable which will extend the overall timetable beyond the legal timeframe for the time str tly nece ary (no more than 3 months).

In case the delay would exceed 3 m hs, the RA Co apporteur (if possible) will be appointed on a temporary basis or if not feasible a other Rapporteur w ll be temporarily appointed for the procedure.

2.12 Inspections

For inspections oordina d by EM the following measures will apply:

For ongoing inspect n req sts hen conduct of an on-site inspection is not deemed possible, the Rapporteurs, inspector and EMA will explore alternative solutions and options (remote inspections, deferred reporting, inform tion from trusted authorities, clock stop, etc.) in advance of discussion at CxMP level

For up oming i pection requests a risk-based approach will be introduced, as follows:

- N w EMA requests for triggered/preapproval inspections will continue but rapporteurs, inspectors and EMA will explore alternative solutions and options (remote inspections, deferred eporting, information from trusted authorities, clock stop, etc.) on a case by case basis.
- New EMA requests for routine/planned on-site inspections are postponed until the safety risks decrease to an acceptable level that allows to conduct an on-site inspection, unless an alternative solution has been identified.

New routine/planned inspection requests will restart as soon as feasible.

The Inspectors Working Groups are involved in developing alternative solutions and options such as guidance on distant assessments/remote inspections.

3. Communication with (Co-)Rapporteurs, scientific committees, the EC and the applicant/MAH

Any change in (Co)-Rapporteurs will be adopted by the CHMP[1], CVMP or PRAC and EMA will inform the applicant/MAH accordingly.

The Rapporteur(s) experiencing delays will inform EMA of the delay. The Rapporteur(s) and EMA will jointly decide on the action to be taken.

Significantly revised timetables, regardless of whether they change the overall timeframe for the procedure or not, will be circulated to the CxMP for adoption where necessary and subsequently sent to the applicant/MAH.

The EC will be asked in advance for their agreement on the revised timetables which extend the procedure beyond the overall legal timeframe. The EC will be sent a list on a regular basis of all timetables that have been revised including those that do not extend the procedure beyond the overall legal timeframe.

In addition to asking the (Co)-Rapporteurs prior to the start of the procedure EMA will survey the (Co)-Rapporteurs at 2 monthly intervals as to any expected delays in the upcoming procedures for which a planned submission date is known as well as for the ongoing procedures. EMA will survey the applicants/MAHs at 3 monthly intervals as to any expected delays in upcoming applications. Both surveys will serve to inform the EMRN about the extent of the impact on the regulatory procedures as well as about the timing of the upcoming workload.

4. Documentation of delays and consequential changes

For each delay reported EMA will keep a log of the justification provided by the Rapporteur(s) and the decision taken.

Revision of timetables will be recorded in the minutes of the relevant Committee meeting and in the assessment report of the procedure. In case the procedure has been extended beyond the overall legal timeframe it will also be reflected in the opinion.

[1] In case of ATMPs also CAT Rapporteurs

Annex 2

COVID-19 BCP measures specific to CMDh and human NAPs

Phases of the CMDh COVID-19 BCP

First Phase CMDh COVID-19 BCP

In accordance with the agreements adopted by the CMDh for the management of exceptional situations prior to the COVID-19 pandemic, the authorisation of medicinal products will continue to be facilitated through the MRP/RUP Zero Day procedures at the request of the MSs. Likewise, the evaluation of products that have been identified as essential for any CMS will be accelerated, as far as possible.

Second Phase CMDh COVID-19 BCP

2.1 Prioritisation and expedited authorisation of new medications or relevant modifications in the context of the pandemic

Regulatory procedures for products considered as critical or directly linked to the COVID-19 outbreak will be prioritised and expedited, as possible.

The CMDh has agreed to perform expedited MRP or RUP procedures via a fast-track timetable (shortened TT) or even in a 0-Day procedure (approved after validation) in order to ensure the granting of a marketing authorisation of relevant products in all the MSs, who need these medicinal products. The same applies to variations concerning the extension of indication for the treatment of COVID-19.

The choice of the procedure depends on the criticality of the product as well as the decision of the RMS and the proposed new CMS.

2.2 Possibility of delaying or stopping non COVID-19 related regulatory procedures

In certain cases, for not COVID-19 related products, the RMS, in consultation with the CMSs, may decide to delay the procedure start or re-start, if this is in the interest of the applicant and/or the RMS/CMSs.

Furthermore, it is exceptionally agreed for DCP/MRP/RUP, renewal and type II variation procedures to allow a "freezing" (holding the timetable at the same procedure Day and restarting it as soon as the response is received or as soon as the RMS AR is finalised) or "rolling back" (bring the procedure back to validation phase or back to clock stop with the usual timeframe of handling responses in the clock stop) of the procedure timetable due to unexpected and COVID-19-related capacity issues within the MS, or when it is not possible for applicants to submit responses due to the COVID-19 pandemic.

2 3 Possible modifications in the reference membership of procedures

As a last option to the aforementioned adjustments in the timelines of the procedures, the CMDh could consider the need to carry out temporary changes in the reference membership to cover exceptional needs of specific procedures. This could be of particular relevance in the case of COVID-19 related products.

As these changes are temporary, they will not imply a formal RMS change, but rather the temporary contribution of some other CMS to lead the evaluation until the completion of the procedures. In this sense, the following options might be valued:

- Replacement of the RMS on a temporary basis with another CMS to finalise the particular procedure where a delay has been reported.
- Replacement of the RMS on a temporary basis for planned submissions of variations relating to th concerned authorised medicine.

In this context of pandemic, it might be recommended to consider the switch of the intended RMS fo specific new marketing authorisation applications, and this will be a joint decision of the rmer assigned RMS, the applicant, and the proposed new RMS.

2.4. Specific measures relating to pharmacovigilance aspects for N Ps

The management of PSURs/PSUSAs, signals and PASS during this pandemic pe iod wil b exactly the same regardless of the authorization route of the involved medicinal products. T erefore, the prioritization principles detailed in the common part of this document will app L kewise, the criterion of case management in the different scenarios will also be common for CAPs and NAPs.

2.5 Inspections

The measures for conducting remote inspections will be ass sed a d agreed at EU level with the involvement of Inspectors Working Groups with rega ds t the general principles and will be applied in the same way by the network.

Third Phase CMDh COVID-19 BCP

The EMRN will decide the need to troduce a ditional mitigation measures for this third phase. The CMDh will provide additional recomm dations for this third phase, if appropriate.

NOTE: All the det ls of t e deci ions taken by the CMDh for the exceptional handling of regulatory procedures in the con xt of the COVID-19 pandemic are available on the CMDh website.
CMDh Procedural guidan e during COVID-19 pandemic. https://www.hma.eu/621.html

Annex 3

COVID-19 BCP measures specific to the CMDv and veterinary NAPs

The CMDv proposed BCP measures for MR/DC procedures based on the scenario elaborated by EMA and HMA. In terms of MR/DC procedures the following should be understood: marketing authorisation procedures, variations (including worksharing applications) renewals and also surveillance (pharmacovigilance). At every stage of a pandemic the safe use of VMPs has to be ensured. Urgent safety issues have to be identified.

The CMDv has also proposed a communication tool for NCAs to inform the network on any issue encountered. It is important that the network is kept informed when a RMS/CMS or an applicant will have delays in sending awaited documents. Each NCA should declare when it considers that its situation has evolved and that a change in status need to be communicated to the network wh tever the status in procedures, RMS or CMS.

First phase

In phase 1 of the EMRN COVID-19 BCP, NCAs are able to continue to fulfil normal reg lator nd surveillance tasks for MRP/DCP (evaluation and monitoring tasks) and CMDv t sks.

Second phase

In the second phase of the EMRN COVID-19 BCP one or more NCA(s) report difficulties in fulfilling normal regulatory and surveillance tasks and, therefore, a first step of prioritisation needs to be applied. Surveillance in order to identify urgent safety issues s uld prevail.

It should be necessary to prioritise the assessment of some roced es depending on several criteria linked to the nature of the procedure and the produc concerned In this case, the RMS, in consultation with the CMSs, may decide to delay the proced e star or re tart, if this is in the interest of the applicant and/or the RMS/CMSs. Furthermo , it is xceptionally agreed for DCP/MRP/RUP, renewal and type II variation procedures to allow a freezing holding the timetable at the same procedure Day and restarting it as soon as the respons s rec ive or as soon as the RMS AR is finalised) of the procedure timetable due to unexpe ted a d COVID-19 elated capacity issues within the RMS, or when it is not possible for applicants to ubmit res onses due to the COVID-19 pandemic. The applicant should inform the RMS timely enoug of a necessary interruption of the procedure and justify that the reason for not being able o res nd is lated to the pandemic.

To solve availabil y issue linked t the COVID-19 situation, the CMDv has agreed to perform accelerated repeat u proc dur via a fast-track timetable (shortened TT). This kind of procedure is possible provided that RMS, new CMS and MAH agreed on it.

Third phase

The th d phase f the EMRN COVID-19 BCP is triggered when the majority of NCAs or the EMA are e erien g i creasing difficulties in fulfilling the tasks as set out in the aforementioned phase 2 desp e the level of prioritisation already applied, and, therefore, additional mitigating measures are need

The need to introduce any additional mitigating measures and to move to phase 3 will be decided on by the EMRN taking into account the outcome of regular reviews.

See also the CMDv website for more information.

PSURs (veterinary medicinal products)

When delays in the assessment of PSURs for NAPs are anticipated or occurring, the RMS or P-RMS should inform the CMS or P-CMS via an e-mail sent to list-v-cmd-psur, specifying if possible the date at which the assessment report is expected to be circulated.

Inspections

For inspections not coordinated by EMA the following measures will apply:

For ongoing inspection requests the inspectors from the supervisory authority will explore ernati solutions and options (remote inspections, deferred reporting, information from trusted autho ies, clock stop, etc.).

For upcoming inspection requests a risk-based approach will be introduced, as follow

- New requests for triggered/preapproval inspections will continue while ternative solutions and options (remote inspections, deferred reporting, information from rusted authorities, clock stop, etc.) will be explored on a case by case basis.
- New requests for routine/planned on-site inspections co ld be postponed until the safety risks decrease to an acceptable level that allows to condu n on-site inspection or alternative solutions and options (remote inspections, deferred rep ting, information from trusted authorities, clock stop, etc.) will be explored n a c e by c se basis.

New routine/planned inspection requests will restart s oon as easible.

The measures for conducting remote inspect ns ll be assessed and agreed at EU level with the involvement of Inspectors Working Groups ith rega ds to the general principles and will be applied in the same way by the network.