



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Points to consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials



Ingram Olkin Forum Series: Unplanned Clinical Trial Disruptions

28 July 2020 presented by Aldana Rosso, Danish Medicines Agency





Disclaimer

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I am employed by the Danish Medicines Agency.

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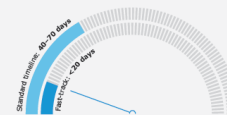
EMA's response to the pandemic

www.ema.europa.eu

Coronavirus disease (COVID-19) ✓
What's new
Guidance for developers and companies
Treatments and vaccines
Availability of medicines
Public-health advice
EMA's governance

EMA Fast-track procedures for treatments and vaccines for COVID-19

EMA is fully mobilised to support the development and marketing authorisation of safe, effective and high-quality therapeutics and vaccines against COVID-19. The Agency has put in place rapid review procedures related to COVID-19 to deliver assessments of high-quality applications from sponsors in the shortest possible timeframes while ensuring robust scientific opinions.



Rapid scientific advice

EMA provides developers with prompt advice to guide on the best methods and study designs to generate the scientifically robust evidence needed to determine the safety, efficacy and quality of treatments and vaccines against COVID-19 in the shortest time possible.



Rapid agreement of PIPs

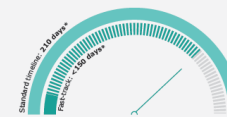
The needs of children have to be considered in the development of every medicine through a paediatric investigation plan (PIP) that is agreed by EMA. During the COVID-19 pandemic EMA expedites the review of applications for agreement of a PIP (or deferrals or waivers as appropriate) for treatments and vaccines against COVID-19 to ensure that development programmes can progress swiftly.



Rolling review**

In a public health emergency, EMA assesses data for promising medicines or vaccines as they become available. Through rolling review, EMA can exceptionally start evaluating data while the development is still ongoing. When the medicine's development is progressed enough for a marketing authorisation application (MAA), the formal assessment procedure can take place in a very short timeframe, because the data have already been scrutinised during rolling review.

Each rolling review cycle requires around 2 weeks, depending on the amount of data



Accelerated assessment

This procedure allows EMA to review the marketing authorisation applications for products of major interest for public health in a shorter timeframe than usual to speed up their approval and availability. It is an option when rolling review is not applicable, where there is an urgent public health need. In practice, assessment timelines will be reduced to the absolute minimum.

* Excluding time given to companies to provide responses
** An ad hoc procedure used in the context of a public health emergency



Extension of indication and extension of marketing authorisation

Medicines that are already authorised for other diseases may be used against COVID-19. EMA is ready to work further



Compassionate use of potential treatments for COVID-19

Compassionate use programmes can be set up by individual EU Member States to give access to treatments under development that have not received a marketing





Motivation

- It is foreseeable that the COVID-19 pandemic will interfere with the conduct of many ongoing trials, also with the collection, analysis and the interpretation of clinical trial data
- EMA Biostatistics Working Party highlights major points that Sponsors could take into consideration in case their trials are affected by the COVID-19 pandemic.



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1 26 June 2020
2 EMA/158330/2020 Rev. 1
3 Committee for Human Medicinal Products (CHMP)

4 **Points to consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials**

7

8

Draft agreed by Biostatistics Working Party	March 2020
Adopted by CHMP for release for consultation	25 March 2020
Start of public consultation	25 March 2020
End of consultation (deadline for comments)	25 April 2020
Update agreed by Biostatistics Working Party	11 June 2020
Adopted by CHMP	26 June 2020

9

Keywords	COVID-19, ongoing clinical trials, protocol deviations, data collection, trial integrity, interpretability, DMC, Scientific Advice
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<https://www.ema.europa.eu/en/implications-coronavirus-disease-covid-19-methodological-aspects-ongoing-clinical-trials>



Safety first

Most importantly, safety of study participants is paramount and must be at the heart of every decision taken, regardless of any potential consequences for an ongoing trial. Beyond this, it is an ethical mandate to proceed with a trial that has been started so that the efforts taken by study participants and physicians can benefit drug development and inform patient care.



Case-by-Case assessment

Implications on clinical trials are expected to be manifold. Impact on recruitment, data collection, analysis and interpretation of results is expected to be different for different trials.



Collect information

- Capture deviations, including those related to the COVID-19 pandemic.
- If possible, continue with data collection and collect information that could be helpful to interpret the results of the trial.



Risk Assessment

COVID-19 potentially affecting trial participants

COVID-19 potentially affecting the conduct of the trial

Implication on recruitment, loss of study participant, interpretation of the treatment effect?



Risk Assessment

Aggregated and blinded data analysis to inform the likelihood of obtaining interpretable results. Focus on quality and reliability of the trial and advise on follow-up actions.

Any analysis bears the risk of unblinding.

Independent Data Monitoring Committee (DMC) recommended.

Estimand framework is well suited to understand how the trial/results may be affected.



Substantial changes to the study protocol necessary?

Modifications such as:

- Changes in the primary and/or important secondary endpoints
- Unplanned interim analyses
- Final analysis with fewer events and/or shorter follow-up time could compromise the interpretation of the results.

Discussion with relevant competent authorities is encouraged.

Seek Scientific Advice at the EMA on these matters early in the process.



Main message

**Record, report,
assess,
and
seek advice
before reacting**

- Patient safety first
- Systematically capture deviations and record related reasons
- Risk assessment of impact of COVID-19 on ongoing trials should be conducted by an independent party.

If measures need to implemented to address pandemic impact:

- Convincing scientific reasons needed to implement changes
- Consult COVID-19 related guidance
- Discussion with relevant competent authorities is encouraged (e.g. through Scientific Advice) early in the process



Next steps

- Continuous scientific discussion expected
- Interaction with stakeholders anticipated
- Further updates of document envisaged based on growing experience

Any questions?



Further information

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