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

The views expressed in this presentation are my personal views and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties or the Danish Medicines Agency.

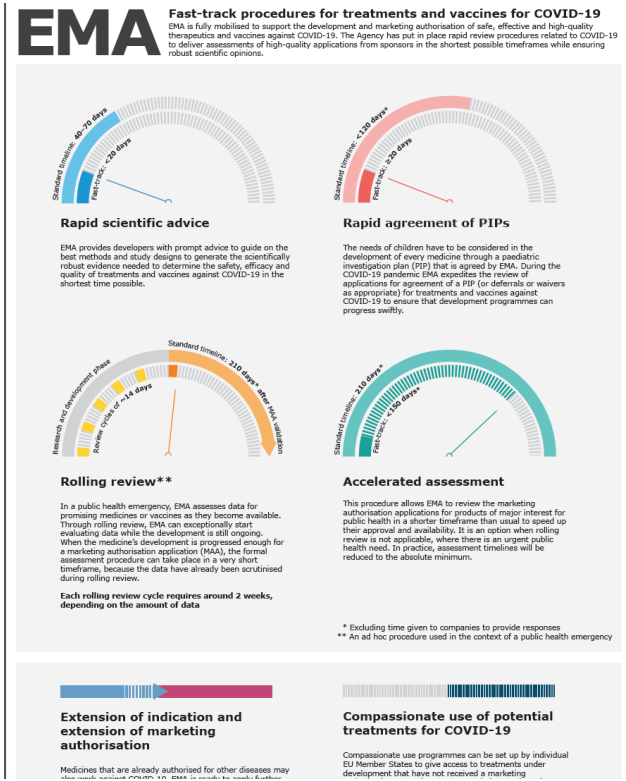
I am employed by the Danish Medicines Agency.

I am not employed by the EMA.

EMA's response to the pandemic

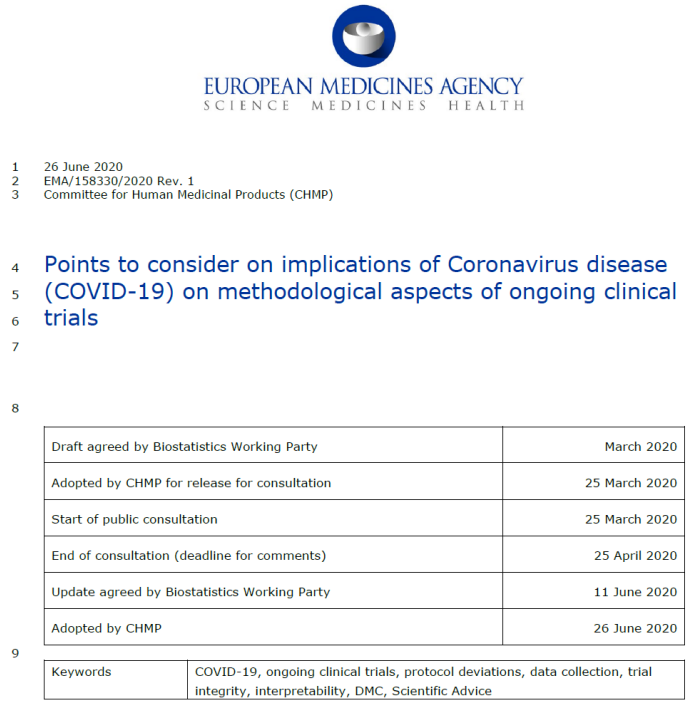
www.ema.europa.eu

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



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.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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

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

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

Keywords	COVID-19, ongoing clinical trials, protocol deviations, data collection, trial integrity, interpretability, DMC, Scientific Advice

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

biostatistics@ema.europa.eu

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

Follow us on **@EMA_News**