EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The EMA regulatory framework for timely approval of new and innovative drugs and vaccines in the pandemic era

XIII FORESIGHT TRAINING COURSE

Challenges for Researchers and Regulators facing the pandemic crisis

23 October 2020

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EMA Health Threat Plan

- **SCOPE:**
  - to provide internal general guidance on EMA activities during a health threat based on the experience from the 2009 pandemic and the Ebola outbreak of 2014-16
  - The plan is drafted to address a more likely bio-health threat, but as per cross-border health threat EU legislation, should be applicable to various acute hazards including threats of chemical, environmental and unknown origin.
  - The focus is human medicines and it does not cover animal health but liaison might be needed in some cases, e.g. zoonosis

EMA activities in support of drug development

- **COVID19 EMA pandemic task force (COVID-ETF):**

EMA scientific committee and working party members with relevant experience, e.g. in vaccines, infectious diseases, preclinical and clinical trial design, paediatric aspects, quality of biological medicinal products

- Early interactions with manufacturers
- Discussions with European Commission (EC), Health Security Committee (HSC), European CDC
- US FDA, Health Canada, International Coalition of Medicines Authorities (ICMRA), WHO on available treatments/vaccines and clinical trial design

EMA pandemic task force

- Exploratory review of current investigational products for treatment or prevention of Emergent disease including TCs with developers.
- identify the most appropriate regulatory pathway to ensure that potential treatments and/or vaccines are approved/made available as swiftly as possible.
- Rapid scientific advice on questions from manufacturers on their development plans, endorsed by CHMP
- Interaction with academia or sponsors/investigators of clinical trials not funded by industry

Inventory of rapid procedures

Development support

- Rapid scientific advice
- Rapid agreement of a paediatric investigation plan and rapid compliance check

Evaluation (initial authorisation & post-authorisation)

- Rolling review
- accelerated assessment for Marketing authorisation, Extension of indication
- Compassionate Use/support to Emergency Use

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4 May 2020
EMA/213341/2020

EMA initiatives for acceleration of development support and evaluation procedures for COVID-19 treatments and vaccines

The European Medicines Agency (EMA) together with the responsible scientific committees and their working parties, and in collaboration with the European Commission, operates rapid procedures to support the development and evaluation of treatments and vaccines for COVID-19. The EMA emerging health threats plan foresees that detailed procedures are set-up to adapt different types of review activities to the needs of the health threat/crisis situation. Whilst respecting the regulatory requirements and established review principles (e.g. independence of experts), these procedures aim, within timelines that are appropriate for the public health emergency situation, to provide most efficient management of product-review activities leading to scientifically sound and robust outcomes.

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Rapid scientific advice

Ad hoc procedure which follows the general principles of the regular scientific advice but with adaptations to facilitate acceleration. Final advice will be adopted by CHMP and the process is enriched with additional expertise from the COVID-ETF.

- **no pre-specified SA request submission deadlines** for developers
- flexibility regarding **the type and extent of the briefing dossier**
- **free of charge** in accordance with the EMA Executive Director Decision
- total review time from start to the final advice letter is **reduced to 20 days**
- To ensure review of suitability and maturity of the planned request for the rapid SA, developers should make the initial contact with EMA (2019-ncov@ema.europa.eu)
- For preliminary plan not yet suitable for formal rapid SA, **early guidance will be provided by EMA and the COVID-ETF**

Rapid agreement of a paediatric investigation plan (PIP) and rapid compliance check

Applications for a PIP, deferrals or waivers for treatments and vaccines for COVID-19 will be reviewed in expedited manner on case-by-base basis. PDCO is responsible for scientific assessment and takes also into account COVID-ETF's scientific input.

- **no pre-specified submission deadlines** for submission of dossiers
- **focused scientific documentation**
- PDCO opinion will be reduced to a **minimum of 20 days** (normally 120 days), EMA decision adopted within 2 days (usual 10 days)
- discuss the plan with **international regulators** during the evaluation
- timelines for a **compliance check** will be defined in accordance with the urgency and can be reduced to 4 days if necessary.

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Marketing authorisation

Products intended for prevention or treatment of COVID-19 will be treated in an expedited manner.

- **Use of rolling review** to accelerate evaluation while still ensuring robust scientific opinion (i.e. last round of RR concludes with no outstanding questions or start last 'RR' data package review as MAA, if all ready incl. PIP decision, expedited validation)
- In case RR is or cannot be used, **possibility of accelerated assessment** i.e. 150 days max (instead of 210d)
- CHMP opinion and assessment report can be adopted via written procedure, in particular in case of RR.
- Rapid translation check (ideally already within RR)
- EC: rapid CD (to be agreed with Commission Services)
- EMA: immediate EPAR publication following CD (awaiting)

Compassionate Use

Certain unauthorised medicinal products may be made available at national level to facilitate the availability to patients of new treatment options that are under development, even more in emergency context.

- Coordination and implementation of a compassionate use (CU) programmes remains **the competence of a Member State**
- EMA can provide **recommendation for a "group of patients" through the CHMP** to favour a common approach across Member States
- NCA should inform EMA if they are making a product available to a group of patients for compassionate use
- Applicant cannot request a CHMP opinion on CU, **only a MS can initiate such request**
- CHMP can accelerate the procedure and issue an opinion in a short timeframe

Scientific question – article 5(3) referrals

Where relevant, an opinion on a scientific matter concerning the evaluation of medicinal product for human use can be drawn up by the CHMP.

Assessment report for Article-5(3) procedure: Medicinal products under development for treatment of Ebola

review of all available data on investigational products for treatment of EVD to support emergency use by MSs

Conditional Marketing Authorisation

On the basis of less comprehensive data and subject to specific obligations

Scope (at least one):

- for **seriously debilitating diseases or life-threatening diseases**;
- to be used **in emergency situations**;
- **orphan** medicinal products.

Criteria (all):

- the **risk-benefit balance is positive**;
- it is likely that the applicant **will be in a position to provide comprehensive clinical data**;
- **unmet medical needs** will be fulfilled;
- the **benefit** to public health **of the immediate availability** on the market of the medicinal product concerned **outweighs the risk** inherent in the fact that additional data are still required.

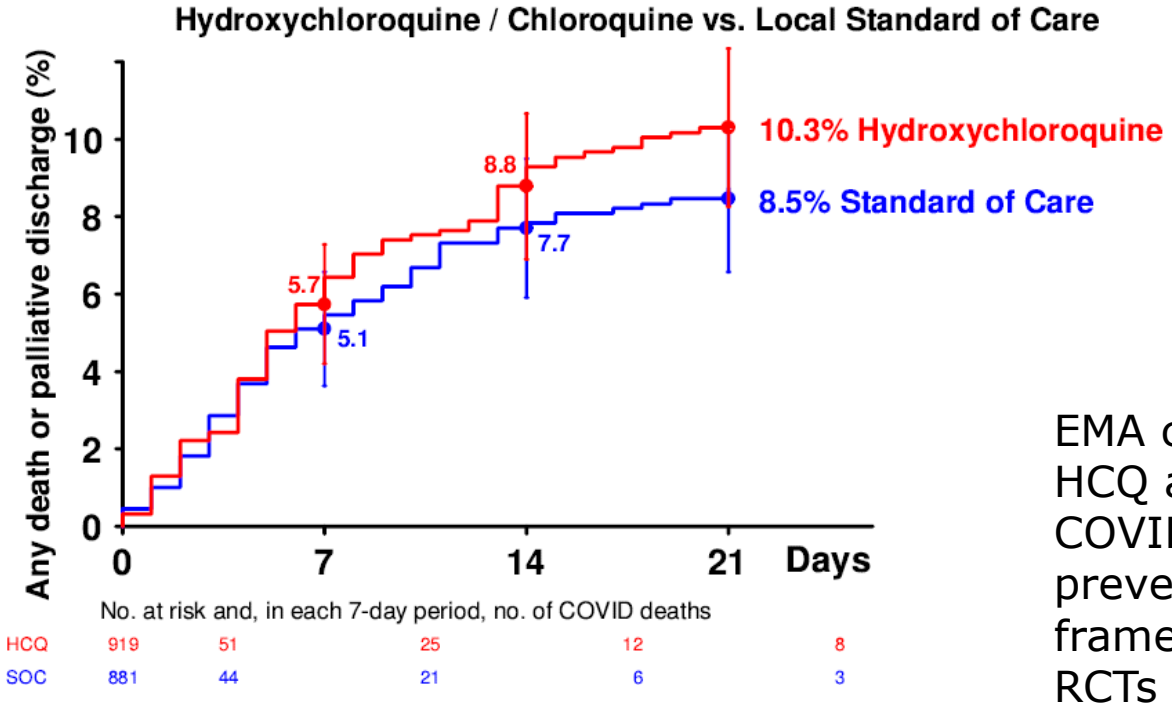
'**unmet medical needs**' means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the Community or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected

Regulation (EC) No 507/2006

Article 58 of Regulation (EC) No. 726/2004

1. *"The Agency may give a scientific opinion, in the context of cooperation with the World Health Organization, for the evaluation of certain medicinal products for human use intended exclusively for markets outside the Community. For this purpose, an application shall be submitted to the Agency in accordance with the provisions of Article 6. The Committee for Medicinal Products for Human Use may, after consulting the World Health Organisation, draw up a scientific opinion in accordance with the provisions of Articles 6 to 9. The provisions of Article 10 shall not apply.*
2. *The said Committee shall establish specific procedural rules for the implementation of paragraph 1, as well as for the provision of scientific advice."*

Successes and failures – Hydroxychloroquine

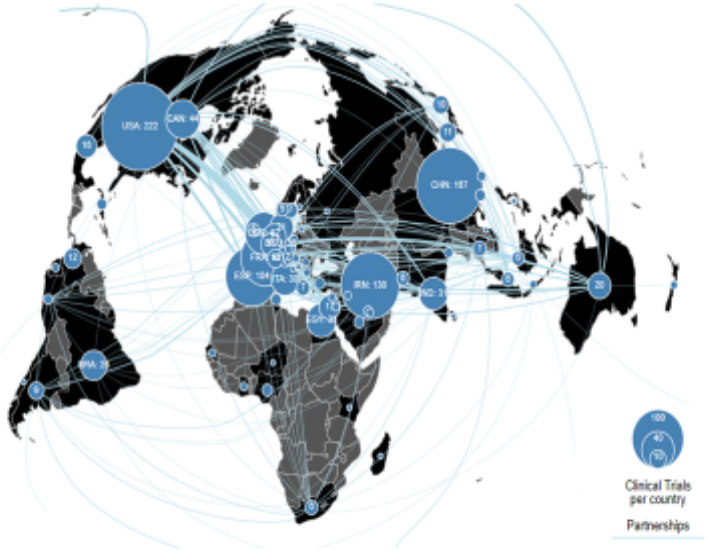


EMA cautioned on the use of HCQ and CQ in the context of COVID-19 treatment and prevention outside the framework of well designed RCTs

What have we learned from the therapeutics RCTs?

A worldwide effort to conduct RCTs. BUT, coordination and size not optimal

▼ Map



Both researchers and regulators must reflect on the need for large collaborative RCTS

Studies registered	1178
Completed	15
Recruiting	644
Not recruiting	515
Suspended	2
Terminated	2

Sample sizes (ranging from 30 – 10000) and endpoints

https://www.covid-nma.com/dataviz/

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ICMRA COVID-related activities

ICMRA, the hub of international collaboration on COVID-19

- COVID-19 Statements
- Technical meetings (18 March, 2, 6 April, 19 May, 22 June)
  - Vaccines (First in Human regulatory requirements, design of Phase III studies)
  - Trials and treatments
  - Observational Studies and RWE
  - Working group(s) being set up for international agreement on vaccines, priority trials, etc.
- bi-weekly Policy meetings

- EMA holds cluster TCs with FDA, HC, MHRA, SwMed and WHO

SUMMARY REPORT

Global regulatory workshop on COVID-19 vaccine development

A virtual meeting, held under the umbrella of the International Coalition of Medicines Regulatory Authorities (ICMRA), convening experts from medicines regulatory authorities, the World Health Organisation (WHO) and the European Commission

18 March 2020

Global regulators discuss data requirements for phase 3 trials of COVID-19 vaccines

Press release 24/06/2020

Under the umbrella of the International Coalition of Medicines Regulatory Authorities (ICMRA), international regulators discussed COVID-19 vaccine development and the necessary evidence required for regulatory decision-making at the second regulatory workshop on COVID-19 vaccines. The meeting was jointly organised by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) on 22 June 2020.

Many researchers around the world are currently working on vaccines against COVID-19 but a rapid authorisation of COVID-19 vaccines will only be possible if robust and sound scientific evidence on vaccine candidates' quality, safety and efficacy is generated. International convergence of data requirements is intended to encourage and accelerate the development of vaccines as a global public health good.

During the workshop, global regulators focused on requirements for non-clinical and clinical data from early phase studies that are needed before proceeding with advanced (phase 3) clinical trials with COVID-19 vaccine candidates in humans. They exchanged views on key aspects, such as eligibility criteria for inclusion of diverse populations, primary endpoints and other methodological considerations related to the design of phase 3 clinical trials.

Concluding remarks

- Regulatory tools for rapid decision making in the context of an emergency are available in the EU and in other regions

- COVID ETF in place to allow proactive and timely regulatory response

- Support to large clinical trials and science based clinical research

- Standards for quality, efficacy and safety are not affected

- International cooperation among regulators and interaction with the scientific community are crucial for a rapid and effective contribution to public health

Thank you for your attention

Further information

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