European marketing authorisation procedure in a pandemic context: challenges and lessons learned

FAMHP Vaccines Symposium

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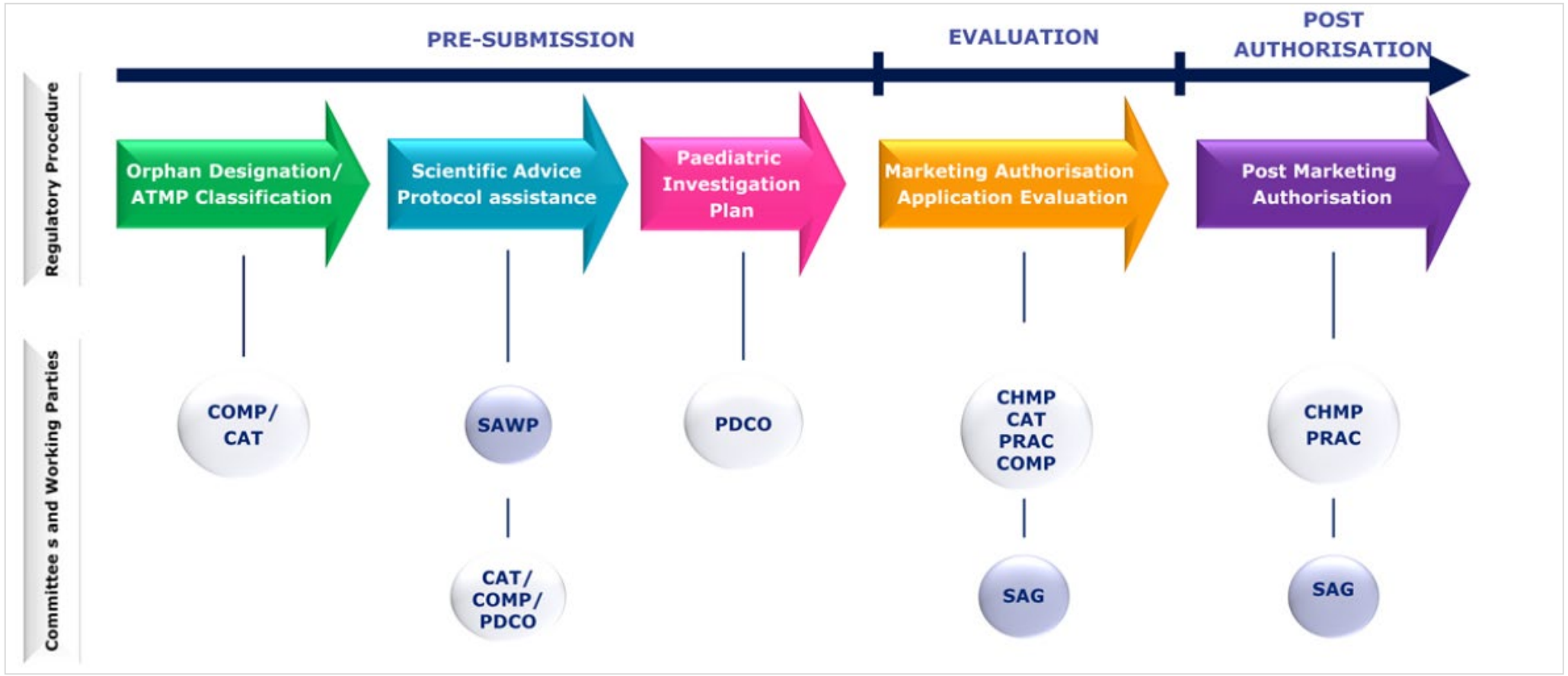
From guided development to accelerated approval procedures (1)

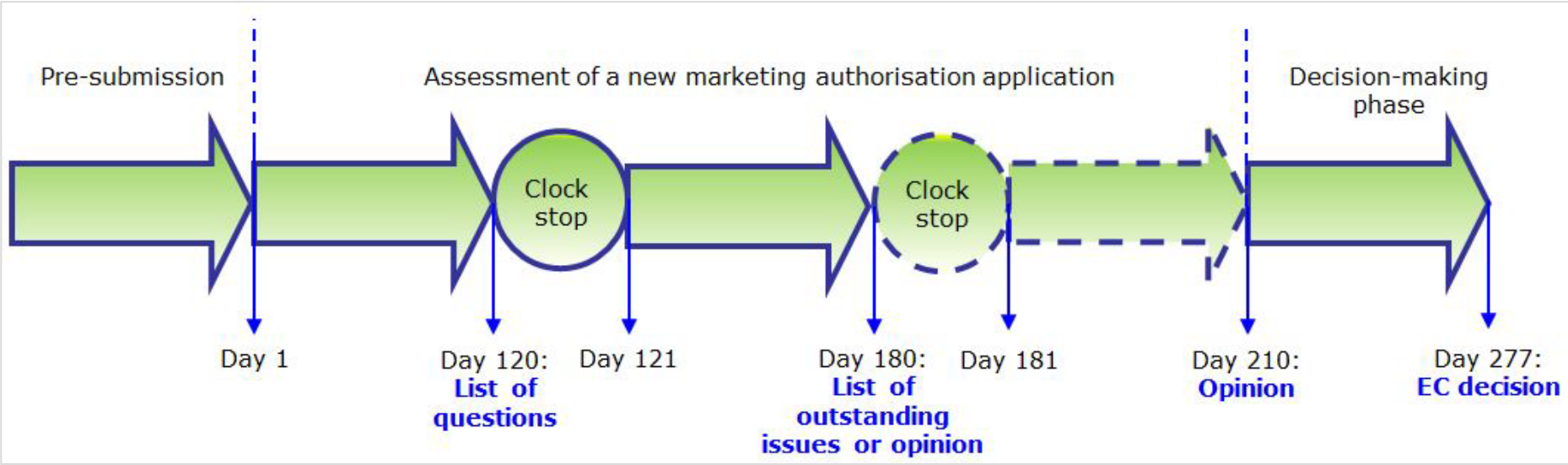
Committees in the regulatory process for human medicines



Source: EMA

From guided development to accelerated approval procedures (2)

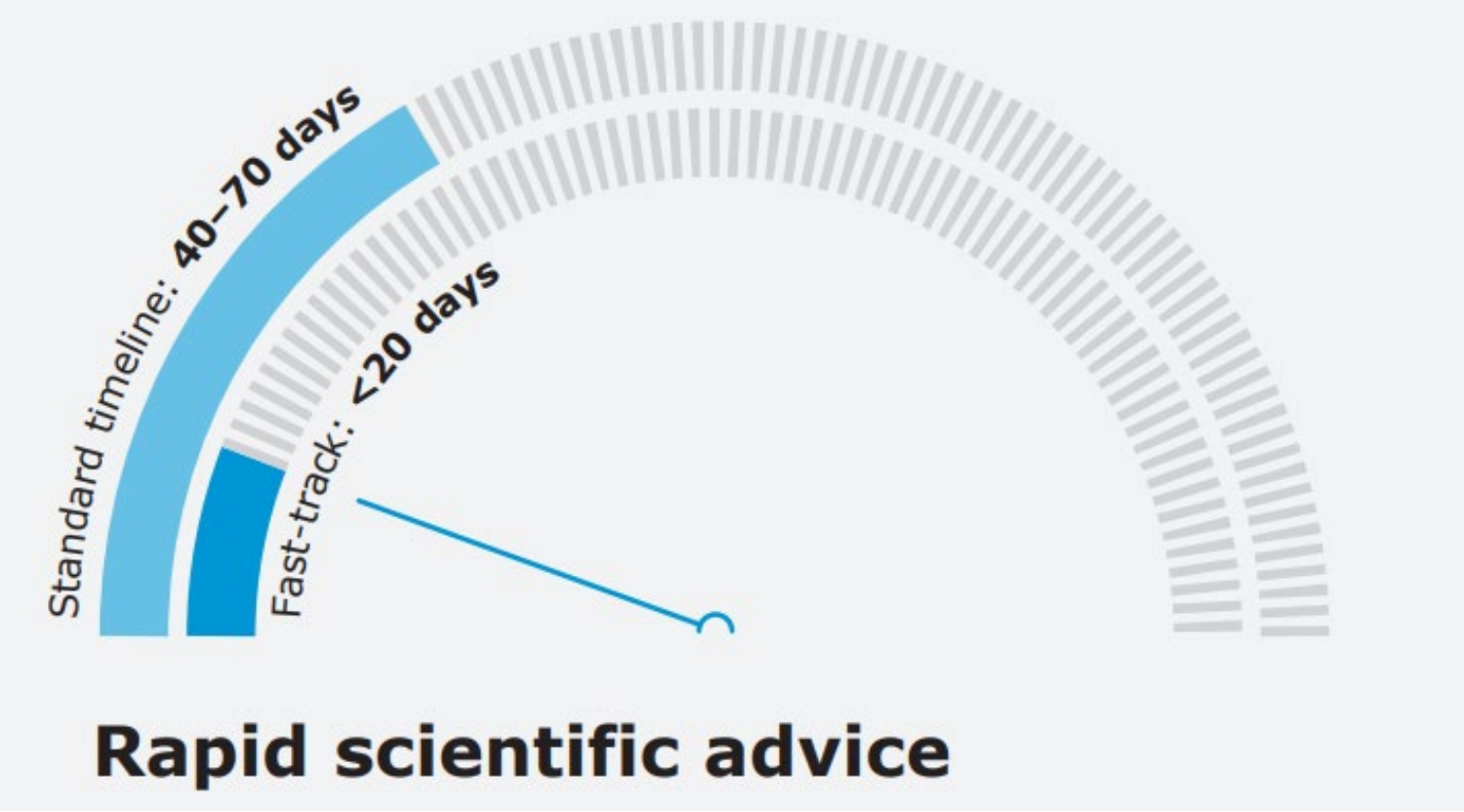
The standard centralised procedure timelines for new marketing authorisation application



Source: EMA

From guided development to accelerated approval procedures (3)

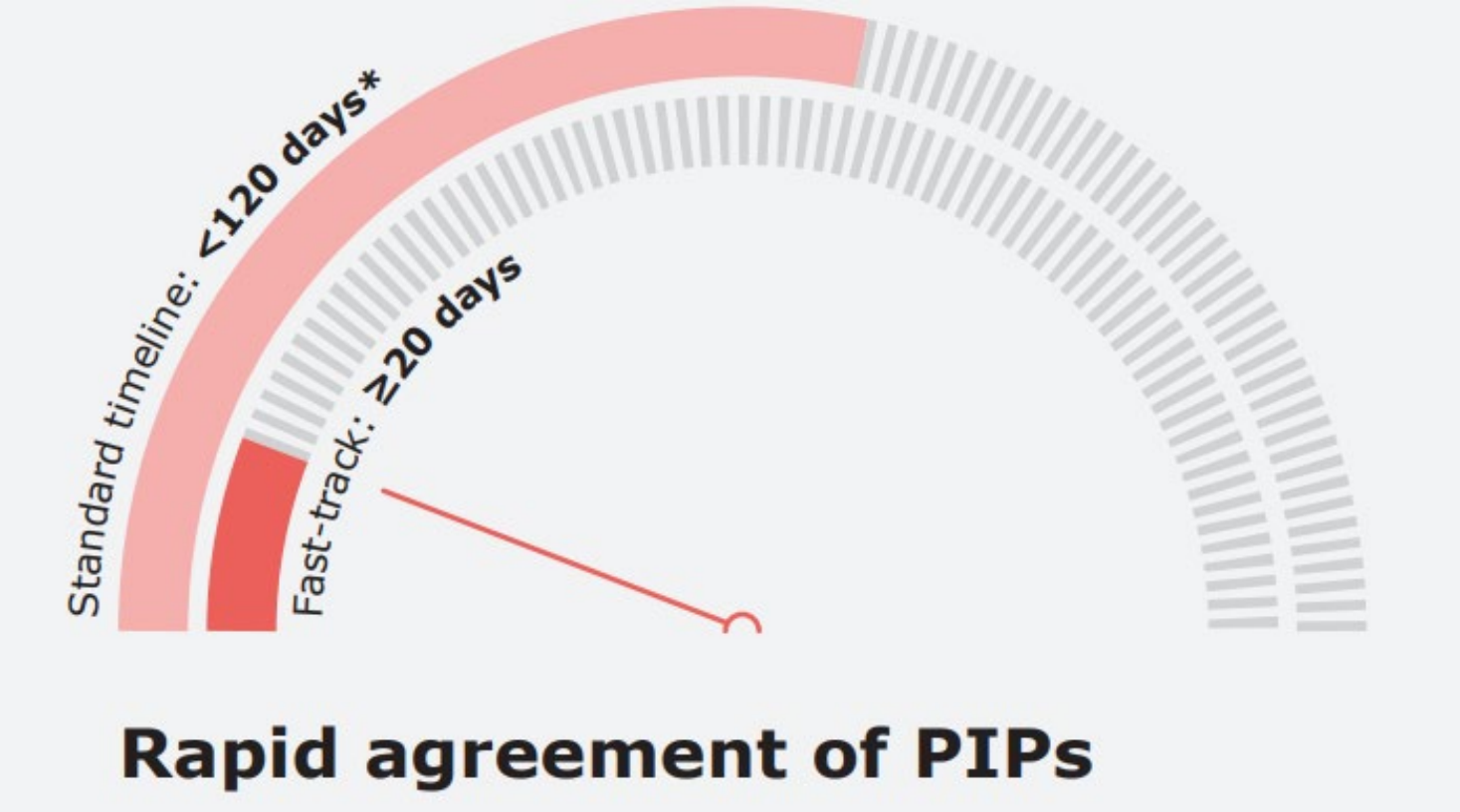
Rapid and agile development support



Source: EMA

From guided development to accelerated approval procedures (4)

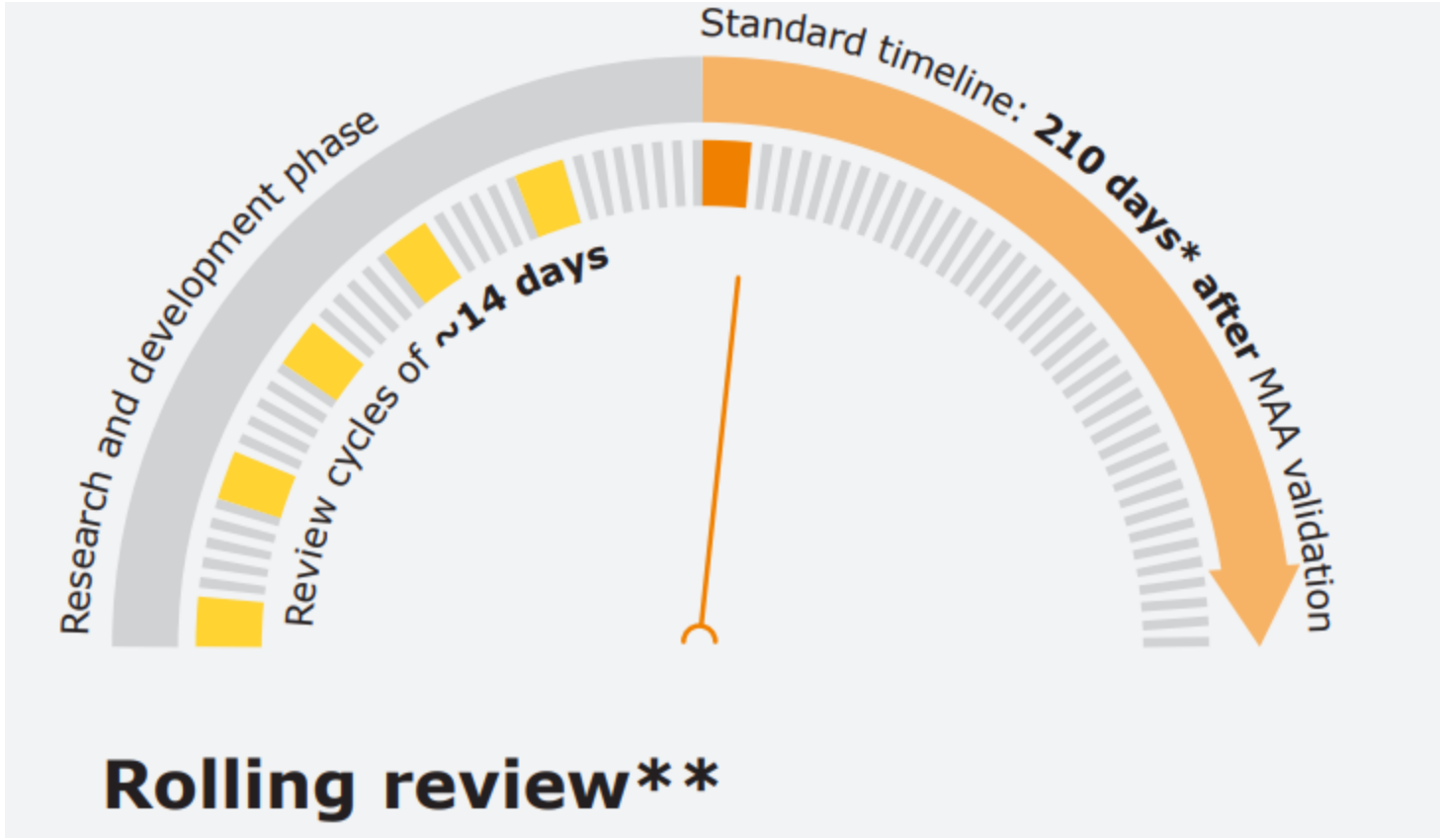
Rapid and agile development support



Source: EMA

From guided development to accelerated approval procedures (5)

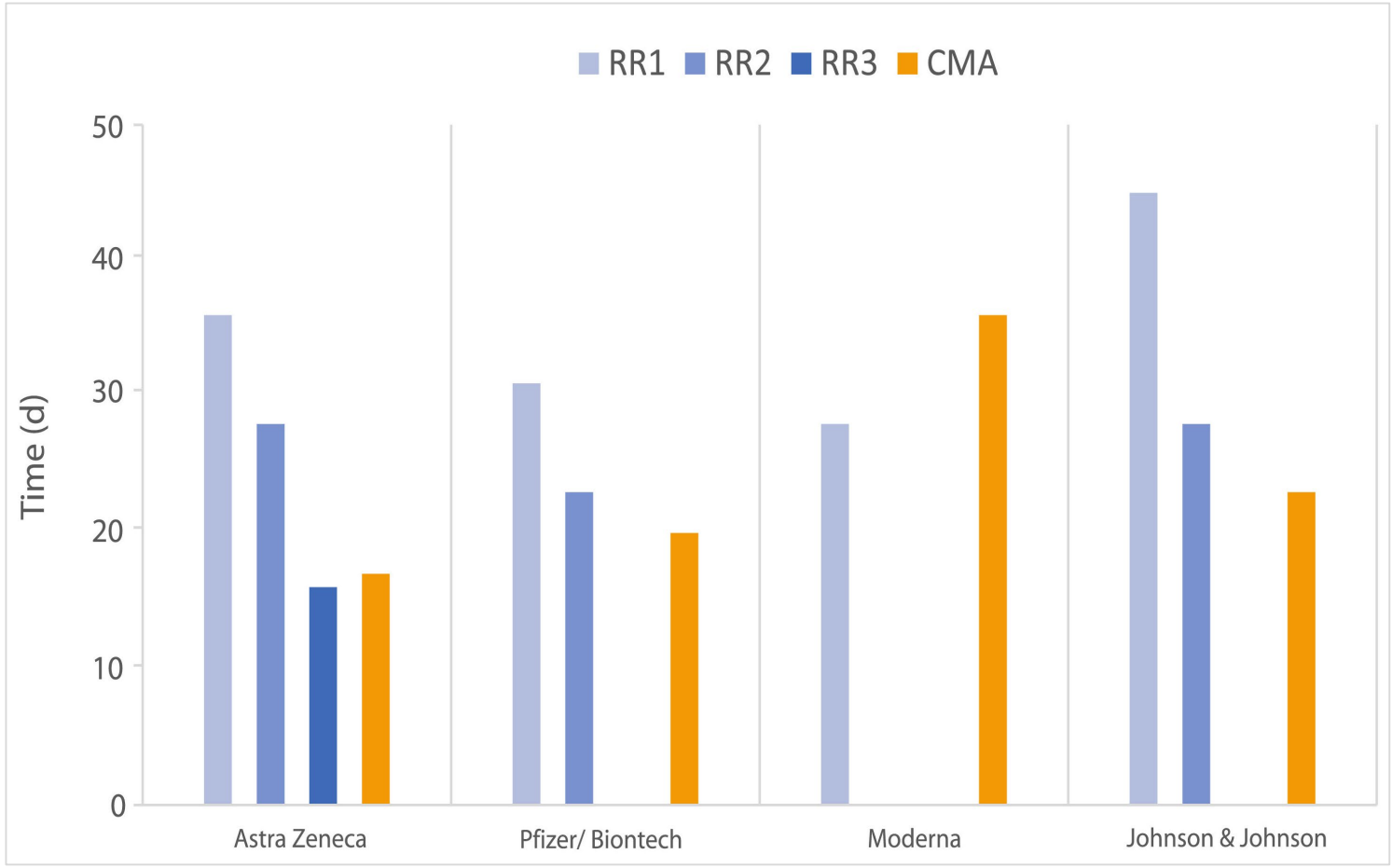
Rolling review and fast-track approval



Source: EMA

From guided development to accelerated approval procedures (6)

Rolling review and fast-track approval



Rolling Reviews During COVID-19: The European Union Experience in a Global Context
Roelie Marinus, BA HM, RN, Sarah Mofid, PharmD, Marya Mpandzou, PharmD, Thomas C. Kühler, PhD
Clinical Therapeutics, volume 44, issue 3, pages 352-363 (March 2022)

From guided development to accelerated approval procedures (7)

Type of Approvals

Standard:
Comprehensive data

Conditional Approval:
- Comprehensive data not available; to be provided after approval
- Must fulfil scope (orphan drugs, emergency threats, serious and life-threatening diseases)
  Approval valid for 1 year, renewable

Exceptional Circumstances:
- Comprehensive data not available and cannot be provided
- Must meet criteria (rarity, medical ethics, state of scientific knowledge)

Source: EMA

From guided development to accelerated approval procedures (8)

Why is CMA the most appropriate tool in the European Union?

Formal approval across the EU: **all member states benefit** from the joint scientific assessment and approval

It has **all the safeguards and controls** in place to ensure high level of protection to citizens during a mass vaccination campaign:

- robust **risk-management and safety monitoring plan**;
- clear **legal framework** for evaluation of **emerging efficacy** and safety data;
- **manufacturing** controls including **batch controls** for vaccines;
- **full prescribing information** and package leaflet with detailed instructions for safe use and storage;
- an investigation plan for use in children (**PIP**);
- **legally binding** post-approval **obligations.**

From guided development to accelerated approval procedures (9)

Safety monitoring

Pharmacovigilance plan for COVID-19 vaccines

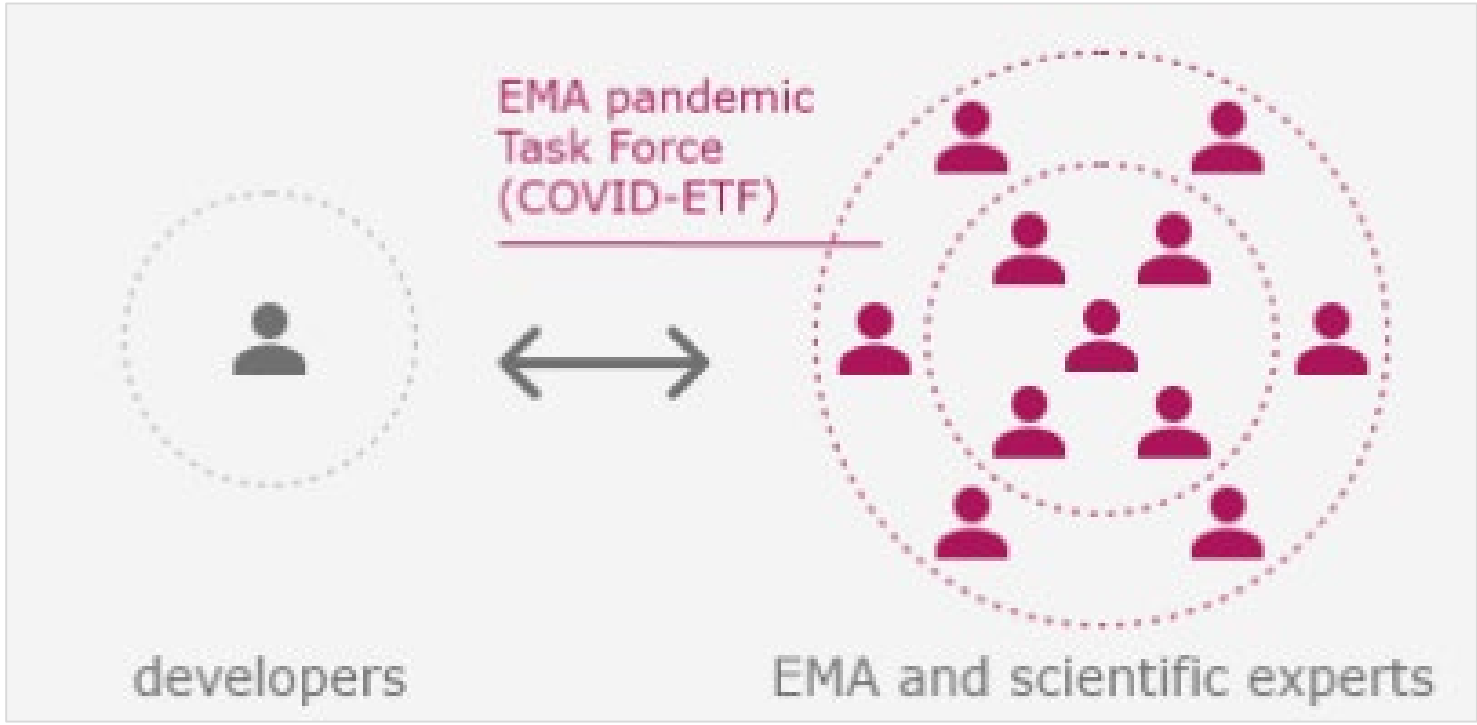
- Core RMP requirements for COVID-19 vaccines
- Monthly summary safety reports (in addition to regular PSURs)
- Collection of exposure data (with the importance of traceability)
- Observational research (Access project, Consign project ….)

Real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 treatments and vaccines and other medicines used for COVID-19. EMA contracted different consortia specialising in observational research to conduct several research projects, including on:

- early safety monitoring of COVID-19 vaccines;
- impact of COVID-19 infection and medicines in pregnancy;
- multicentre cohort studies on the use of medicines in COVID-19 patients;
- natural history of coagulopathy and use of antithrombotic agents in COVID-19 patients.

From guided development to accelerated approval procedures (10)

Mobilising expertise from across the European network



Source EMA

In April 2020, as part of its health threats plan to fight COVID-19, EMA established the **COVID-19 EMA pandemic Task Force (COVID-ETF).** The group brought together the best expertise from the European medicines regulatory network and ensured a fast and coordinated response to the pandemic.

From guided development to accelerated approval procedures (11)

International collaboration

EMA works closely with other European partners, including the European Commission, the Health Security Committee and the European Centre for Disease Prevention and Control (ECDC), and with international partners such as the WHO and regulators from affected countries (ICMRA).

OPEN

EMA is running a pilot project called **OPEN**. It allows medicines regulators from outside the European Union and the World Health Organization to take part in EMA's scientific evaluations of **COVID-19 vaccines and treatments**.

From guided development to accelerated approval procedures (12)

Transparency

	Standard practice	COVID-19 medicines
Scientific advice	No information published	List of medicines that have received scientific advice or guidance from COVID-ETF published
Compassionate use opinion	Published in Compassionate use after CHMP opinion	News announcement published within 1 day of CHMP opinion
Start of rolling review	Not applicable	News announcement published within 1 day of start of review
Marketing authorisation application	Active substance and therapeutic area listed in Medicines under evaluation	Update: Vaccine / treatment page updated; news announcements published on case-by-case basis
Product information	Published and updated in all EU languages with EPAR	Published (in English) within 1 day of positive CHMP opinion; published in other EU languages with EPAR. Updates to be expedited for major post-authorisation changes

From guided development to accelerated approval procedures (13)

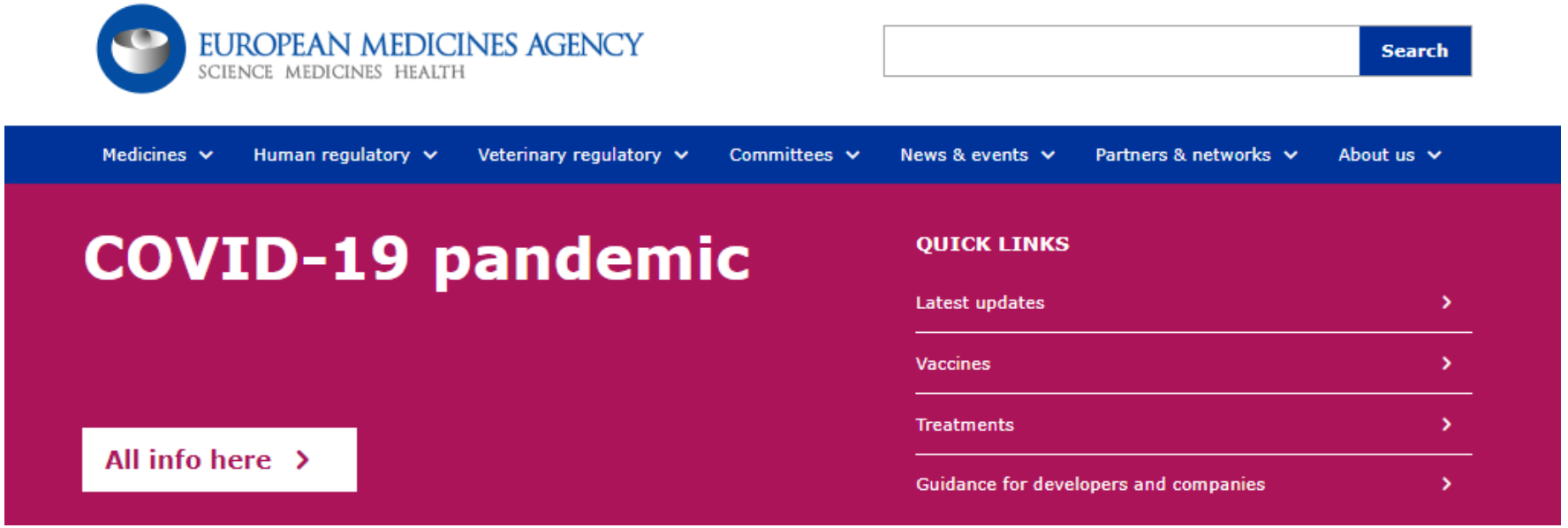
Transparency

Publication of European public assessment report (EPAR)	Published at least 2 weeks after marketing authorisation and updated following changes to the authorisation.	Published as soon as possible and ideally within 7 days of marketing authorisation.* Updates to be expedited for major post-authorisation changes *EPARs can only be published once all necessary steps are completed, which is not always possible within 7 days
Risk management plan (RMP)	Summary of RMP published	Full body of the RMP (plus Annex 4) published. Updated RMPs also published after major post-authorisation changes
Clinical trial data	Publication suspended until further notice	Trial data published on Clinical data website after marketing authorisation; additional trial data also published after major changes to authorisation
Application for extension of indication	Not announced	Update: Vaccine / treatment page updated; news announcements published on case-by-case basis
Monthly safety updates for vaccines	No information published	Published monthly for approved COVID-19 vaccines and ad-hoc as needed.
Assessment of safety signals	Information published with PRAC meeting highlights as necessary	Information on start and finalisation of procedure published with PRAC meeting highlights routinely

From guided development to accelerated approval procedures (14)

Crisis communication and stakeholder engagement

One of EMA's top priorities throughout the pandemic has been providing the general public with factual, complete and up-to-date information about its activities to fight the pandemic in a timely manner.



Additional measures (1)

Regulatory flexibility

- Flexibility in the submission of renewal applications and the application of the sunset clause
- Extended validity of **GMP and GDP certificates**, and time-limited **manufacturing, import and wholesale authorisations** for sites in and outside the European Economic Area (EEA) until the end of 2022
- For new sites/facilities in the EEA that have never been inspected and authorised, a **distant assessment/remote inspection** may be conducted in order to evaluate if the site could be authorised without a pre-approval inspection.
- Flexibility in the **labelling and packaging requirements** to facilitate the movement of medicinal products within the European Union
- **Serialisation exemptions** (limited in time, submission of progress reports …)
- ….

Additional measures (2)

Regulatory flexibility

- Optimising capacity by facilitating more extensive use of **MNAT**
- No formal appointment of a **Peer Reviewer,** for COVID-19 products taken over by **ETF**
- Introduction **Co-Rapporteur Critique** concept
- Working on better **predictability of submission** dates and reduce last minute postponements of submissions to allow better advance **planning** for rapporteurs/assessors.

EMA extended mandate – Regulation (EU) 2022/123 (1)

The new **EU regulation reinforcing EMA's role** in crisis preparedness and management became applicable on 1 March 2022.

- The **new Emergency Task Force (ETF**), which will take over the activities of the current COVID-19 EMA pandemic Task Force (COVID-ETF). The ETF will provide scientific advice on medicines with the potential to address public health emergencies and will also support EMA's committees in the evaluation and safety monitoring of such medicines.

- The **Medicines Shortages Steering Group (MSSG),** which will be tasked with monitoring and mitigating shortages of medicinal products in certain crisis situations.

EMA extended mandate – Regulation (EU) 2022/123 (2)

The new Emergency Task Force (ETF)

- ETF established with formal legal mandate as an **advisory and support body on medicines for public health emergencies and preparedness**
- Regulation sets out objectives and composition, but allowing flexibility & membership based on expertise
- **Strengthened** existing ETF responsibilities building on successful experience during past emergencies & COVID-19

Scientific advice and support to clinical trials

- assessed **directly** by ETF
- free of charge & fast-track for clinical trials and protocols
- **support study conduct**

Scientific reviews

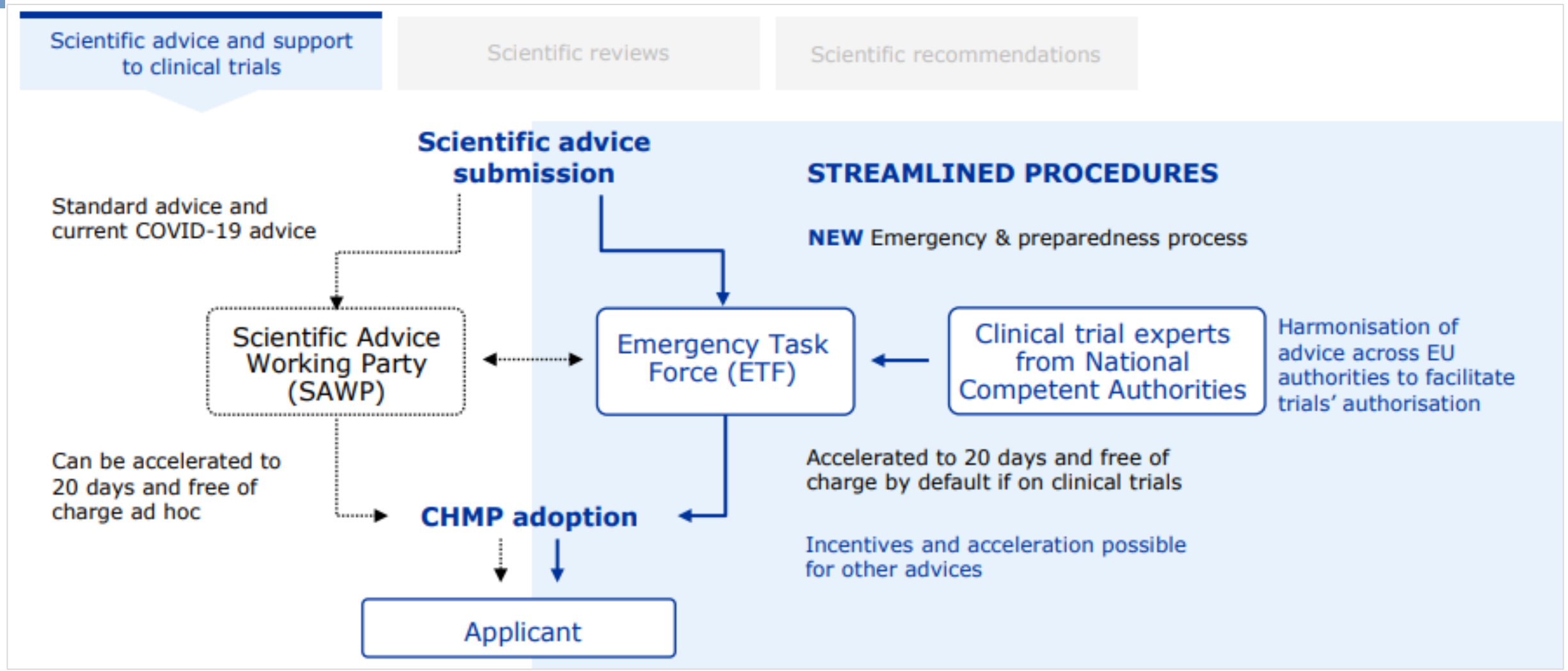
- **systematic** assessment of evidence on medicines

ETF recommendations

- **on medicines not yet authorised**
- on scientific or **public health matters**

Source EMA

EMA extended mandate – Regulation (EU) 2022/123 (3)



Source EMA

EMA extended mandate – Regulation (EU) 2022/123 (4)

Scientific advice and support to clinical trials | **Scientific reviews** | Scientific recommendations

KEY BENEFITS

• Systematic review and recommendations **on medicines targeting the emergency**, published by EMA:	• **Reduce use of medicines with insufficient evidence** (e.g. hydroxychloroquine, ivermectin, inhaled corticosteroids in COVID-19) • **Increase safe and harmonised use across EU** ahead of authorisation (e.g. COVID-19 vaccines mix&match & safety during pregnancy)
• Screening evidence on medicines in the pipeline to prepare for potential marketing authorisation application:	• **Improve access to medicines** (amount of evidence needed to start rolling review)

Source EMA

EMA extended mandate – Regulation (EU) 2022/123 (5)

Scientific advice and support to clinical trials | Scientific reviews | **Scientific recommendations**

Systematic recommendations to relevant Committees on medicines for emergency:

- pre-authorisation: paediatric plans, rolling review applications, Risk Management Plans
- post-authorisation: applications for major changes in use of medicines, e.g. vaccine boosters, critical pharmacovigilance issues
- use of investigational products or compassionate use programs - can be evaluated by ETF directly **(article 18(3) ETF recommendations)**
- recommendations or position statements on scientific or **public health matters** related to the emergency
  - including joint recommendations with other bodies such as ECDC

Source EMA

Revision of the Pharmaceutical legislation (2)

Contact

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