The National Academies of SCIENCES ENGINEERING MEDICINE

EUROPEAN MEDICINES AGENCY

An Overview of Emergency Use Authorizations and Similar Authorities

The Food and Drug Administration's Emergency Use Authorization
Lessons Learned from the Past to Guide the Future: A Workshop

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"There are more ways than one to skin a cat…"

- In the context of a public health emergency, what are our responsibilities to the public we serve?
- Timely availability and access to quality, safe and effective vaccines, drugs and diagnostics
- COVID-19 has shown us that regulators, regardless of their resource setting, face common problems, but we may have different solutions to those questions and lessons to learn

The European emergency response toolkit

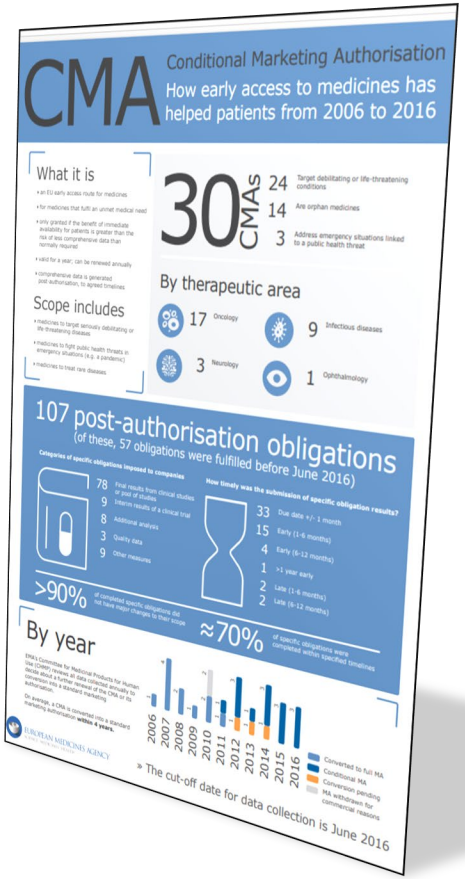
- Conditional Marketing Authorisation, supported by informal 'rolling review'
- **Fast-track review and approval**, based on **less comprehensive** data than normally required. The available data must support a positive benefit/risk profile with **obligation** that applicant provides the comprehensive data in the future.

  (a) Benefit-Risk balance of the medicine is positive;
  (b) Likely that the applicant will be able to provide comprehensive data post-authorization;
  (c) Medicine fulfils an unmet medical need;
  (d) Benefit of the medicine's immediate availability to patients is greater than the risk inherent in the fact that additional data are still required.

- In case of a public health emergency, quality and non-clinical data may also be less comprehensive

EU conditional marketing authorization

- Introduced in 2006
- Used >60 times since then, including 13 times in 2020
- All 4 EU-approved vaccines under conditional MA
- Expectation that they will pass to regular approval *(cf. exceptional circumstances, where they don't)*
- Active follow-up of post-authorization obligations
- Used for two pandemic vaccines in 2009/2010, for pandemic preparedness influenza vaccine in 2016 and Ebola vaccine (Ervebo) in 2019



Hope for the best, but prepare for the worst

- EMA health-threats plan set up after 2009 H1N1 pandemic
- Put in place process for rolling reviews (administrative arrangement)
- Dedicated platform to manage rolling reviews, interactions with applicants and our network of experts (Emergency Task Force)
- Ready-to-go: Legal framework, procedures, resourcing plans worked out in advance

EMA OPEN Pilot: collaborative assessment and reliance

- OPEN lets WHO and medicines regulators from outside the EU take part in EMA scientific evaluations – currently just for COVID-19
- Drivers: sharing scientific expertise, tackling common challenges, enhancing transparency on regulatory decisions
- Pilot launched December 2020 with TGA Australia, Health Canada, MHLW/PMDA Japan, Swissmedic and WHO
- Participate in scientific assessments and COVID-19 pandemic task force
- Experts keep full scientific and regulatory independence; participate under existing confidentiality arrangements; have no role in EMA B/R decision

OPEN convergence for approval timelines

	EMA	Australia	Canada	Japan	Switzerland	WHO
Comirnaty	21-Dec-20	25-Jan-21	09-Dec-20	14-Feb-21	19-Dec-20	31-Dec-20
Spikevax	06-Jan-21	09-Aug-21	23-Dec-20	21-May-21	12-Jan-21	30-Apr-21
Vaxzevria	29-Jan-21	15-Feb-21	26-Feb-21	21-May-21		15-Feb-21
Janssen	11-Mar-21	25-Jun-21	05-May-21		22-Mar-21	12-Mar-21

- Approval timelines converge as experience with pilot grows
- Onwards reliance on WHO EUL where EMA is reference NRA (e.g. >40% of all regulatory actions by African regulators)

International collaboration – ICMRA
International Coalition of Medicines Regulatory Authorities

- Informal group of leaders of medicines regulatory authorities that provides strategic directions for enhanced collaboration, improved communication and approaches to jointly address common challenges
- 34 participating authorities, plus WHO as Observer
- Major focus on aligning and convergence in the COVID-19 pandemic response
- WHO led exercises on regulatory agilities, including 'Deep Dive' on use of EUAs
- Analysis and best practice recommendations from 13 regulators, due to be published later this month on ICMRA website www.icmra.info

Some common themes, some differences

Deep dive exercise generated a comprehensive collection of information

Findings expand upon broader ICMRA-WHO regulatory agilities review report

Response to pandemic: Accelerated enhanced transparency measures

Diversity of instruments/measures

Commonalities exist which could inform model/practices to deal with future pandemics

Accelerated development of technical and administrative guidance documents

All respondents exercised regulatory agilities in responding to the pandemic

Each NRA will have lessons learned to further improve their response during a future pandemic

Have the tools in place from the beginning

- Almost all regulators used or introduced flexibilities or agilities as part of response. Preference for clear legal basis and authority, over administrative arrangements
- Enhanced transparency and communication with developers and public
- Approvals mostly time-limited, e.g. one year, duration of emergency, public health need for the product
- Linked to (enforceable) obligation to generate sufficient data for 'regular' marketing authorisation
- Authority to rely on assessment of others, including inspections (including hybrid arrangements)

Weighing Benefit/Risk vs 'Enough data' in a public health emergency

- Regulatory standards must be maintained, important to reassure public confidence in process and the vaccine or drug
- Risk-based approach to what is reasonable (or enough) S/E/Q data for emergency or conditional approval, with ongoing generation of data towards regular approval
- Rolling submissions and reviews (formal or informal) are resource intensive but many regulators used them to expedite review and approval
- International convergence (through ICMRA) on minimum data package – avoid multiple development plans at time of public health emergency

Ongoing data generation and safety monitoring

- Enforceable obligations to complete ongoing and planned studies designed to confirm Benefit/Risk profile is key to emergency or conditional approval
- Risk management plans, that sets out safety studies and reporting obligations
- Many regulators introduced flexibilities for post-approval CMC changes, but industry must play its part to ensure site readiness and in-depth product knowledge
- Again, transparency of post-authorisation obligations and results is important (especially for other regulators who relied on your initial assessment)

Some thoughts for the workshop

- **Access** and **availability** is key. Does the licensing framework match national/regional procurement or vaccination recommendation rules?
- **Enforceability** of post-approval commitments: counterpart of early access accelerated review and approval – can they be enforced?
- **Time-limited** emergency approvals give leverage and flexibility to regulators
- **Transparency** is common theme: Benefit/Risk basis of approvals, ongoing studies, post-approval obligations; more transparency needed during emergencies; creates common science base for public health decisions; allows for **reliance**
- Can public health emergencies be used as a **vehicle for unprecedented information** sharing on reviews, inspections, vigilance?
- What is **industry's role** in this?

Value of reliance as a regulatory tool in the COVID-19 pandemic

- Having regulatory provisions that **enable** reliance, gives us additional tools to address the challenges posed by the pandemic
- Near **real-time information sharing and collaboration** was key to informing NRA and WHO regulatory decisions, requirements, communications and plans for COVID-19 products (especially through ICMRA)
- **OPEN Pilot** is seen by partners as important collaboration opportunity for assessment and approval of COVID-19 products
- **Enhanced transparency** helps public confidence, and regulatory alignment
- WHO-led global assessment and NRA approvals **accelerated access** in LMICs

Reflections and lessons we have learnt

- From a regulatory perspective – the international community has been successful
- Vaccines have been authorised on a global scale in record timelines that exceeded initial estimates
- EUA and conditional marketing authorisations **have worked** for COVID-19 vaccines less so for therapeutics (‘no magic bullet’, yet)
- For therapeutics, marginal and inconsistent results, small numbers in trials, methodological limitations have caused challenges
- Exemptions and waivers for labelling, languages and shelf-life have facilitated vaccine rollout
- Fit-for-purpose ‘**ready to go’ regulatory frameworks** benefits developers and regulators – and public health

Reflections and lessons we have learnt

- International cooperation needed for **well-designed** and **powered** trials
- Wide-scale use during health emergencies will always generate safety signals not seen in trials; need **international pharmacovigilance** collaboration
- Public confidence easily dented by **inconsistent or mis-communication**
- Don’t underestimate **resource investment**, ultimately it saves global resources
- Challenges of global **supply and procurement** remain

Thank you

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