EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Preparedness for paediatric COVID vaccine trials

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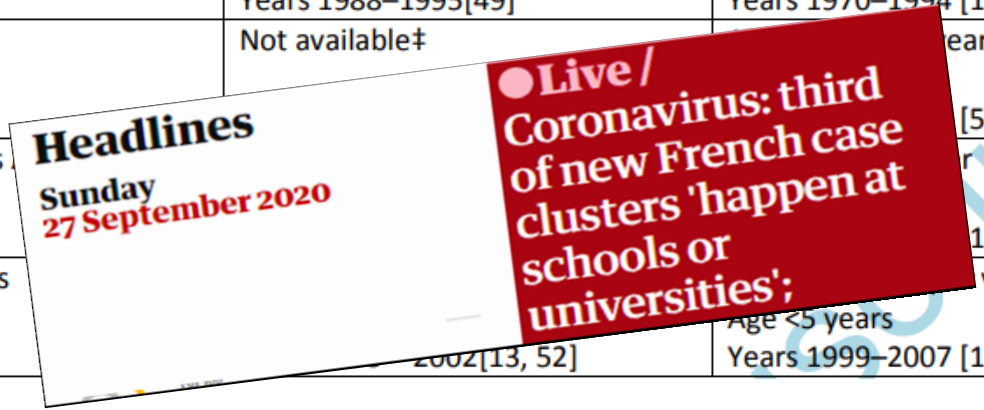
Enpr-EMA
Monday 28 September 2020

- elimination of the virus from circulation
- reduction of viral circulation in the whole population;
- protection of specific groups (at risk; health workers; etc..)
- geographical containment
- outbreak response to sporadic clusters
- a mix of the above

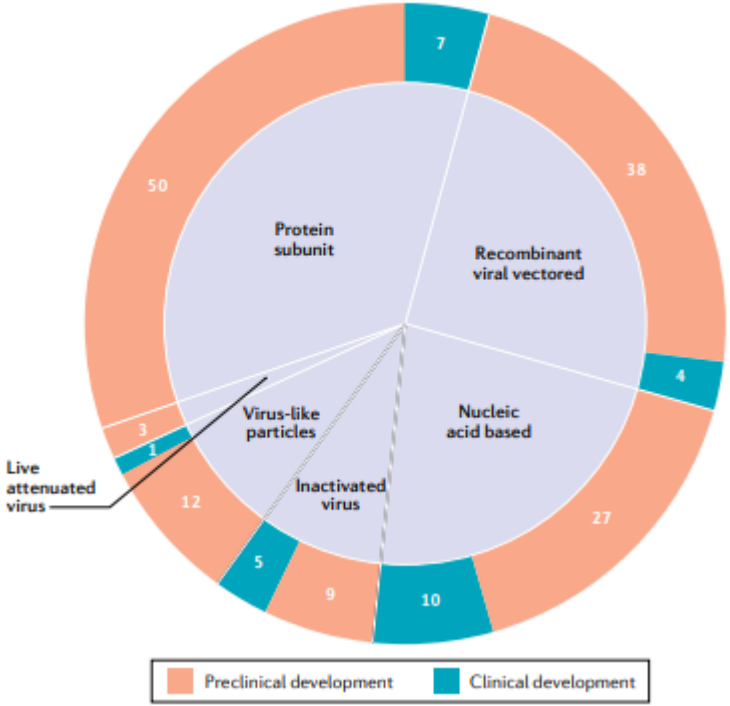
Do we need COVID vaccines in children?

Virus	Hospitalizations/year	Deaths
COVID-19	15.4 per 100,000 ages 0-4 years 8.7 per 100,000 ages 5-17 years Through 8/22/2020[7]	103 children Age ≤18 years Through 08/26/2020 [11]
Varicella	4–31 per 100,000 Age <20 years Years 1988–1995[49]	50 children per year Age <15 years Years 1970–1994 [14]
Rubella	Not available‡	ear [50]
Hepatitis		r 15]
Rotavirus	2002[13, 52]	year Age <5 years Years 1999–2007 [13, 53]



Development of SARS-Cov2 vaccines

- Many different vaccines, many uncertainties, **new technologies**
- **Accelerated** development and approval
- **Rapid vaccination** to occur in millions or billions
- **Safety critical**: Unexpected or rare serious ADRs could negatively affect vaccination campaigns and increase vaccine hesitancy
- Need of systems in place to rapidly **detect** and **minimise** serious risks to patients
- **Transparency** and **communication** is key



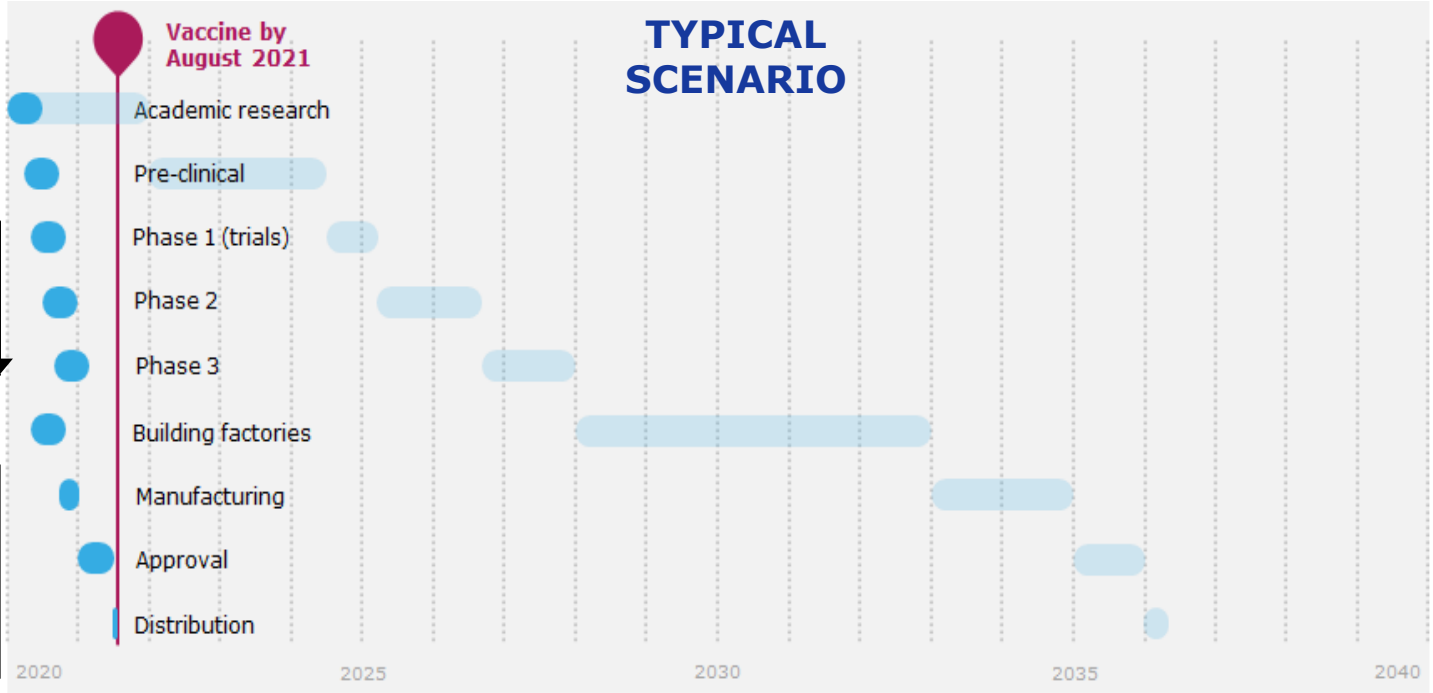
https://www.nature.com/articles/s41577-020-00434-6

From Research to Distribution

PANDEMIC SCENARIO

Collection of adequate data for safety and efficacy

European population ~ 500 M= To vaccinate ½ pop in a year requires ~1.000.000 vaccinations/day



Modified from https://www.nytimes.com/interactive/2020/04/30/opinion/coronavirus-covid-vaccine.html

Vaccines currently in phase 3

COVID-19 Vaccine developer/manufacturer	Vaccine platform	Type of candidate vaccine	Number of doses	Timing of doses	Route of Administration	Phase
						Phase 3
University of Oxford/AstraZeneca	Non-Replicating Viral Vector	ChAdOx1-S	1		IM	ISRCTN89951424 NCT04516746 NCT04540393
CanSino Biological Inc./Beijing Institute of Biotechnology	Non-Replicating Viral Vector	Adenovirus Type 5 Vector	1		IM	NCT04526990 NCT04540419
Gamaleya Research Institute	Non-Replicating Viral Vector	Adeno-based (rAd26-S+rAd5-S)	2	0,21 days	IM	NCT04530396 NCT04564716
Janssen Pharmaceutical Companies	Non-Replicating Viral Vector	Ad26COVS1	2	0, 56 days	IM	NCT04505722
Sinovac	Inactivated	Inactivated	2	0, 14 days	IM	NCT04456595 669/UN6.KEP/EC/2020
Wuhan Institute of Biological Products/Sinopharm	Inactivated	Inactivated	2	0,21 days	IM	ChiCTR2000034780
Beijing Institute of Biological Products/Sinopharm	Inactivated	Inactivated	2	0,21 days	IM	ChiCTR200003478 NCT04560881
Moderna/NIAID	RNA	LNP-encapsulated mRNA	2	0, 28 days	IM	NCT04470427
BioNTech/Fosun Pharma/Pfizer	RNA	3 LNP-mRNAs	2	0, 28 days	IM	NCT04368728

World Health Organization

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

Development Requirements from International Regulators

- **Non-clinical data** needed to support first-in-human (FIH) clinical trials

- **to characterize immune response** from animal models, including potential enhanced disease (ED) (e.g. neutralizing antibody vs total antibody responses; Th1/Th2 balance)

- Postvaccination challenge **data from NHPs** (ED) valuable, but should not delay ph3 trials: case by case decision depending on construct and NC/C data available. Other potential models: hamsters, ferrets, transgenic mice…

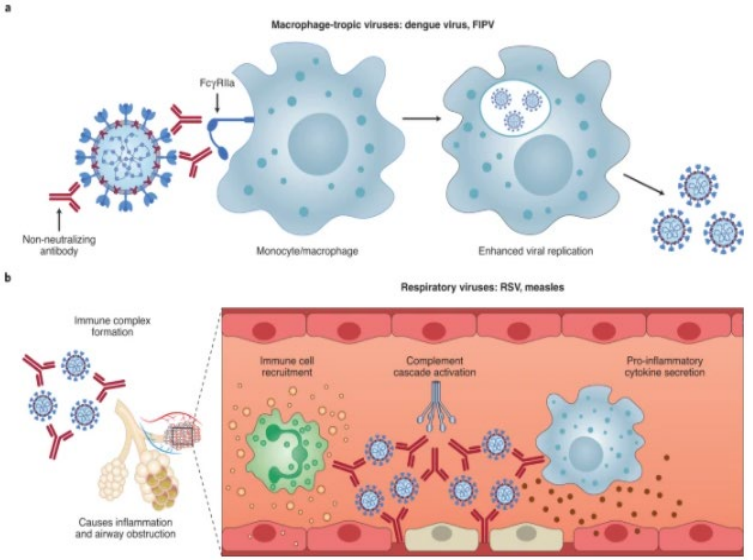

ICMRA

SUMMARY REPORT

22 June 2020

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

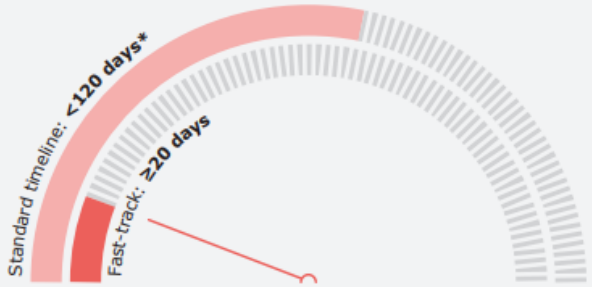


https://www.nature.com/articles/s41564-020-00789-5

Considerations for phase 3 clinical trials

- **Before Phase IIb/III studies, safety data from early phase trials need to be favourable. Preliminary relevant immunogenicity data to support selected dose and schedule**
- safety and immunogenicity for each dose level/age group to be included in late stage trials, to support general safety and immunogenicity of the vaccine candidate (e.g. subjects older than 55 years if included in phase 3 trials)
- **Phase 3 Primary endpoint**: lab-confirmed COVID-19 of any severity
- **Secondary endpoints** can include prevention of infection and disease severity
- Stringent criteria for efficacy to be specified; Interim analysis to assess for ED or futility
- Safety evaluation, size safety database and F-UP in same range as other preventive vaccines. Pre-specified criteria for study halt/pause in study protocol
- **Important to plan for paediatric assessment of safety and effectiveness** (safety may be different as compared to adults). Initial licensure likely to be in adults

Supporting paediatric development: RAPID PIPs



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.

FDA U.S. FOOD & DRUG ADMINISTRATION

EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH

2 June 2020

FDA / EMA Common Commentary on Submitting an initial Pediatric Study Plan (iPSP) and Paediatric Investigation Plan (PIP) for the Prevention and Treatment of COVID-19

Given the global public health crisis resulting from the coronavirus disease 2019 (COVID-19) pandemic, FDA and EMA are providing procedural assistance to sponsors and applicants who anticipate submission of pediatric product development plans for new drugs and biological products for the treatment or prevention of COVID-19. FDA and EMA are issuing this Common Commentary to streamline administrative processes and facilitate efficient submission of an initial Pediatric Study Plan (iPSP) and Paediatric Investigation Plan (PIP). This Common Commentary addresses only the submission of an iPSP and PIP for a drug or biological product for treatment or prevention of COVID-19.

Considerations and open questions in paediatric COVID vaccines development

- B/R in children the main driver (including direct and indirect effects, e.g. allowing attendance of school; role of children in transmission?)
- Which information on safety and efficacy needed before starting studies in children? (Some adult (efficacy) clinical trials will include adolescents)
- Younger children studied for immunogenicity: usefulness of existing knowledge of paediatric immune response to SARS-Cov2?
- From which age to start vaccination?
- How to plan for many vaccines and for relative effectiveness? (many vaccines tested at the same time; no multi-arm trials for vaccines)

Any questions?

Further information

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