COVID-19 pandemic
Regulatory approval of vaccines at EMA

16th PDI Forum on vaccination
3 December 2020

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EMA activities during emerging health threats and pandemics

- EMA operates under the framework of the Health Threat Plan (Decision 1082/2013/EU on serious cross-border threats to health): internal guidance on activities during a health threat based on the experience from the 2009 flu pandemic and the Ebola outbreak of 2014-16
- Crisis-related regulatory activities (interaction with manufacturers and data evaluation) led by a dedicated group since 2009: **EMA Pandemic Task Force (ETF)**, whose mandate was expanded to cope with COVID-19
- Includes key reprs of the main EMA scientific committees & working parties with relevant experience, e.g. in vaccines, infectious diseases, preclinical and clinical trial design, paediatric aspects, quality of biological medicinal products; civil society reprs; EC reprs

How EMA contributes to faster approval of COVID-19 vaccines

Development support

- Rapid scientific advice (from 70 to 20 days) and informal TCs with developers
- rapid endorsement by PDCO of paediatric investigation plans (from 120 to 20 days)

Evaluation support (new and repurposed products)

- Rolling review (ETF reviews data to start RR)
- accelerated assessment for Marketing authorisation (from 210 to 150 days) & Extension of indication
- Compassionate Use/Emergency Use Authorisation

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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.

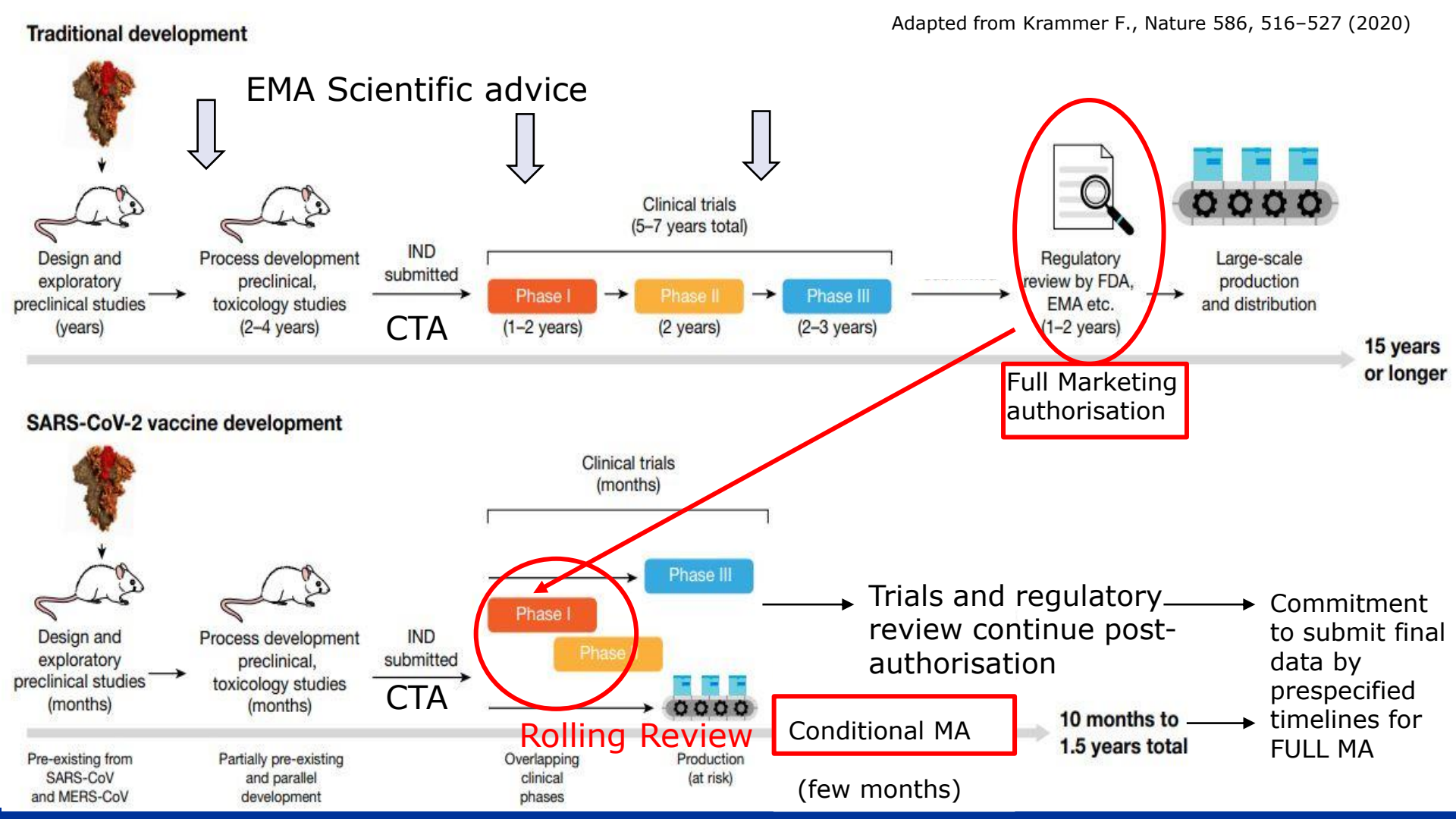
EMA initiatives for acceleration of development support and evaluation procedures for COVID-19 treatments and vaccines

Responsibilities of the COVID-ETF

- Review data of products in pipeline, identify promising candidates to engage in preliminary discussions; review study protocols and comment on quality, pre-clinical and clinical developments
- Provide scientific support in collaboration with CTFG* to facilitate clinical trials conducted in the European Union for the most promising products
- Contribute to product assessments acting as Peer Reviewer and as forum for discussion on the rolling data assessment
- Contribute to PRAC activities on emerging pharmacovigilance issues; provide scientific input to committees and other EMA groups as needed
- Prepare scientific position/input to public comms
- Interactions with international regulators and other stakeholders

*CTFG: clinical trials facilitation group

Adapted from Krammer F., Nature 586, 516–527 (2020)



Scientific Advice procedures for COVID-19 vaccines

- 25 SA finalised and 4 currently ongoing; this online table lists all products which have received advice from COVID-ETF either formally via SA or informally via oral interactions
- Standard assessment process (accelerated) plus the additional peer review of the COVID-ETF
- Vaccines/companies who received formal rapid SA:
  - **Virus vector**: Janssen (Ad26-S), AstraZeneca (ChAd S), MSD/IAVI (replication competent rVSVΔG-S), MSD/Themis (live attenuated measle vector encoding S protein), Krystal Bio (replication deficient HSV-1 vector expressing 4 SARS-CoV-2 proteins: S, N, E, M)
  - **Subunit adjuvanted**: Sanofi (rSΔTM-AS03), Novavax (rS Matrix adjuvant), Seqirus (rS-clamp –MF59), Clover Bio (rS trimer-Tag-AS03)
  - **mRNA/DNA**: Curevac (mRNA S-LNP), Moderna (mRNA S-LNP), Sanofi (mRNA S-LNP), Takis (DNA vaccine encoding RDB-S)
  - **Virus-like particle**: Kentucky Bio (inactivated tobacco mosaic viral particle conjugated with RBD-S)

Ongoing Rolling Reviews (RR) for vaccines

- RRs packages contain pre-agreed amount of data, start with manufacturing and pre-clinical, evaluation time depends on content – when overall the data enough to decide if vaccine is safe and efficacious, a MA application is submitted and processed rapidly including Commission Decision

- **AZD1222 vaccine** (AstraZeneca): RR started 30 Sept – top line efficacy and safety data available

- **BNT162-b2 vaccine** (Biontech/Pfizer):
  - RR started 5 October - top line efficacy and safety data available
  - CMA application started 1 December – ETF /CHMP final opinion 29 December at the latest

- **mRNA1273 vaccine** (Moderna):
  - RR started 16 Nov - top line efficacy and safety data available
  - CMA application started– ETF/CHMP final opinion 12 January at the latest

- **Ad26.COV2.S** (Janssen): RR started 1 December

*Conditional Marketing Authorisation

EMA considerations on COVID-19 vaccine approval

- published 16 Nov, Q&A for the general public to follow in the next few days

- At least one well-designed large-scale (>30,000) phase 3 efficacy and safety trial, including at least 25% older adults >65YOA and people with comorbidities, who are most at risk of severe COVID-19 and death, ethnical minorities

- Trials to be designed based on stringent success criteria: demonstrate an efficacy rate >50%
- Efficacy endpoints: prevention of COVID-19 disease of any severity in people who were not previously infected with SARS-CoV-2, prevention of infection, prevention of severe disease, disease amelioration

- Safety data required as a minimum: several thousands (uncommon risks (those that occur in between 1/100 and 1/1000 vaccinated persons) followed up for at least 6 weeks post-last dose when most side effects occur– trials should continue for 2 years or more for longer term safety and efficacy data

- Post-authorisation safety monitoring (rare/very rare side effects) and effectiveness studies are paramount

Evidence in immunocompromised (IC) individuals

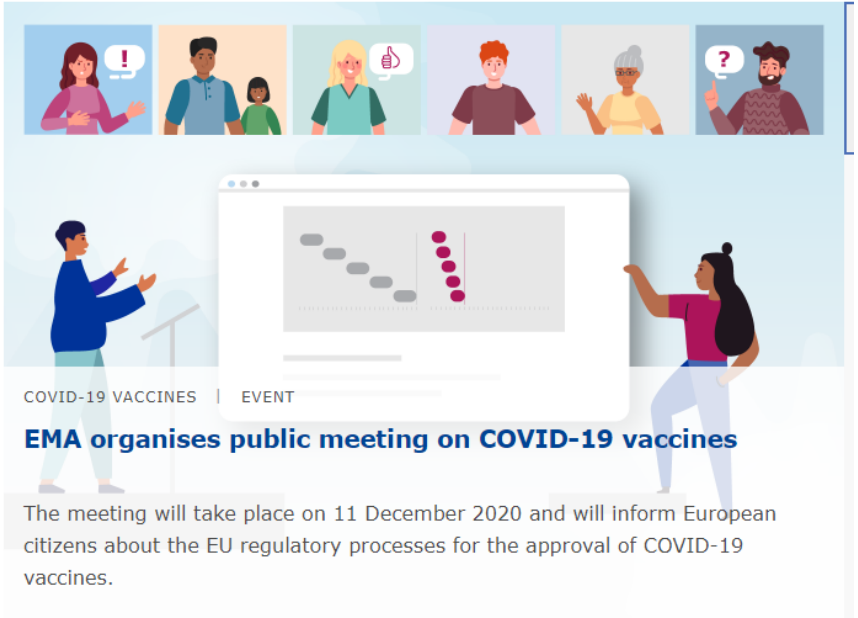
- many challenges with the inclusion of IC in vaccine trials: vulnerable population and various factors to consider e.g. underlying disease or reason for the immunocompromised state, the degree of immunodeficiency, other medical treatments
- Thus difficult to include such people in the initial large-scale clinical trials designed to test the safety and efficacy of a vaccine for the general population or to generalise results from people with reduced immune function of differing causes
- expected that safety and immunogenicity data in IC people would be generated after authorisation
- Post-authorisation safety monitoring and effectiveness studies (how well a vaccine works in real life) will provide additional information

Conclusions

- Existing processes to support vaccine development and data evaluation have been accelerated and adapted to the specificities of the COVID-19 pandemic scenario
- Global collaboration with regulators (ICMRA) and scientific community crucial for a rapid and effective contribution to public health
- Stringent criteria for phase 1/2 and phase 3 trial design and stringent requirements for vaccines approval - **Standards for quality, efficacy and safety are not affected**
- Dedicated resources and flexible procedures (RR and CMA) for evaluation of priority COVID-19 vaccines to avoid any delays and bottlenecks
- **COVID-19 Vaccines will only be approved upon compelling demonstration of efficacy and safety** before they are used in the general population
- Post-authorisation obligations: manufacturing and trials complete dataset, robust systems for safety and effectiveness monitoring of vaccine use in real life in the EU

Public stakeholder meeting on COVID-19 vaccines on 11 December

- To provide further insight into the ongoing work on COVID-19 vaccines, and how vaccines are developed, evaluated, approved, and how safety is monitored;
- To listen to the public and stakeholder groups on their needs, expectations and any concerns.



Any questions?

Further information

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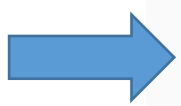
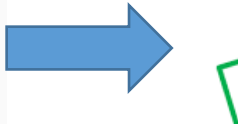
Vaccine accessibility in the EU

Leire Solis
IPOPI

16th PID Forum on Vaccines and PIDs
3rd December 2020, virtual Forum



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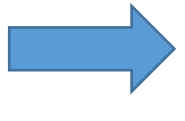
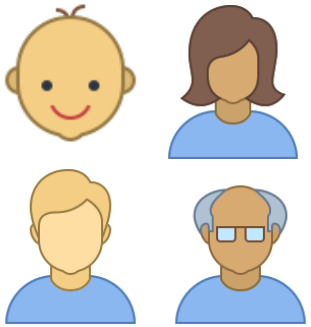




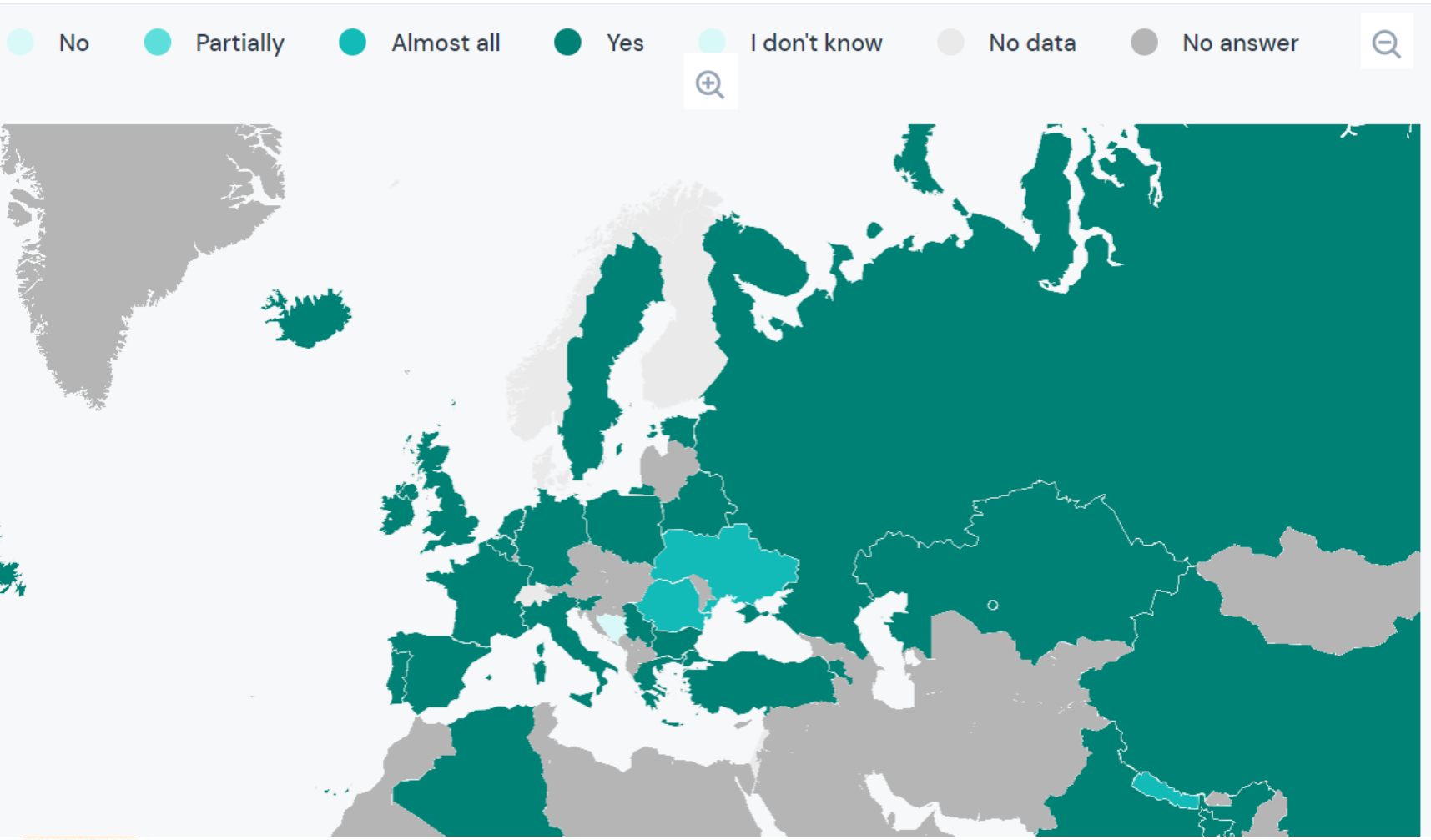
“*Good health is central to wellbeing and depends [… on] fair and equitable access to healthcare*”

“*many patients do not benefit from that innovation, because medicines are either unaffordable or unavailable*.”

Source: Pharmaceutical Strategy for Europe

[COM(2020)761 final]

Are vaccines available?



What matters to you?

WHAT PRINCIPLE ARE YOU INTERESTED IN?

Treatments

WHAT CRITERIA ARE YOU INTERESTED IN?

Vaccines availability

How to read

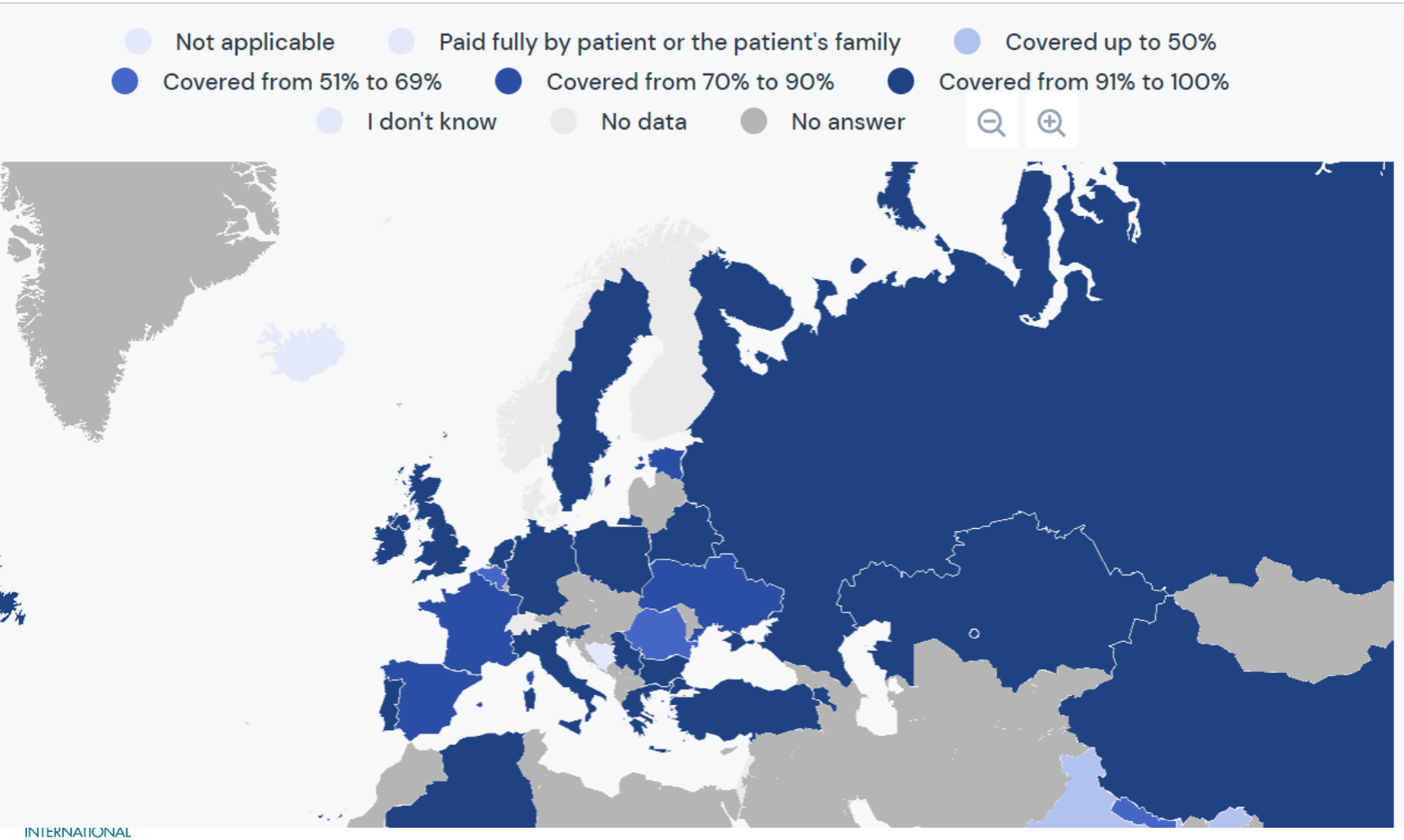
Source: https://pidlifeindex.ipopi.org

Access to medical care

Percentage of population reporting unmet health care needs due to barriers: economic (very expensive), geographic (far away) or waiting list

Source: https://www.mscbs.gob.es/estadEstudios/estadisticas/docs/presentacion_en.pdf

Are vaccines covered?



What matters to you?

WHAT PRINCIPLE ARE YOU INTERESTED IN?

Universal health coverage

WHAT CRITERIA ARE YOU INTERESTED IN?

Vaccines reimbursement

How to read

Source: https://pidlifeindex.ipopi.org

Are vaccines covered?

- Dual system (most covered / some not) can be translated into:

Vacuna frente al rotavirus

El rotavirus es un tipo de virus que produce cuadro de diarrea, vómitos y fiebre en bebés y niños muy pequeños. Como en todos los cuadros infecciosos, el grado de severidad dependerá de muchas causas y puede ir desde un cuadro de gastroenteritis leve, hasta uno grave con necesidad de ingreso hospitalario.

Existen dos tipos de vacuna contra el rotavirus, ambas se administran vía oral:

- Rotarix®: precisa 2 dosis. La primera dosis debe ser después de las 6 semanas de vida, pero no más tarde de las 12 semanas. La última dosis no se debe dar más tarde de las 24 semanas. Su precio es de 93.66 € aproximadamente.
- RotaTeq®: precisa 3 dosis. La primera no se debe poner antes de las 6 semanas de vida y no más tarde de las 20 semanas. La última dosis no se debe dar más tarde de las 32 semanas de vida. Su precio es de 69.50 €

Source (update from January 2020)**:**
https://saludextremadura.ses.es/ventanafamilia/contenido?content=vacunas-no-financiadas

IPOPI INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

Are vaccines covered?

- Dual system (most covered / some not) can be translated into:

Vacuna frente al virus del papiloma humano (VPH)

El virus del papiloma humano se asocia al cáncer de cuello de útero, cáncer anal, cáncer de pene y cáncer orofaríngeo. También es el responsable de las verrugas genitales o condilomas y lesiones precancerosas en la zona genital. Es un virus que su contagio es sexual, es decir, entra dentro de las infecciones de transmisión sexual (ITS). En la gran mayoría de los casos esta infección desaparece sin causar ningún problema, pero en otros, el virus persiste durante muchos años en el organismo llegando a producir cáncer.

Actualmente en España se comercializan 3 vacunas que previenen la infección de los tipos de VPH que producen con mayor probabilidad cánceres: Gardasil®, Gardasil 9® y Cervarix®. Las tres están indicadas tanto para niños como para niñas.

En Extremadura la vacuna está financiada en chicas a partir de los 12 años de edad. Sin embargo, no está financiada para los varones. Se puede comprar en las farmacias con receta médica.

Las dosis van a depender de la edad. Para niño de entre 9 y 14 años, se recomienda 2 dosis, mientras que, en mayores de 14 años, son 3 dosis las recomendadas.

El precio por dosis de Cervarix® es 121,81 €, de Gardasil® 155.91 € y de Gardasil 9® 172,55 €.

Source (update from January 2020)**:**
https://saludextremadura.ses.es/ventanafamilia/contenido?content=vacunas-no-financiadas

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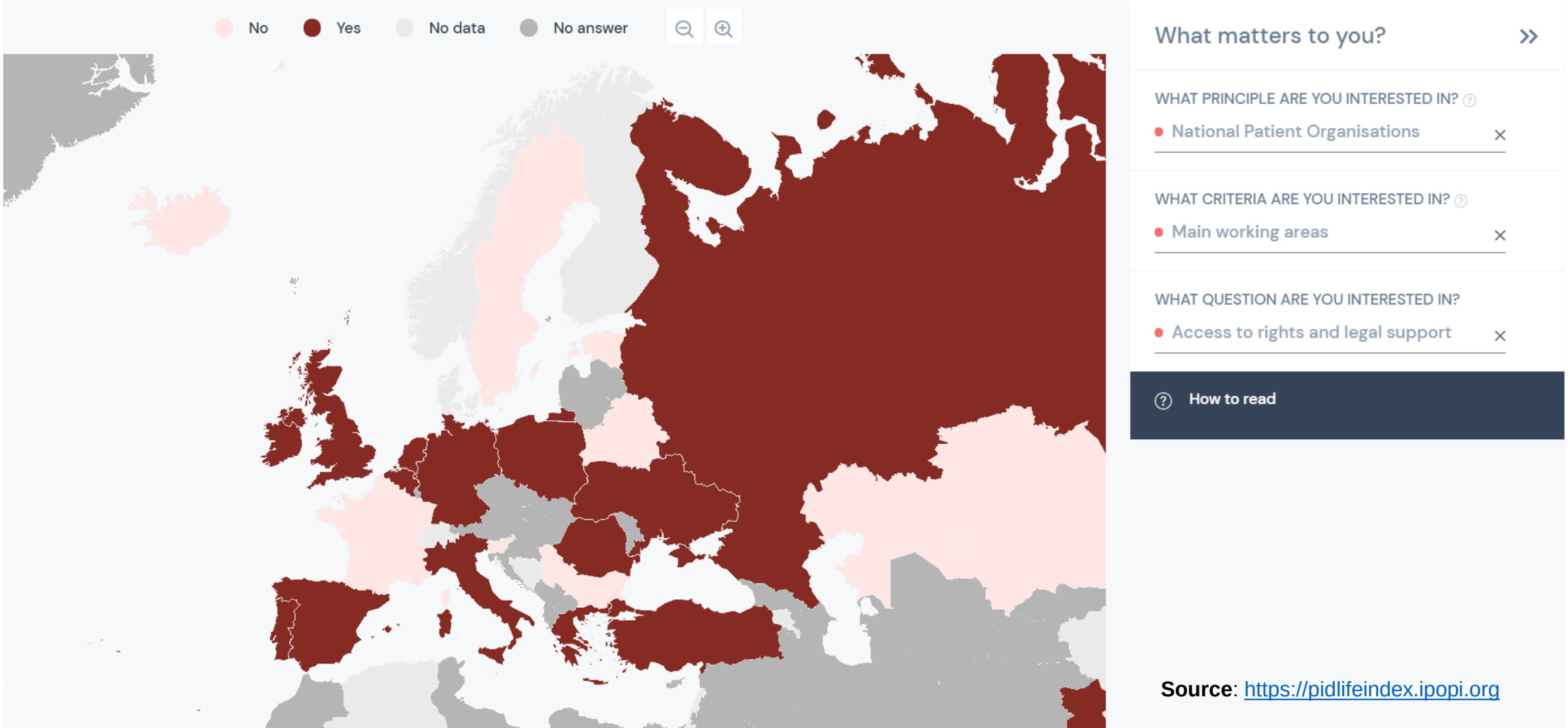
Food for thought



Source: https://pidlifeindex.ipopi.org

To sum up

- Vaccination is key to prevent diseases in the general population and in patients with PIDs.
- A marketing authorisation is not the end of the road.
- A vaccine can be available, but is it really accessible to all patients in need?
- We welcome EU initiatives that promote vaccine R&D but also patient accessibility to them.

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Thank you for your attention