

CEPI



Covid-19 Vaccines Risk Management Planning: Stakeholders Experiences and Perspectives

A COVAX Vaccine Safety Working Group Webinar

April 28th 2021

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Throughout the workshop, **please ask any questions in the “Q&A” function only.**

During the discussion sessions, please **“Raise Your Hand”** if you want to say something. If called on by the moderator, **you will be unmuted to intervene.** Please **turn on the camera on during your intervention only.**

For any technology issue please contact via direct message in the Zoom chat **user WeDo.**

For any logistical issue please contact mireia@wedo-projects.com or please contact via direct message in Zoom chat **Mireia Manent**

This workshop will be **recorded**. Recording might be shared after the webinar.

Please be mindful of the diverse audience attending the meeting when participating in open discussions.

Agenda

Time (PDT)	Session	Speaker
(2:30 pm CET)	<i>Tech check</i>	
(2:50 pm CET)	Attendees start to arrive	
(2:50 pm CET)	Platform and webinar dynamics slide & instructions	
3:00 pm CET	Workshop welcome	Daniel Brasseur (COVAX) Katharina Hartmann (COVAX)
3:00 pm CET	Introduction	Rogério Gaspar (WHO) Jakob Cramer (COVAX)
3:10 pm CET	Regulators' Experience and Expectations	
	Presenters: <ul style="list-style-type: none"> • Petra Doerr (WHO) • Emil Cochino (EMA) • Helaine Carneiro Capucho (Brazil) • Juan Roldan (Chile) • Mojisola Christianah Adeyeye (Nigeria) Joint Q&A	Moderator: Daniel Brasseur (COVAX) Q&A curator: Gabrielle Breugelmans (COVAX)

Agenda

Time (PDT)	Session	Speaker
3:40 pm CET	Industry Experience & Perspective	
	Presenters: <ul style="list-style-type: none"> • Sarah Frise (AstraZeneca) • Jamie Wilkins (Pfizer) • Marc Ceuppens (J&J) • Polina Dombure (Gamelaya, Inpharmatis) • Jiayi Wang (Sinovac) 	Moderator: Katharina Hartmann (COVAX) Q&A curator: Gabrielle Breugelmans (COVAX)
4:10 pm CET	Round table	
	Panelists: <ul style="list-style-type: none"> • Shanthi Pal (WHO) • Nora Dellepiane (former WHO PQ) • Emil Cochino (EMA), • Helaine Carneiro Capucho (Brazil) • Juan Roldan (Chile) • Christianah Adeyeye Mojisola (Nigeria) • Corinne Jouquelet-Royer (IFPMA) • Alexander Precioso (DCVMN) 	Moderator: Katharina Hartmann (COVAX) Q&A curator: Gabrielle Breugelmans (COVAX)
4:50 pm CET	Summary and Closure	Shanti Pal (WHO) Jakob Cramer (COVAX)
5:00 pm CET	End of meeting	

Daniel Brasseur (COVAX)

Katharina Hartmann (COVAX)

**Workshop
Welcome**

Rogério Gaspar (WHO)

Jakob Cramer (COVAX)

Workshop Introduction

Regulators' Experience and Expectations

Regulators' Experience and Expectations

**Petra Doerr
(WHO)**

WHO Good Reliance Practices



COVID-19 Vaccines Risk Management Planning - Stakeholders Experiences and Perspectives

28 April 2021

Evolving Science and Regulatory Challenges

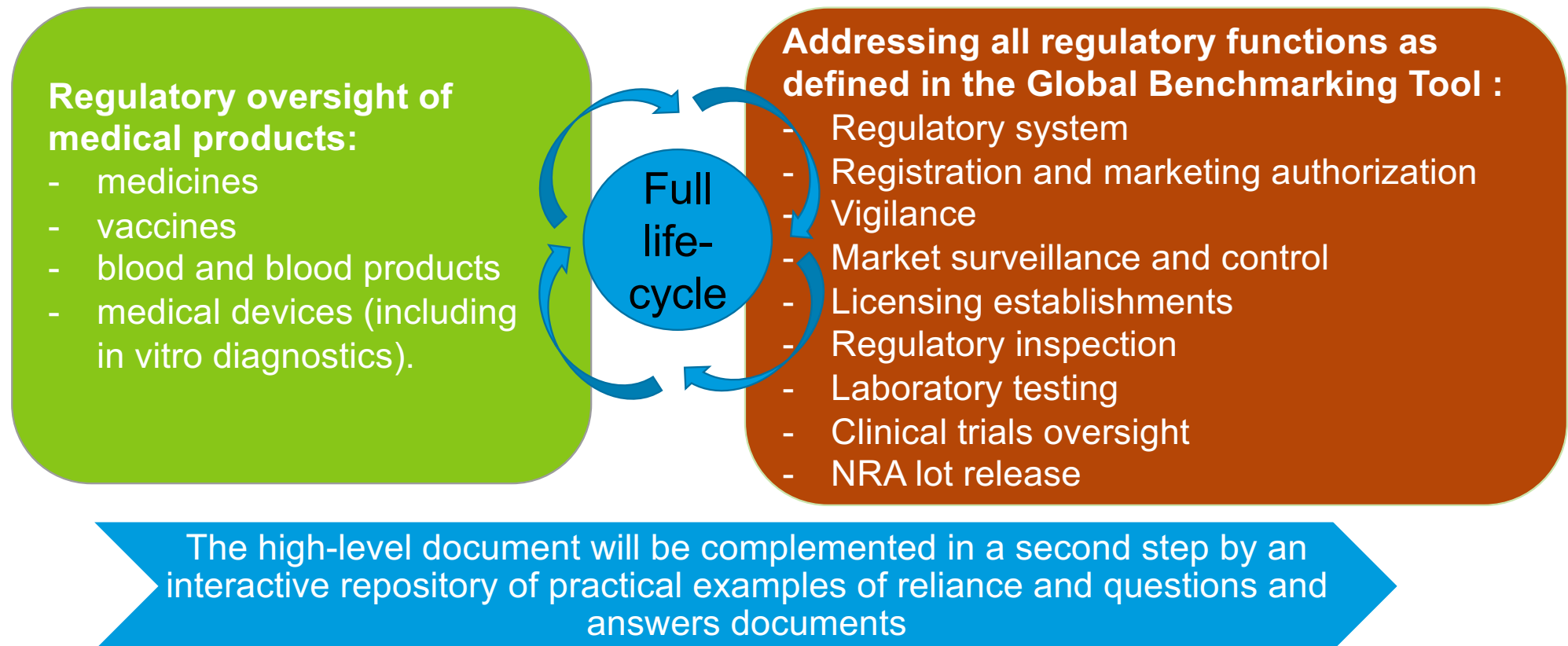
- Globalization of markets
- Sophistication of health technologies
- Rapid evolution of regulatory science
- Increasing complexity of supply chains
- Transparency and growing public expectations
- Lack of global regulatory resources



Importance of international cooperation to ensure the safety, quality and efficacy/performance of locally used medical products

Make best use of available resources and expertise, avoid duplication and concentrate regulatory efforts and resources where most needed

WHO Good Reliance Practices - Scope



Link to GReIP (Annex 10 of 55th report of ECSP): [9789240020900-eng.pdf \(who.int\)](https://www.who.int/publications/m/item/9789240020900-eng)

Principles of Reliance



International cooperation essential to ensure the safety, quality and efficacy/performance of locally used medical products.
No regulatory authorities even the best resourced one can do it alone.



Make best use of available resources and expertise, avoid duplication and concentrate regulatory efforts and resources where most needed.
Promote a more efficient approach to regulatory oversight, thereby improving access to quality-assured, effective and safe medical products over the entire life-cycle.



The act whereby the regulatory authority in one jurisdiction takes into account and give significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information in reaching its own decision.



The relying authority remains independent, responsible and accountable regarding the decisions taken, even when it relies on the decisions, assessments and information of others.

WHO Good Reliance Practices – Principles

Universality

Applies to all NRAs irrespective of their levels of maturity or resources

Sovereignty of decision-making

NRAs maintain independence, sovereignty and accountability

Transparency

Key enabler to adopting new, more efficient ways of conducting regulatory operations. NRAs to be transparent about their reliance approaches

Respect of national/regional legal basis

Coherent with national/regional frameworks and policies

Consistency

Established for specific and well-defined categories of products and processes

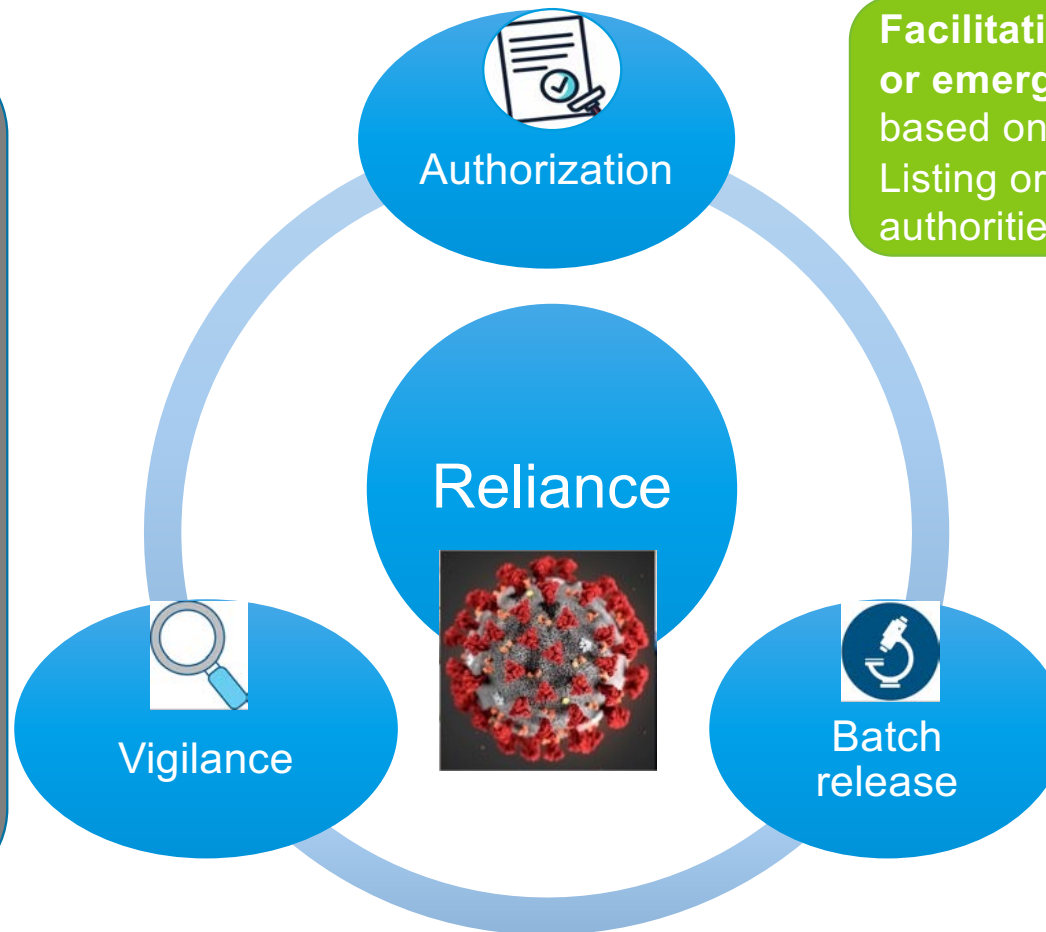
Competency

Build and maintain appropriate competencies and scientific expertise

Application of reliance in Public Health Emergencies

Use of reliance and work-sharing encouraged

WHO Covid-19 vaccines safety surveillance manual encourages reliance, review of risk management plans at regional and WHO prequalification level, pharmacovigilance inspections, etc.
<https://www.who.int/publications/i/item/10665338400>



Facilitation of authorization for use or emergency authorization based on WHO PQs Emergency Use Listing or stringent regulatory authorities approvals

Avoid retesting of vaccines **through reliance on the batch release testing from releasing NRAs/NCLs** (through the WHO-National Control Laboratory Network for Biologicals)

Thank you



World Health
Organization

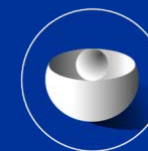
WHO

20, Avenue Appia
1211 Geneva

Switzerland

Regulators' Experience and Expectations

**Emil Cochino
(EMA)**



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Covid-19 Vaccines Risk Management Planning EMA perspective

Covid-19 Vaccines Risk Management Planning: Stakeholders Experiences and Perspectives

Presented by Emil Cochino on 28 April 2021
Risk Management Specialist - Human Medicines Division - European Medicines Agency

An agency of the European Union





EMA coreRMP19 guidance, recommendations, requirements

= additional requirements and guidance for the RMP of COVID-19 vaccines

Existing guidance applies*: EU Good Pharmacovigilance Practices: Module V (Risk Management Systems), P I Vaccines, P II Biologicals; EU RMP Template, other vaccine development clinical guidance (e.g. pandemic requirements for influenza vaccines)

coreRMP19 v1.0 published 13 November 2020, updated version currently in drafting:

https://www.ema.europa.eu/en/documents/other/consideration-core-requirements-rmps-covid-19-vaccines_en.pdf

* <https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/good-pharmacovigilance-practices>

<https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/pharmacovigilance/risk-management/risk-management-plans>

https://www.ema.europa.eu/en/documents/scientific-guideline/influenza-vaccines-non-clinical-clinical-module_en.pdf

https://www.ema.europa.eu/en/documents/scientific-guideline/interim-guidance-enhanced-safety-surveillance-seasonal-influenza-vaccines-eu_en.pdf



coreRMP19 content (1)

- Additional COVID-19 specific topics to be addressed in the safety specification, including missing information and AESI
- Additional topics for discussion as part of Safety Specification, to facilitate discussion with regulators and assessment: e.g. reactogenicity, impact of formulation, management of multiple doses, long term follow-up
- Existing sources to consider for the list of AESI
- When and how to follow and present AESI (i.e. follow-up questionnaires, with periodic reports)
- Methods for signal detection adapted to pandemic use (to be described in RMP)
- Content and periodicity of the Monthly Summary Safety Reports (further developed with the experience of up to four months submissions);



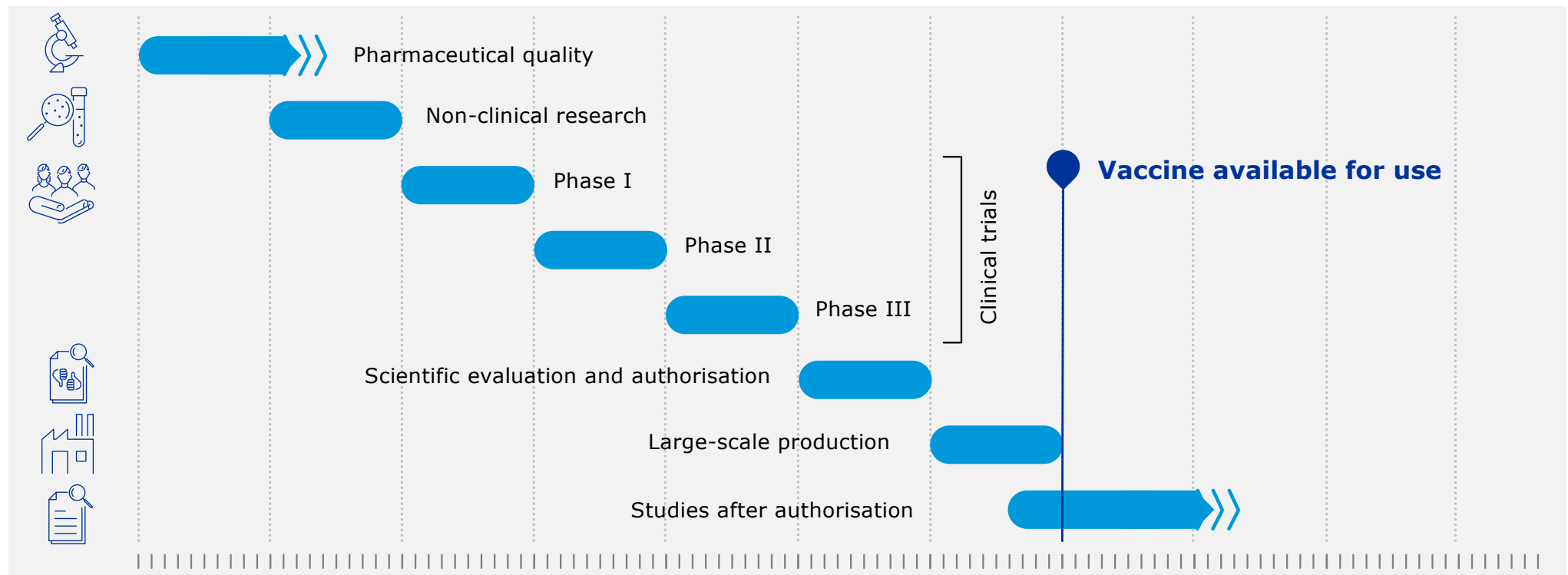
coreRMP19 content (2)

- General recommendation for use of enhanced passive surveillance systems; designs to be avoided
- Use of vaccination cards, stickers for traceability, additional electronic methods (barcode and/or QR codes) to be considered for traceability and risk communication.
- Key elements of PASS design: e.g. rapid start, fast data generation, frequent reports, using results of ongoing EU efforts; considerations on when a PASS should be considered.
- EU projects that are likely to generate useful element for designing and conducting a PASS, or conducting safety surveillance that can be used for regulatory purposes by the MAHs
- Transparency measures: RMP full body and Annex 4 (ADR reports follow-up questionnaires) are published on EMA website for all COVID-19 vaccines

e.g. https://www.ema.europa.eu/documents/rmp-summary/comirnaty-epar-risk-management-plan_en.pdf ; https://www.ema.europa.eu/documents/rmp-summary/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-risk-management-plan_en.pdf

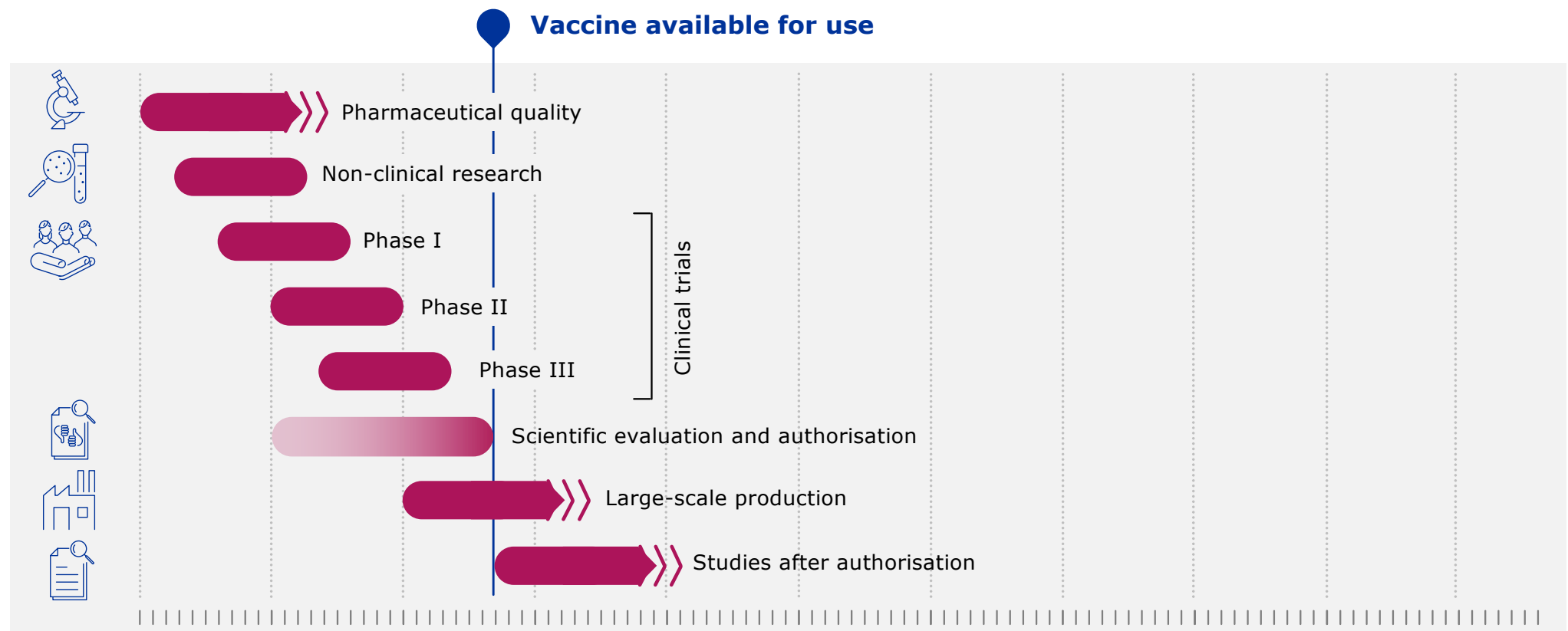
NEW INFORMATION MATERIALS ON COVID-19 VACCINES

Standard vaccines compared with covid-19 vaccines



NEW INFORMATION MATERIALS ON COVID-19 VACCINES

Standard vaccines compared with covid-19 vaccines



Rapid approval processes in the EU

Early support for vaccine developers:

EMA provides scientific advice and a dedicated Task Force (COVID-ETF)





Experience with RMP assessment - RR + initial MA application

- ✓ RMP available only in later rolling reviews submissions, sometimes at the time of the clinical trial data reports generation
- ✓ One cycle for RMP assessment, two at best (e.g. third rolling review + CMA application)
- ✓ First four vaccines in EU:
 - Creating precedents while ensuring consistency
 - Accounting for individual CT data submission
 - Sync with CHMP evaluation and PI finalisation (most important risk minimisation activity)
 - Defining the conditions of the MA (imposed studies)
- ✓ Improving the process from one product to the next = taking parts of the RMP earlier in the RRs: relevance of pre-clinical data; common safety concerns; signal detection during pandemic; defining the AESI; agreeing the monthly summary safety report content requirements; TRACEABILITY tools; studies concepts/synopsis.



EU lessons learned – pre-authorisation

- ✓ Use 2009-2010 pandemic lessons learned and recommendations
- ✓ Preparedness plans adapted to the new pandemic situation (e.g. https://www.ema.europa.eu/en/documents/other/pharmacovigilance-plan-eu-regulatory-network-covid-19-vaccines_en.pdf)
- ✓ Severe disruption of work environment, travel, medical access = challenges for MAH staff fulfilling PhV obligations, Rapporteurs' assessment teams, and EMA staff
- ✓ Flexibility of the EU Network: focused efforts; long assessment hours, weekends included
- ✓ Early and frequent dialog with Manufacturers: rapid scientific advice, interaction with COVID-ETF, pre-submission meetings
- ✓ Transparency for requirements and assessment with an enhanced communication to the general public (support confidence in vaccines and assessment process)



Any questions?

Further information

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Telephone +31 (0)88 781 6000

Send us a question Go to www.ema.europa.eu/contact

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Regulators' Experience and Expectations

**Helaine Carneiro Capucho
(ANVISA, Brazil)**

COVAX / WHO Vaccine Safety surveillance Webinar

Regulators' Experience and Expectations

Brazilian Experience

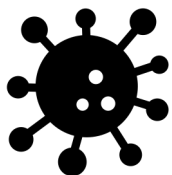
Helaine Capucho, PhD.

Pharmacovigilance Manager



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THE CHALLENGE

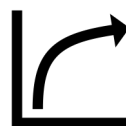


NEW DISEASE



FASTER STUDIES

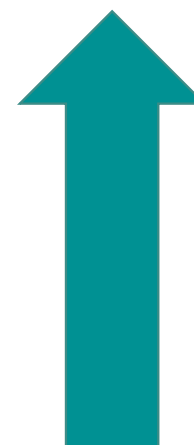
UNCERTAINTY



SHORT LIFE-CYCLE
TECHNOLOGY



QUICK DISTRIBUTION AND
LARGE SCALE



RISK

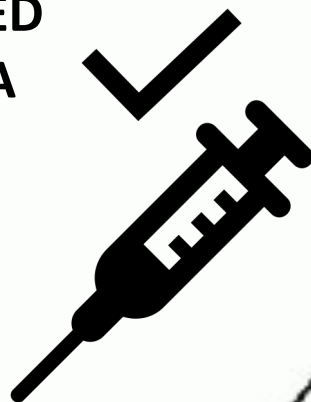


GREATER NEED
FOR SURVEILLANCE



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**VACCINES
AUTHORIZED
BY ANVISA**



SINOVAC/BUTANTAN

Emergency Use Authorization

OXFORD/ASTRAZENECA/FIOCRUZ

Registration

PFIZER

Registration

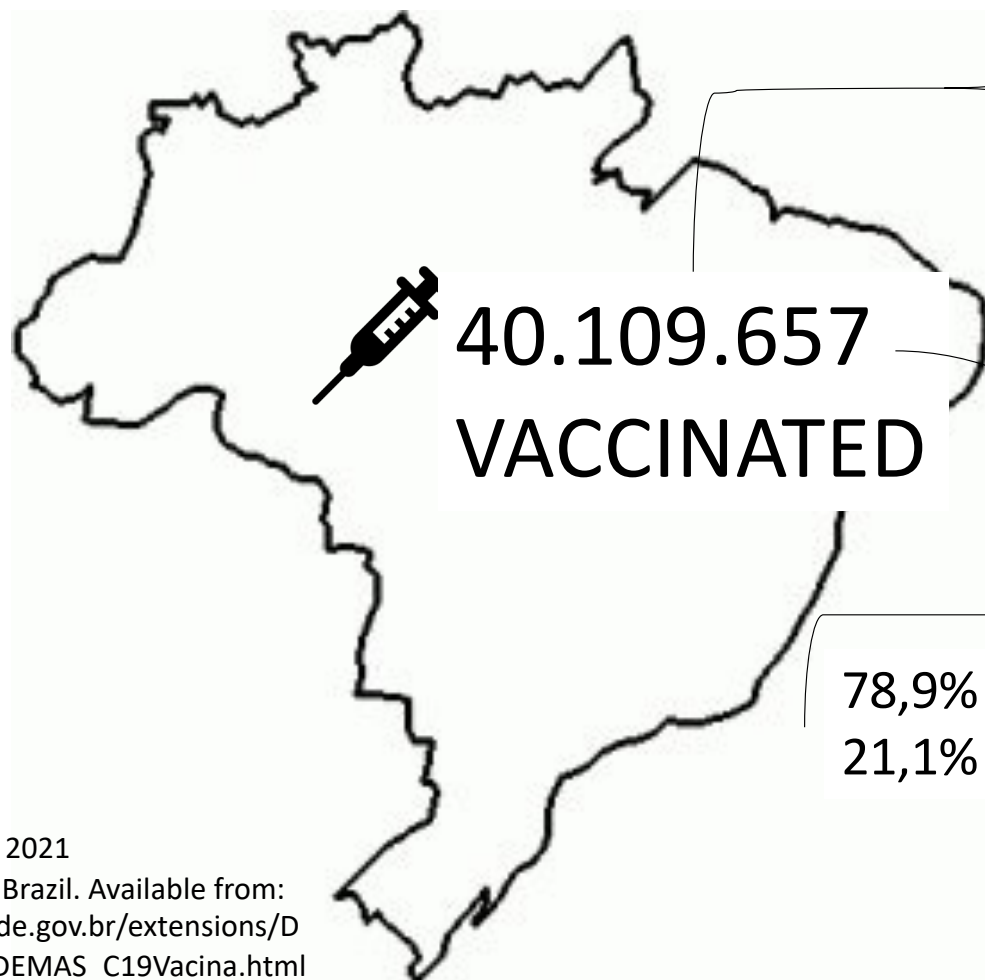
JANSEN

Emergency Use Authorization

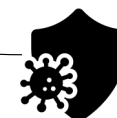
Anvisa, Brazil. Available from
https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2021/covid-19-quadro-de-analises-de-vacinas-pela-anvisa?_authenticator=49168e13d276eeb6de2df4a423e2a4eee9c563bc



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FIRST DOSE
27.882.030



SECOND DOSE
12.227.627

78,9% SINOVA/CBUTANTAN
21,1% OXFORD/ASTRAZENECA/FIOCRUZ

Data from April 27, 2021
Ministry of Health, Brazil. Available from:
https://qsprod.saude.gov.br/extensions/DEMAS_C19Vacina/DEMAS_C19Vacina.html



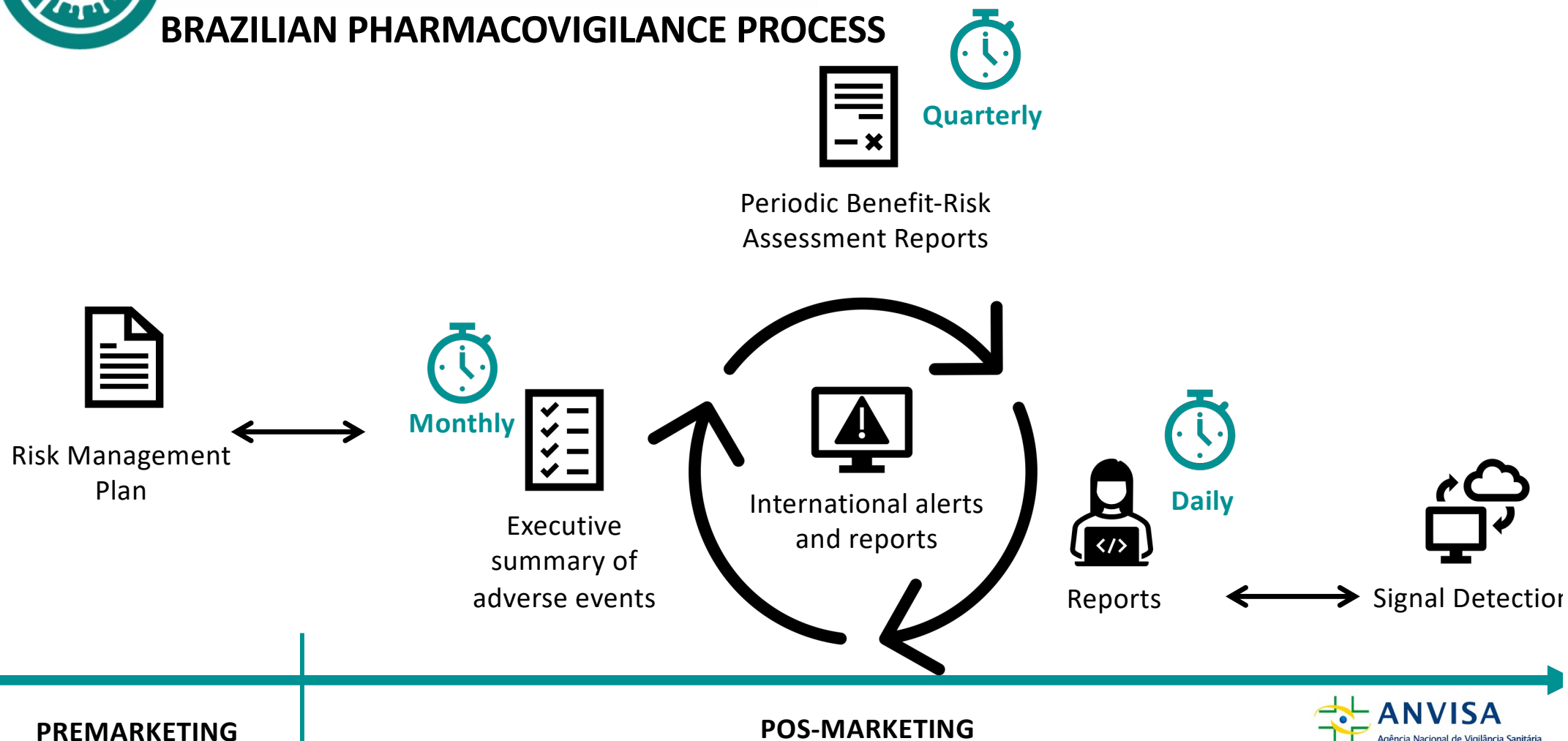
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BRAZILIAN PHARMACOVIGILANCE PROCESS



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BRAZILIAN PHARMACOVIGILANCE PROCESS





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ADVERSE EVENT FOLLOWING IMMUNIZATION

FLOW REPORTING



Diagrama de fluxo do sistema de farmacovigilância:

- VigiMed** (top left) → **Análise de causalidade** → **Pharmacovigilance Office Anvisa** (top center)
- e-SUS Notifica** (bottom left) → **Análise de causalidade** → **Comitê de Respostas Rápidas PNI** (bottom center)
- Pharmacovigilance Office Anvisa** ↔ **Comitê de Respostas Rápidas PNI**
- Pharmacovigilance Office Anvisa** → **VigiMed** (top right)
- VigiMed** (top right) → **VigiBase** (Uppsala Monitoring Centre/WHO, represented by a teal cylinder)
- VigiBase** → **Signal Detection** (represented by a monitor and cloud icon)
- Signal Detection** → **Vigilyze** (top right)
- VigiMed** (top right) → **Vigilyze**
- Vigilyze** → **Notificações** (represented by a person with a laptop icon) → **e-SUS Notifica**

Logotipo da **ANVISA** (Agência Nacional de Vigilância Sanitária) no canto inferior direito.



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COMMUNICATIONS AND ALERTS



CORONAVÍRUS • COVID - 19 • VACINA



COMUNICADO GGMON 004/2021

Vacinas contra a COVID-19

07 de abril de 2021

ULA DA VACINA OXFORD/ASTRAZENECA/FIOCRUZ



olicita alteração de
vacina de Oxford

everá incluir a possibilidade de
de casos muito raros de
anguineos associados à
penia - diminuição do número
as no organismo.

riscos.

la da vacina Oxford/Astrazeneca/Fiocruz para incluir no item
Precauções” as possíveis ocorrências tromboembólicas com
evento muito raro observado em alguns países
em a recomendação de continuidade da vacinação com o
nte, uma vez que, até o momento, os benefícios superam os



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COMUNICADO GGMON 001/2021

Agência Nacional de Vigilância Sanitária - Anvisa

Assuntos > Notícias > 2021 > Vacinas contra a Covid-19 não são intercambiáveis

VACINA

Vacinas contra a Covid-19 não são intercambiáveis

A Anvisa alerta para que a administração da primeira e da segunda doses da vacina contra a Covid-19 seja realizada com vacinas do mesmo fabricante.

Publicado em 25/03/2021 16h33 Atualizado em 26/03/2021 09h49

A Anvisa alerta os profissionais de saúde e a população para que a administração da primeira e da segunda doses da vacina contra a Covid-19 seja realizada com vacinas do mesmo fabricante.

Não existe, até o momento, informação sobre intercambiabilidade* entre as vacinas utilizadas no Brasil, ou seja, não há dados que sustentem que a troca de fabricantes de vacinas entre a primeira e a segunda dose produza resposta imune ao Sars-CoV-2.

A identificação dessa troca entre a primeira e a segunda dose da vacina deve ser informada às autoridades de saúde.

SOBRE O LOTE EM INVESTIGAÇÃO

O lote suspeito – ABV5300 – é fabricado pela Astrazeneca e não é utilizado no Brasil.

Mais recentemente, Alemanha, França, Itália, Espanha, Irlanda, Chipre e Indonésia também suspenderam, temporariamente, a aplicação da vacina Oxford/AstraZeneca contra a Covid-19.



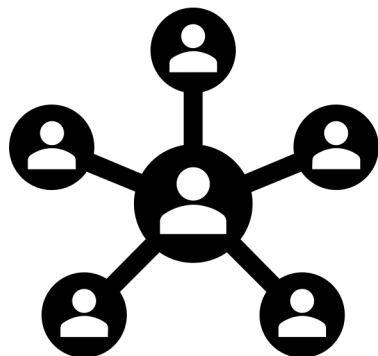
ANVISA

Agência Nacional de Vigilância Sanitária



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THE CHALLENGE



**INTEGRATE SYSTEMS
USED IN BRAZIL**



ANALYZE CAUSALITY QUICKLY



**COMMUNICATING RISKS
WITHOUT REDUCING
ADHERENCE TO VACCINATION**



CORONAVÍRUS • COVID - 19 • VACINA

AN OPPORTUNITY



GREATER NEED
FOR SURVEILLANCE



A WORLD GOAL



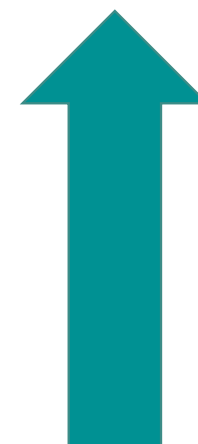
USE OF INFORMATION
TECHNOLOGIES IS
ACCELERATED



GREATER INVOLVEMENT
OF THE POPULATION



DISSEMINATION OF
HEALTH INFORMATION



PHARMACOVIGILANCE



CORONAVÍRUS • COVID - 19

Thank you!

farmacovigilancia@anvisa.gov.br

helaine.capucho@anvisa.gov.br

Agência Nacional de Vigilância Sanitária - Anvisa



www.gov.br/anvisa

Regulators' Experience and Expectations

**Juan Roldan-Saelzer
(ISPC, Chile)**

Experience on Pharmacovigilance Planning/Risk Management Plans

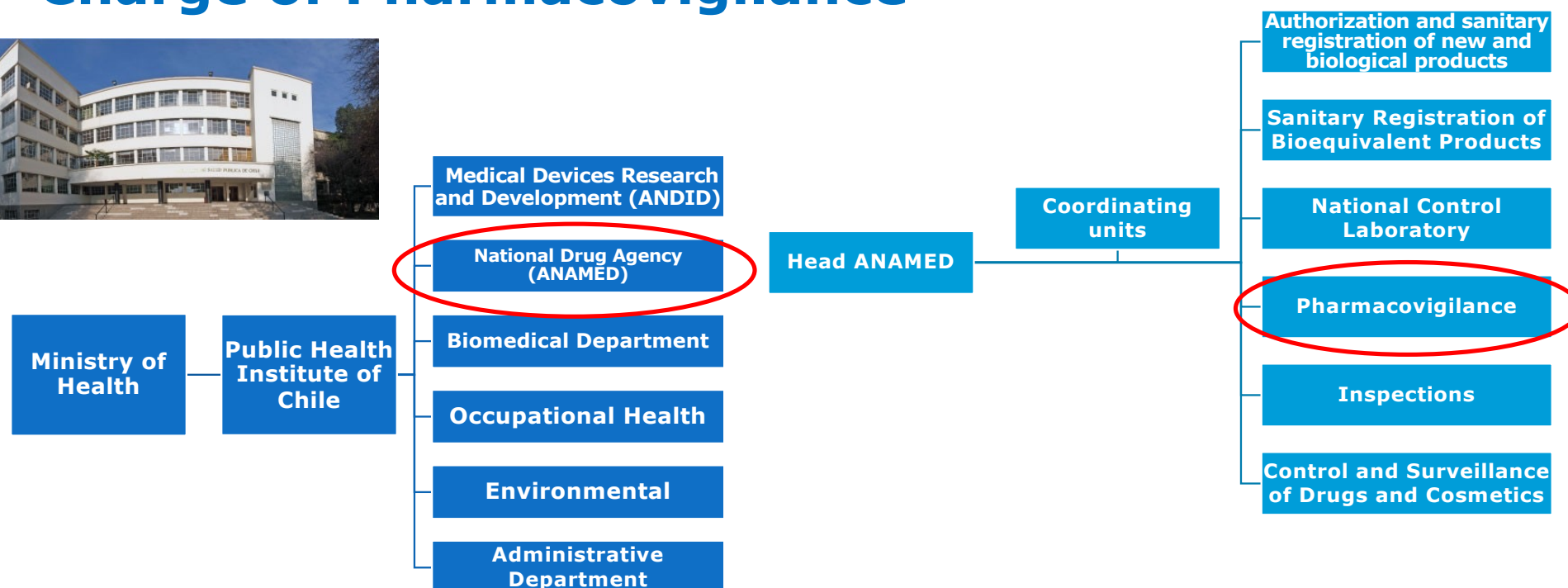
Engaging the stakeholders in Chile

WHO – COVAX Vaccine Safety WG workshop

Pharm. Juan Roldan-Saelzer, PhD
Head (S) Department National Drugs Agency
Public Health Institute of Chile

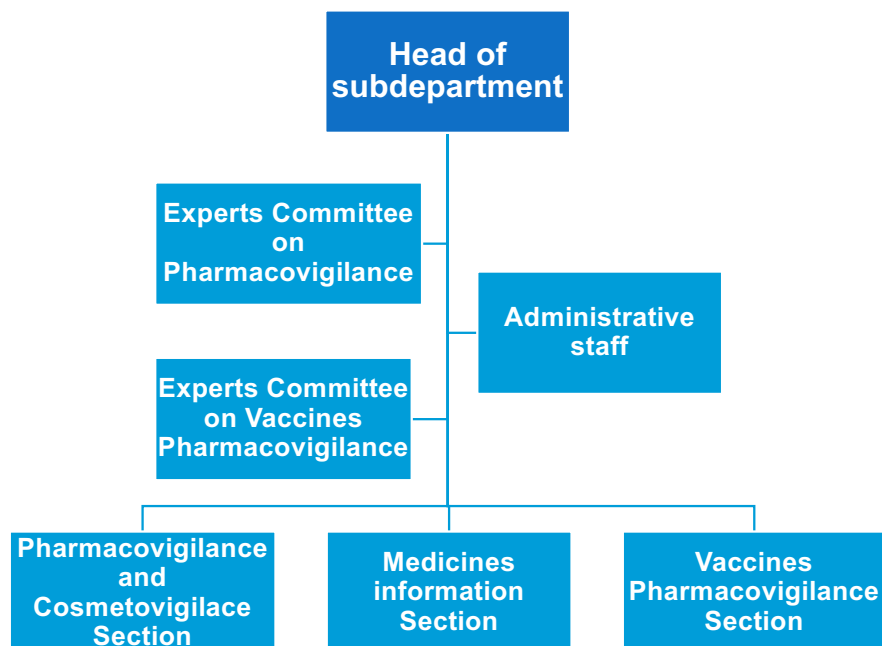
April 28, 2021

Organization chart Health Regulation Authorities in Charge of Pharmacovigilance



A reference institution of the State, which promotes and protects population health, strengthening sanitary control through **surveillance, authorization, inspection, research and technology transfer**, complying with high standards of quality and excellence.

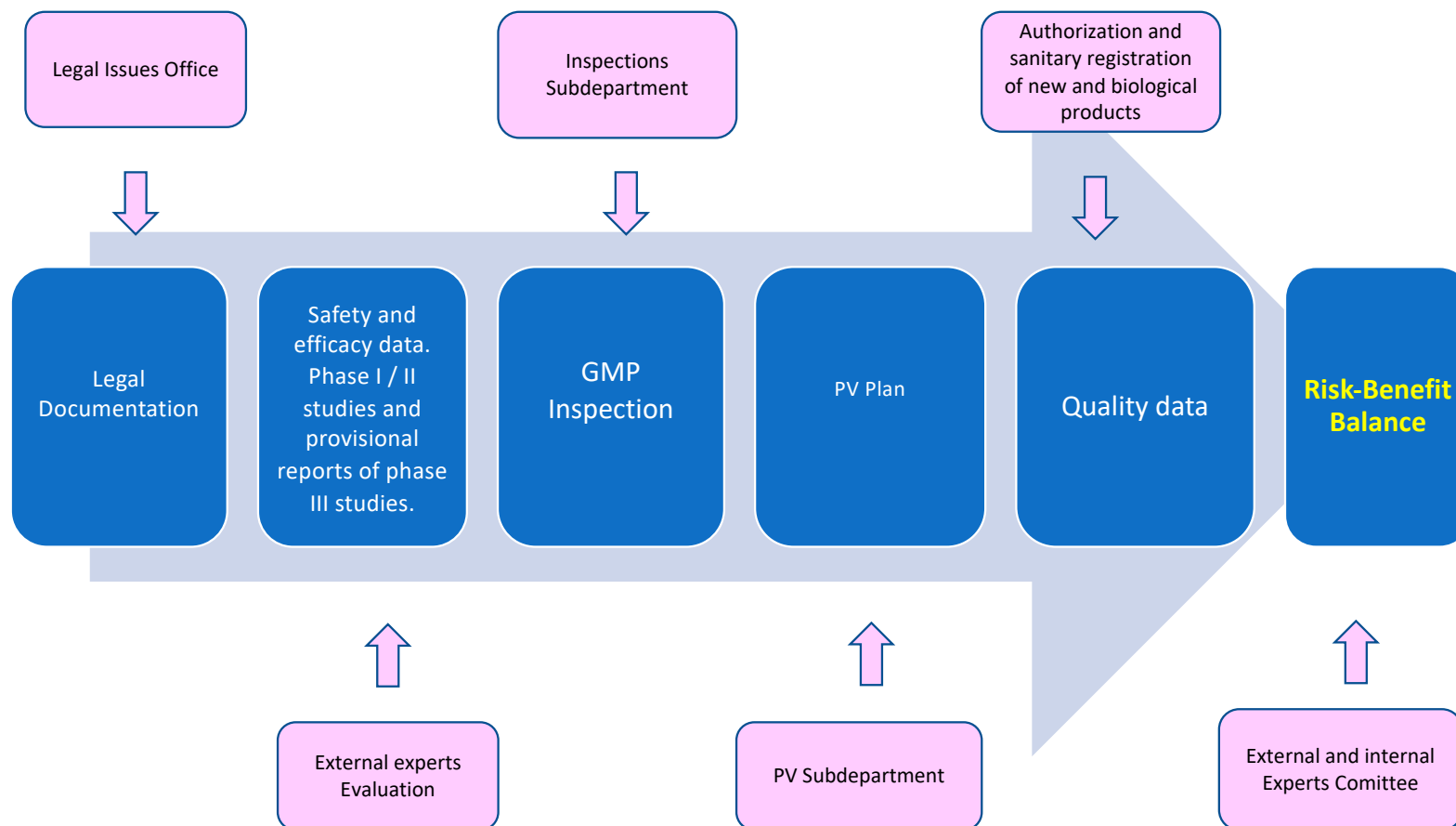
Pharmacovigilance Subdepartment



- **Expert Committee on Pharmacovigilance**
- **(4 external members):**
 - 2 doctors.
 - 2 pharmacists.
- **Expert Committee on Vaccine Pharmacovigilance**
- **(6 external members)**
 - 5 doctors.
 - 1 nurse.
 - Additional experts according to need
- **Team:**
 - 11 Pharmacists
 - 3 pandemic supporting Pharmacists
 - 2 administrative staff



COVID-19 vaccines – Evaluation Process



Pharmacovigilance activities for COVID-19 vaccines



Participation in:

- Committee for clinical trials and evaluation of adverse events
- Review of medical records for emergency authorization
- External and internal Experts Committee

Routine PV:

Reception and evaluation of spontaneous AEFI Reports

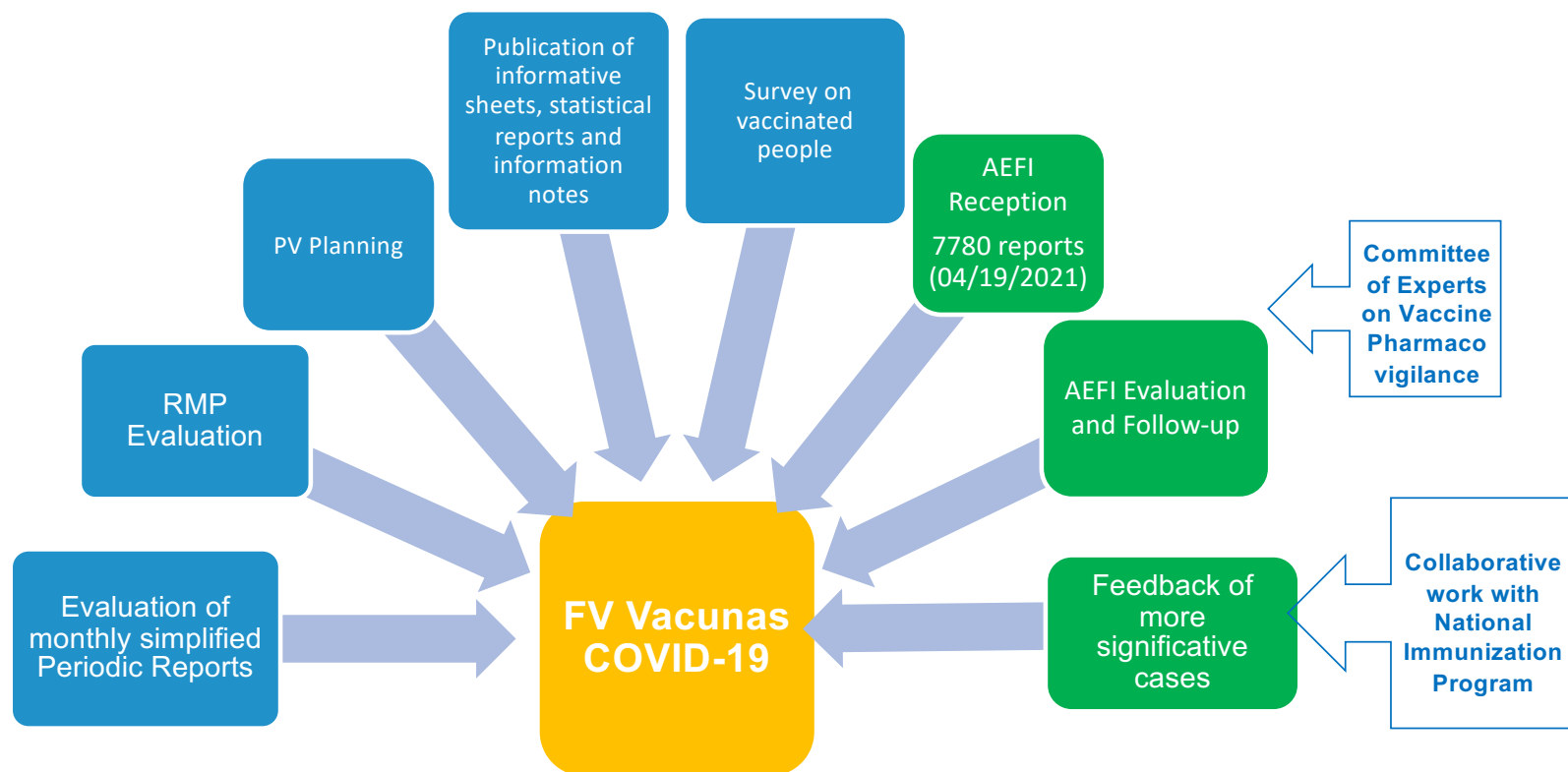
Patient safety survey:

Follow-up of vaccinated people through the email registered in the National Immunization Registry

Evaluation of risk management plans, monthly simplified safety reports, and safety reports



Pharmacovigilance activities for COVID-19 vaccines

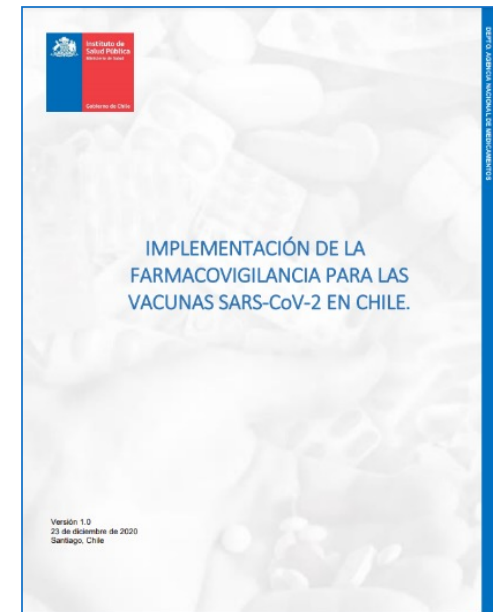
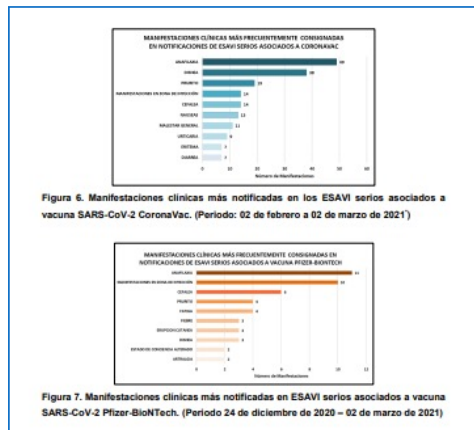
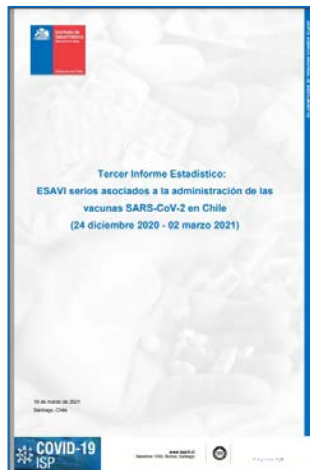


<https://www.ispch.cl/isp-covid-19/notas-farmacovigilancia/>

Pharmacovigilance activities for COVID-19 vaccines

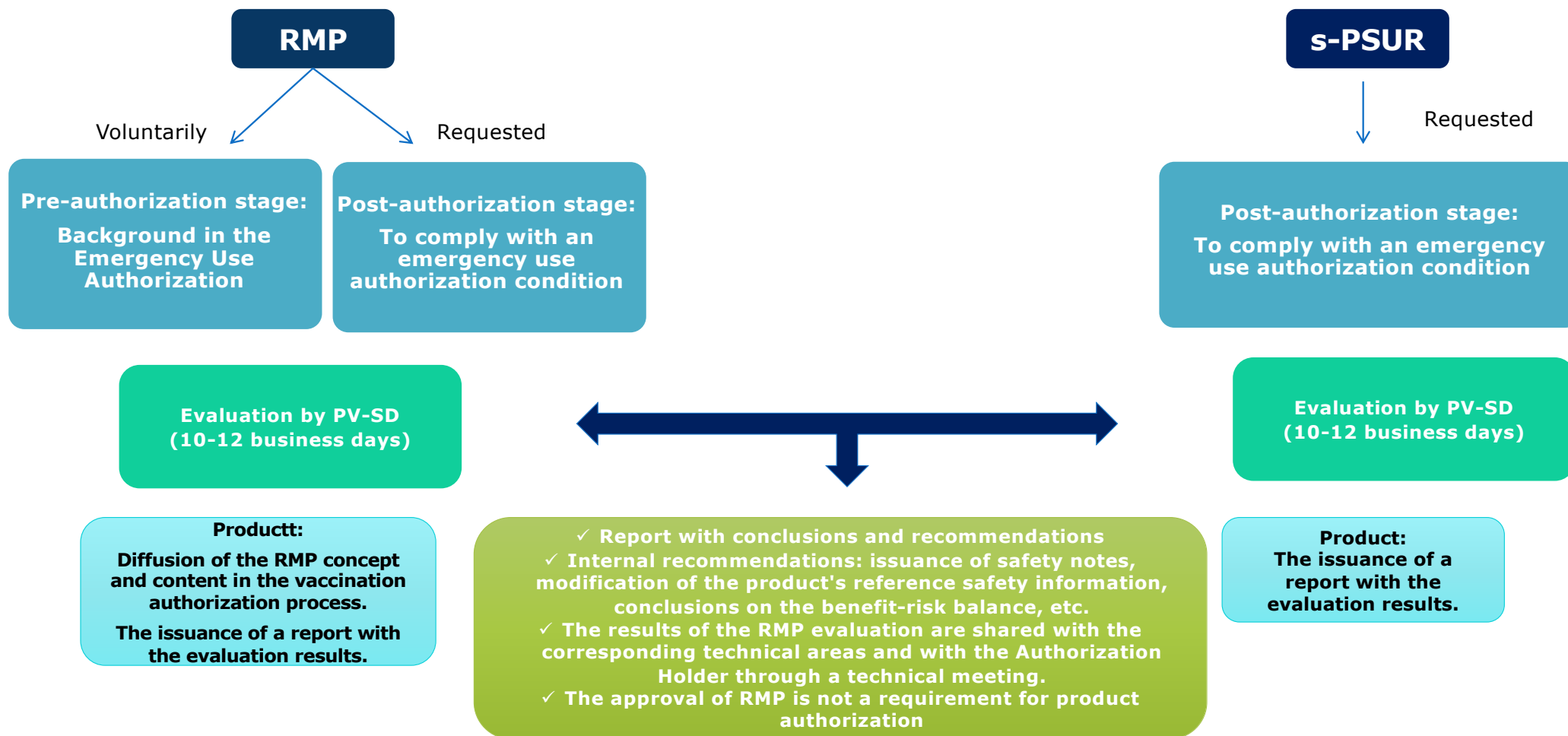
Safety data sheets
Statistical reports
Informative notes

Guidelines for the
pharmacovigilance of SARS-CoV-2 vaccines in Chile.
Includes information for the submission of RMP



Spontaneous reports received:
7780 reports (04/19/2021)

General application and evaluation process for RMP and s-PSUR of COVID-19 vaccines



Strengths, limitations and challenges of the Chilean strategy in PV for Covid-19 vaccines

Strengths

- It is useful for monitoring the safety profile of COVID-19 vaccines.
- Source for signal detection (identify new risks).
- Contributes to health decision making.
- Allows to keep the safety information of COVID-19 vaccines up to date.
- Allows evaluation of the overall benefit-risk balance of COVID-19 vaccines.
- Trained personnel are available to carry out the activity.

Limitations

- Complexity of the evaluation (extensive documents with high informative content).
- Limited human resources and high volume of documents.
- Heavy workload, requiring exclusivity to perform the activity.
- Short evaluation times in order to manage the demand of documents susceptible to evaluation.

Challenges

- Strengthen staff capacities in regard to the evaluation of this type of documents.
- To have more professionals available to carry out the activity.
- Improve the timeliness of document evaluation, as well as making recommended actions as part of the evaluation results.
- Continuously improve the evaluation process and those derived from its results.
- Share experiences with other countries in the region regarding the evaluation of these documents.



GRACIAS

INSTITUTO DE SALUD PÚBLICA DE CHILE

Regulators' Experience and Expectations

**Mojisola Christianah Adeyeye
(NAFDAC, Nigeria)**

Covid-19 Vaccines Risk Management Planning (RMP): Stakeholders Experiences and Perspectives

Presented by
Prof Mojisola Christianah Adeyeye

At The
COVAX Vaccine Safety Working Group Webinar
28th April, 2021

Outline

- Structure of RMP
- Risk Management Planning
- Requirements for Pharmacovigilance Planning
- Post Authorization Safety Studies
- Requirements for Periodic Safety Update Report/Periodic Benefit Risk Evaluation Report (PSUR/PBRER)
- Need for Risk Management Planning
- Responsibility for RMP and NRA Responsibility
- COVID-19 Vaccine Pre-Authorization Safety Preparedness and Experience
- NAFDAC and International Regulatory Cooperation
- NAFDAC Activities
 - Lessons learnt
 - War Forward
- Conclusion

STRUCTURE OF THE RISK MANAGEMENT PLAN IN NIGERIA

The RMP consists of seven parts:

- Product overview
- Safety specification
- Pharmacovigilance plan
- Plans for post-authorization efficacy studies (PASS)
- Risk minimization measures (including evaluation of the effectiveness of risk minimization measures)
- Summary of risk management plan
- Annexes

Risk Management Plan (RMP)

Overview

- The **overall aim of risk management** is to ensure that the benefits of a particular medicinal product exceed the risks by the greatest achievable margin.
 - Dynamic document that should be updated throughout the life cycle of medicinal product(s).

Safety Specifications

- Current knowledge about the **safety profile, benefits and the risks** of the vaccine or medicinal product,
- Key information on **plans for studies** and other activities to gain more data on missing information,
- Plans for **risks minimization and assessment** of effectiveness

Requirements for Pharmacovigilance Planning

There is need to focus PV planning in the following areas:

- Specific activities for collection, compilation, assessment and reporting of AEFI to NRA
- Monthly safety summaries in addition to routine PSURs
- Post-authorization safety studies
- The establishment of sentinel sites, as part of active surveillance system for COVID-19 vaccine safety
- Provision of educational materials and implementation of technology-driven tracking system of vaccine administered e.g., barcode stickers

Requirements for Pharmacovigilance Planning

Monthly safety summaries should include:

- A summary of **vaccine distribution** (number of doses, locality of distribution)
- Global numbers (with country of origin) and **analysis of AESIs reported** in individuals following immunization, following the Brighton Collaboration recommendations for COVID-19 vaccines
- **Numbers of deaths and relevant case histories**, including observed over expected analysis
- In addition to 6 months PSUR/PBRER, a **monthly safety summary focusing on AESI** should be submitted or more frequently as the situation requires

Other requirements defined in the regional annex

- Challenges such as large volume of reports of adverse events following immunization (AEFIs) associated with a mass vaccination campaign should be considered and reflected in the planning document

Post Authorization Safety Studies (PASS)

- PASS should be considered and reflected in RMP if planned clinical trials and routine activities do not provide enough information for the complete characterization of important identified and potential risks

Further studies to consider under PASS include:

- A study to further investigate the **safety in pregnant women** and pregnancy outcomes
- **Study in pediatrics and young children** who were not studied on during clinical trials
- **Effectiveness studies** are key in this section of the RMP.
- It is recommended that the MAHs make use of the existing/established efforts that could provide brand-specific data reliably and timely

Requirements for PSUR/PBRER

- Periodic Safety Update Report/Periodic Benefit Risk Evaluation Report shall be submitted to the Agency immediately upon request or in accordance with the following:
 - Where a medicinal product has been on the market, the following periodicity shall apply;
 - For new drug molecules, at least every six (6) months for the first two (2) years, annually for the following three (3) years, and every five (5) years, at the time of renewal of license.
 - For products already being marketed elsewhere, existing PSUR/PBRER shall be submitted to the Agency not later than thirty days after submission of documents requesting for Certificate of Registration in Nigeria.
 - For listed medicinal products (provisional registration), the Certificate of Registration holder shall submit a PSUR/PBRER every six (6) months for the two (2) year listing period.

Requirements for PSUR/PBRER...

Each vaccine manufacturer/**MAH should be responsible for submitting PSUR/PBRERs** for its own products to the Agency according to the following timelines:

- Within **70 calendar days** of the data lock point (day 0) **for PSUR/PBRERs/ covering intervals up to 12 months** (including intervals of exactly 12 months); and
- Within **90 calendar days** of the data lock point (day 0) for PSUR/PBRERs covering intervals in excess of 12 months;
- PSUR/PBRER reporting should be **linked to the risk management systems of the medicinal product**

Need for Risk Management Planning

- The uptake of COVID-19 vaccines once authorized is anticipated to be very high which may lead to a high volume of suspected adverse reaction reports and other safety data.
- Passive and active safety monitoring are integral to the evaluation of efficacy and safety of vaccines.
- Prompt detection and evaluation of new information on the benefit-risk balance of these vaccines, timely communication and a high level of transparency will be key to protect public health and ensure the public's trust in the vaccines and in the regulatory system



Responsibilities for RMP

An applicant/marketing authorization holder is responsible for:

- Having an appropriate risk management system in place
- Ensuring that the knowledge and understanding on the product's safety profile, following its use in clinical practice, are critically reviewed.

Responsibilities for RMP...

- Should **monitor pharmacovigilance data to determine whether there are new risks** or whether risks have changed or whether there are changes to the risk-benefit balance of medicinal products
- Should **designate a qualified person responsible for pharmacovigilance (QPPV)** (or a global QPPV for international vaccine manufacturers) for monitoring its safety; and to clearly present the **contact information and qualifications of the QPPV** to the NRA

NRA Responsibilities

- Clear **guidance** and **requirements for PV**
- Contribute to **regional annex for RMP** to establish criteria for study site selection
- Provide **oversight** for study implementation
- Guidance to MAH on requirements for routine **communication of study findings**, adhoc communications for urgent emerging issues
 - Implement a coordinated routine communication plan with stakeholders
- Ensure a **national committee** is ready to review any national PASS data

COVID-19 Vaccine Pre-Authorization Safety Preparedness and Experience

- Collaboration with all relevant stakeholders NPHCDA, NCDC, WHO, UNICEF, AUDA NEPAD, MHRA, CDC, etc
- Multi-Agency Technical Working Group established to enhance planning and safety surveillance
- Development of the COVID-19 Vaccine Regulatory preparedness plan
- Deployment of the AEFI form on the Med Safety App
- Training of health workers on the use of Med Safety App
- Deployment of PV focal persons and champions for the Med Safety App to the field to monitor vaccination and upload reports real time

COVID-19 Vaccine Pre-Authorization Safety Preparedness and Experience...

- Planned the conduct of enhanced/targeted **passive surveillance of COVID-19**
- Planned the pilot testing of the **Traceability system** using the COVID-19 Vaccine introduction
- Developed **the CEM protocol for active surveillance** for COVID-19 vaccine monitoring
- Inaugurated the **National Expert Committee on AEFI Causality Assessment**
- WHO at the continental level has built the capacity of the National Expert Committee on AEFI Causality Assessment in **Nigeria (NAFDAC and NPHCDA)**.
 - All these efforts are geared towards ensuring appropriate safety monitoring, causality assessment and adequate information sharing on safety concerns on COVID-19 vaccines.

NAFDAC and International Regulatory Cooperation

- Pre-vaccine roll out **regulatory meetings** - International Coalition of Medicine regulatory Authorities (**ICMRA**)
- Pre-vaccination **World Health Organization** meetings, workshops
- The imminent arrival of COVID vaccines has created an urgent demand for a strong, coordinated, **multi country approach to safety monitoring**
- Post-vaccination **AEFIs, AESIs sharing among ICMRA members**
- The African Union Smart Safety Surveillance (**AU 3S**) coordinated by AUDA NEPAD and MHRA as technical partner is one such co-operation.
 - Four countries National Regulatory Authorities namely: Nigeria, Ghana, Ethiopia and South Africa are participating in the programme

NAFDAC and International Regulatory Cooperation

- Capability trainings on data collection tools for Adverse Events Following Immunization (AEFIs), signal detection and management, safety communication and risk benefit assessments have been conducted across the four countries.
- Landscape assessment of the safety surveillance system was also conducted to identify key gaps and mitigation strategies
- AU-3S Joint Signal Management Group has been established with participants from the four countries as members
- Aggregated safety data harvested from the Med Safety App from the four countries provides source of data for signal detection
 - This provides continental approach to safety monitoring and signal management.

NAFDAC Activities (Examples)

- General awareness education on use of COVID-related commodities
- Debunking unproven claims for cures of COVID-19 and (Ongoing)
 - *Press releases*
 - *NAFDAC and Your Health*
- Guidance for some regulatory processes and Outcomes
 - *COVID-related clinical trials (Therapeutics, Cohort event Monitoring)*
 - *Therapeutics submissions and approvals (Sanitizers: 26-----250) companies; therapeutics – Remdesivir (Compassionate ground permit)*
 - *Medical Devices – testing kits, face masks,*
 - *Manufacturing of personal protective equipment (PPEs)*
 - *Approved the first Nigerian-made medical face mask and protective gown*
 - *Herbal medicines' submissions (Over forty submissions and fifteen Listing approvals)*
 - *Guidance on COVID-19 vaccines preparedness – first NRA in Africa*

NAFDAC Activities (Examples)

- Training of Traceability Technical Working Group by GS1 Technical officers
- Development of In-Country track and trace plan
- Pre-NAFDAC approval of COVID vaccine studying of SRAs assessment reports
- Vaccine Committee review of COVID vaccine dossiers

- Monitoring of Adverse Events Following Immunization
 - *Med Safety App (launched November 2020)*
 - *GS1 technology-driven traceability (launched October 2020)*
 - *Training and deployment of personnel for field safety monitoring (1st quarter 2021)*

Challenges with Routine/Expected Pharmacovigilance Activities

- Despite the deployment of the Med Safety App, a large number of AEFIs are not reported particularly when they are considered mild or non-serious .
- **Downloading and use of the App** still a challenge even with literate users. Sustained awareness and sensitization required.
- **AEFI reports are mainly received from urban and semi-urban areas** with good network coverage. There are few AEFI reports from rural areas due to poor internet penetration and low levels of literacy with the ownership and use of smartphones
- **Undue reliance on other sister agencies** to support data collection at the periphery leading to delays
- **Poor transmission of investigation forms for serious** AEFIs from the States to the National

Lessons learnt

- Targeted multi-stakeholder engagements is a very important factor to continually detect and report AEFIs during and post vaccination .
- **Trainings** to improve implementation of Policy (NPC staff and all PV stakeholders on Covid-19 vaccines roll-out).
- **Electronic data collection tools fully deployed (e-Reporting and Med Safety App)**
- Increase in number of AEFI reports during on-field sensitization and vaccine monitoring however, **post-exposure studies required to monitor effectiveness of vaccines**

In summary,

- Capacity strengthening, electronic data collection tools, online platforms for direct ADR reporting alongside local, national and international stakeholder engagement is critical towards strengthening systems for PV in Nigeria.



Way Forward

- Awareness Creation, Intense sensitization and Enlightenment campaigns
 - Social media
 - Radio and Television
 - Community sensitisations
- Sustained Implementation of country plans
- Increased vaccination via tackling vaccine hesitancy in the populace
- Safety monitoring of medical products (medicines and vaccines) and reporting of ADRs/AEFIs associated with the use of medicines and vaccines using electronic and online reporting tools.
- Monitoring of effectiveness of PV interventions



Conclusion

- Safety monitoring of COVID-19 vaccines is key to characterizing the full safety profile of the vaccine
- Collaboration between the NRA and vaccine manufacturer/MAHs is critical
- Adequate minimization measures put in place in the RMP should be well implemented in conjunction with the NRA oversight



Thank You

Industry Experience and Perspective

Industry Experience and Perspective

Sarah Frise & Jamie Wilkins
(Astra Zeneca) (Pfizer)

Covid-19 Vaccines Risk Management Planning: Stakeholders Experiences and Perspectives

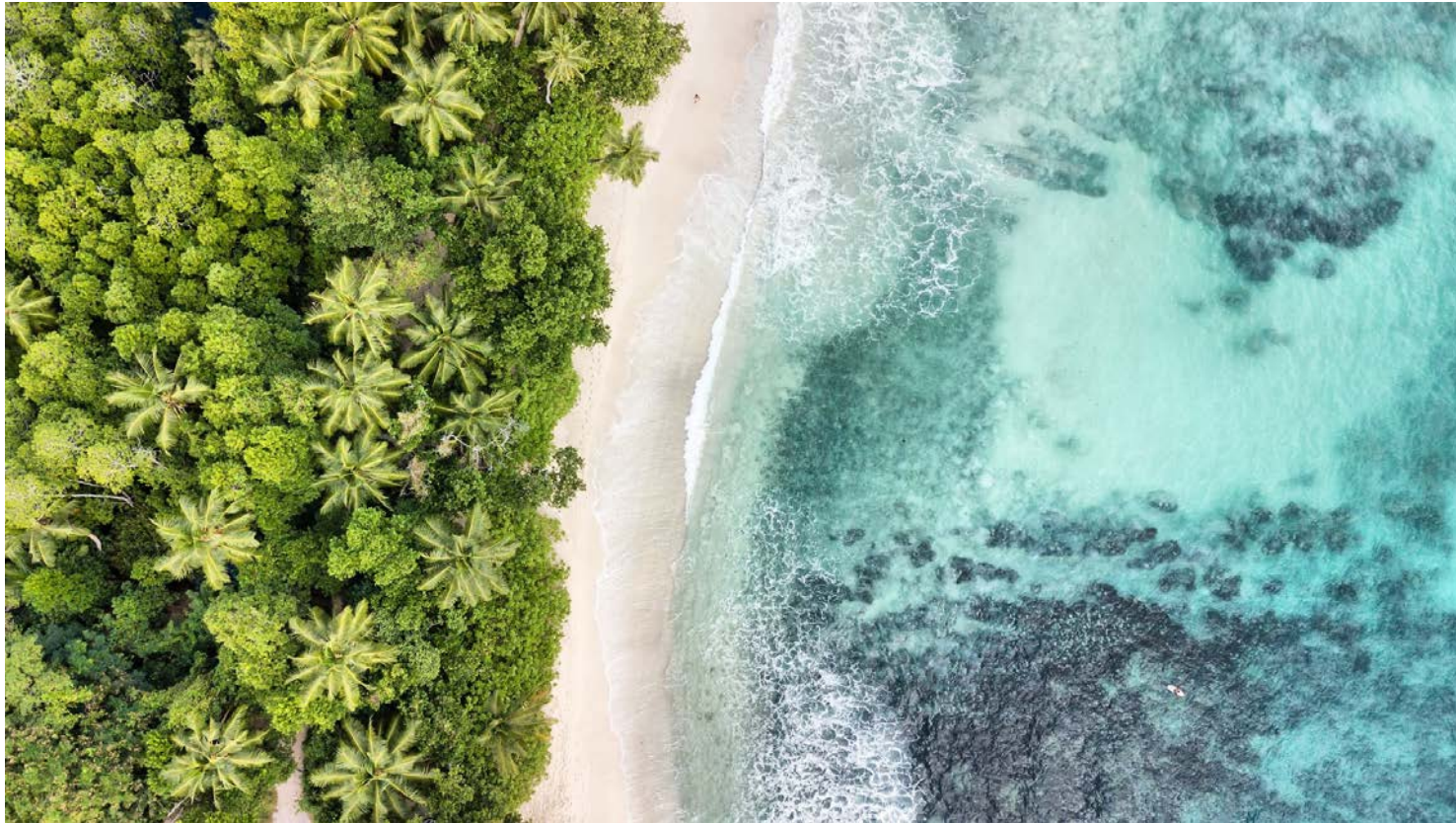
Industry Experience & Perspective

28th April 2021

Jamie Wilkins, Pharm.D., Pfizer Worldwide Safety

Sarah Frise, MSc, Ph.D., Head of Risk Management, Astra Zeneca

WHO Risk Management Plan (RMP) Preparation & Submission: A matter of perspective



Global Risk Management Submission Requirements:



MHRA: RMP Plus²

- GVP V revision 2 template
- + Routine PV
- + Bi-weekly meetings
- + Monthly sPSUR (summary report)
- + Traceability (UK)
- + Numerous PASS (& different)



US FDA: Pharmacovigilance Plan (PVP)

Based on E2B

- + Routine PV
- + Action Plan for Safety Issues
- + Observational Studies



WHO: RMP³

- Based on GVP V rev 2 template
- + Regional Annex



EMA: RMP Plus¹

- GVP V revision 2 template
- + Routine PV
- + Traceability (EU)
- + Signal Detection methods
- + Monthly Summary reports
- + Numerous PASS

1. As per EMA COVID-19 vaccine - https://www.ema.europa.eu/en/documents/other/consideration-core-requirements-rmps-covid-19-vaccines_en.pdf
2. MHRA guidance: PV and RM requirements for COVID-19 vaccines in the UK (not published)
3. COVID 19 Vaccines: Safety surveillance manual: <https://www.who.int/publications/i/item/10665338400>

A number of uncertainties initially:



Process for
review/approval?
Who/What/How?



RMP documentation for
WHO- approach and
strategy?



Length of review?

A core
organizational
Risk
Management
stance provides
agility.

- Core organizational stance on information contained within major regulatory Risk Management Documents:
 - Identified Risks
 - Potential Risks
 - Missing Information
 - Routine PV
 - Studies
- Organizational position on elements to include in core risk management documents vs. appropriate information for addendum
- Provides ability to quickly mobilize for submissions; formatting may differ based on regulatory requirements however, content is consistent.

Challenges and Opportunities

Potential Challenges

- Unknown requirements
- Co-existing products in certain countries (COVAX supply vs. approved/authorized product via typical process)
- Additional requests and clarifications from WHO
- Implementation of pharmacovigilance in LMICs

Potential Opportunities

- Unique perspective during pandemic
- Innovative methods of implementing requirements
- Global knowledge sharing
- RMP structure for LMICs
- Flexibility and agility

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Industry Experience and Perspective

**Marc Ceuppens
(Janssen)**



COVID-19 Vaccines Risk Management Planning: Stakeholders Experiences and Perspectives

The Janssen Experience

Marc Ceuppens, MD – Janssen Global Medical Safety – 28/04/21

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Nelly Velez, *The World Among Us*
Artwork from Gilda's Club



Background

- Format

- Core Risk Management Plan

- Template EMA/164014/2018 Rev.2.0.1: Guidance on Format of the Risk Management Plan (RMP) in the EU – in Integrated Format, 31-Oct-2018 and Considerations on core requirements for RMPs of COVID-19 vaccines EMA/544966/2020
 - Support development EU-RMP, US PV Plan, meet Local Country requirements (Addenda)

- Learnings from Ad26.ZEBOV vaccine

- Accelerated development

- Evolving knowledge COVID-19
 - AESI: Identification, case definition and background incidences
 - Parallel development with Phase 3 trials conduct
 - Addressing 'Missing Information' and further risk characterisation through PA(S)S program

Challenges

- Exposure data
 - Product specific
 - Stratification age – gender – racial/ethnic origin
- Reliable background incidences for Observed/Expected calculations
- Meeting multiple country expectations
 - The rapid development of new and updated COVID-19 vaccine-specific local/regional regulatory guidance
 - Local epidemiology data (population exposure, concurrent disease, ...)
 - AESI selection
 - PA(S)S requirements
 - Post-marketing periodic reporting
- PA(S)S set-up and roll-out
- Assessing effectiveness risk minimisation tools
 - Monitoring and reporting AEFIs through local surveillance



Thank You

Nelly Velez, *The World Among Us*
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Industry Experience and Perspective

**Polina Dombure
(Inpharmatis)**



Sputnik V (Gam-Covid-Vac)

Risk Management Plan preparation

Success and Challenges

28.04.2021

By Dr. Polina Dombure, CEO, Inpharmatis Group



Collaboration



- **National Research Center of Epidemiology and Microbiology n.a. N.F. Gamaleya** is the world's leading research institution founded in 1891
- The Center successfully created the world's first Ebola virus vaccine. A MERS vaccine is currently in advanced stages of clinical trials. Both vaccines are based on the human adenovirus vector platform used for Sputnik V
- The Center runs one of the world's only "virus collection" and has its own vaccine production facility



- **Sovereign Wealth Fund of Russia** established in 2011
- RDIF has played a key role in fighting COVID-19 in Russia. The Fund has selected and funded the most promising testing system (COVID-19 SmartAmp), drug (Avifavir) and vaccine (Sputnik V) for COVID-19
- RDIF is supporting the development of Russia's COVID-19 vaccine by the Gamaleya Center
- RDIF has the exclusive license for the sale and manufacture of Sputnik V vaccine in international markets



- 20+ years of proven experience operating in the EU, Russia and CIS region
- Partnership with leaders in pharmaceutical and medical device industry - proven compliance with high-quality standards
- Consulting for RDIF & Gamaleya on Sputnik V from the beginning – providing high level scientific and medical expert advice
- EMA / WHO Rolling Review Procedures for Sputnik V vaccine
- Global Pharmacovigilance Set Up fulfilling the requirements EU, WHO and acting as EU QPPV, as well as centralised management of all safety data for Sputnik V vaccine

Developer of Vaccine

Authorised for production and distribution outside of Russia

Global Pharmacovigilance for Sputnik V

Inpharmatis Role

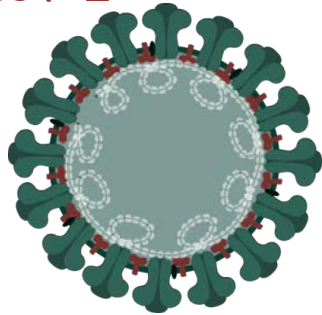
- Regulatory support in WHO & EMA Rolling Review Procedure
- Global Pharmacovigilance provider for Sputnik V vaccine
- Global ADR collection / Case Processing / Case Submission
- Global Pharmacovigilance database management
- Global Literature Search
- Aggregate Report Preparation
- Signal Detection
- CMO, CRO and local PV partners management & support
- Medical Information Management
- Regulatory Intelligence etc.



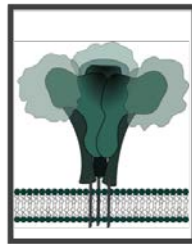
Sputnik V Product Presentation

Sputnik V short overview

SARS-CoV-2

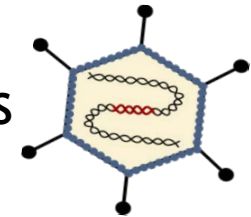


Glycoprotein S



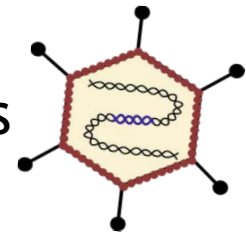
Component 1

rAd26-S



Component 2

rAd5-S

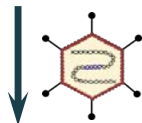
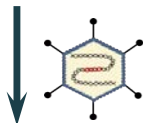


10^{11} viral particles (vp) per dose for both rAds

VACCINATION REGIMEN:

Component 1

Component 2



0

21

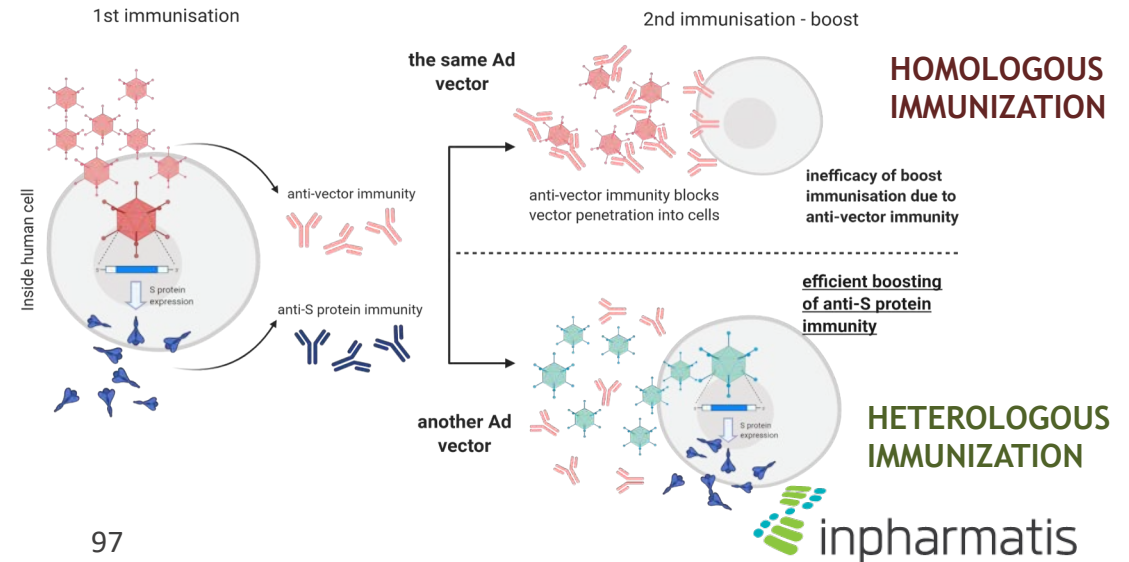
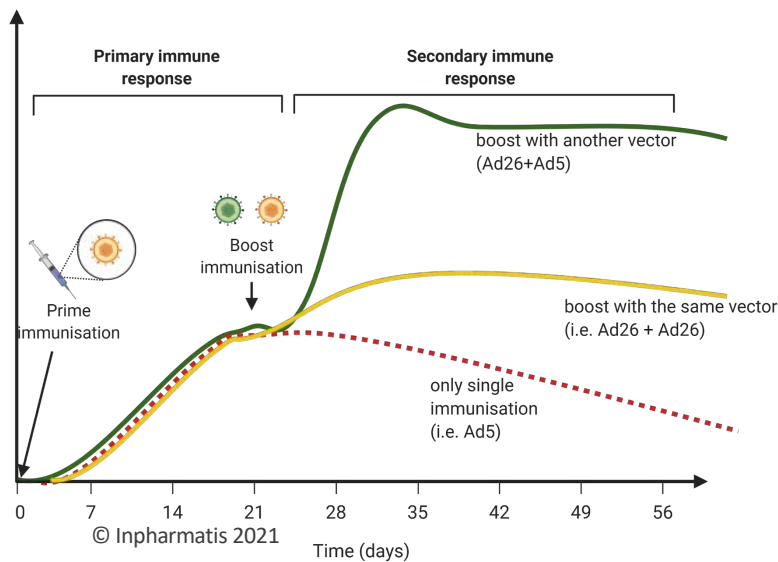
DAYS



Sputnik V Short Overview:

Advantages of heterologous prime-boost immunisation

- Boosting of the primary immune response is important for a long-lasting immunity
- Prime immunization induces anti-vector immunity which affects efficacy of the boost immunisation
- Heterologous prime-boost immunisation might overcome anti-vector immunity
- rAd26 and rAd5 are distinct vector serotypes with a low probability to induce cross-serotype immunity





Phase III Results

Phase III: Interim Report

Primary Endpoint

- Proportion of trial subjects with COVID-19 disease developed

Secondary Endpoint

- The percentage of trial subjects with mild, moderate, severe, and extremely severe COVID-19

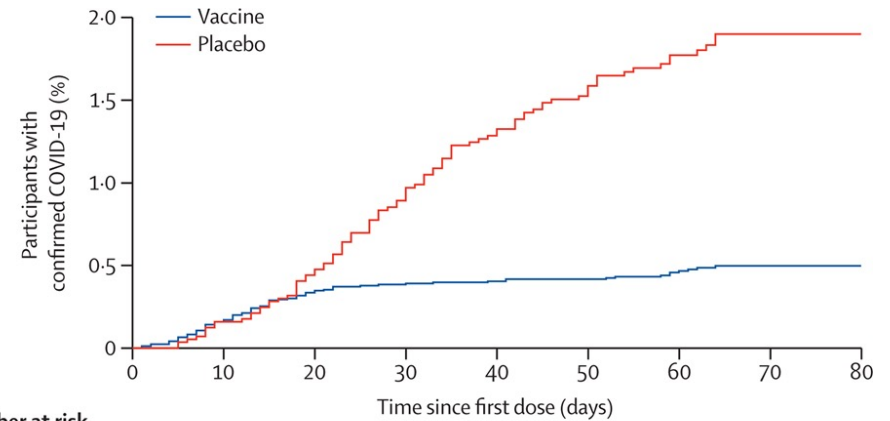
Secondary Endpoint / Immunogenicity

- Percentage of trial subjects with a fourfold or more increase in the titer of SARS-CoV-2 glycoprotein-specific antibodies
- Interferon gamma concentration in T-cells after repeat stimulation with the SARS-CoV-2 glycoprotein
- Geometric mean virus-neutralizing antibodies titre
- **Secondary Endpoint / Safety:** Incidence and severity of adverse events (including adverse events of a particular interest) in the study subjects

Phase III Efficacy: Interim Analysis

Overall from 21 days after dose 1					●	91.6 (85.6-95.2)
Age strata	18-30				●	91.9 (51.2-99.3)
	31-40				●	90.0 (71.1-96.5)
	41-50				●	91.3 (73.7-96.9)
	51-60				●	92.7 (81.1-97.0)
	>60				●	91.8 (67.1-98.3)
Sex	Female				●	87.5 (73.4-94.2)
	Male				●	94.2 (87.2-97.4)
Moderate/severe cases					●	100 (94.4-100.0)
Anytime after dose 1					●	73.1 (63.7-80.1)
From 14 days after dose 1					●	87.6 (81.1-91.8)

0 25 50 75 100



Number at risk
(number of COVID-19 cases)

Vaccine	16 427 (0)	15 338 (35)	15 117 (61)	14 683 (66)	10 970 (70)	6 686 (71)	3 314 (77)	398 (79)
Placebo	5 435 (0)	5 121 (10)	5 046 (30)	4 895 (54)	3 662 (71)	2 223 (87)	1 106 (92)	133 (96)

• The efficacy of the Sputnik V vaccine is 91.6% (95%CI: 85.6-95.2), based on the interim analysis of 78 confirmed COVID-19 cases: 16 cases in vaccine group (n=14964) and 62 cases in placebo group (n=4902). Calculation was based on the analysis of data of volunteers who received both doses of the vaccine or placebo

• From 15 to 21 days after the first dose, efficacy was 73.6% (p=0.048)

• The efficacy of the Sputnik V vaccine is comparable within different age and sex groups

Phase III Interim Safety

The safety study included **21 862 volunteers**, who received at least one dose of vaccine or placebo.

During the study among 21 862 volunteers (who received at least one dose), 70 episodes of SAE not related to COVID-19 were recorded in 68 volunteers: in 45 volunteers from the vaccine group and 23 volunteers from the placebo group.

No one of registered SAEs was associated with vaccination.

There were **no vaccine-related deaths** reported.

There were 3 SAEs reported in the vaccine group 3 days after administration: renal colic, deep vein thrombosis, and extremity abscess (third finger). SAE was diagnosed on the basis that in all three cases the event required hospitalization for study participants. **No association was found between SAE and the vaccine administration.**

The most common adverse events were influenza-like illness and local reaction. During the study, among volunteers 60+, 3 episodes of AEs grade 3 or more, not associated with vaccination, were recorded: in the vaccine group an exacerbation of urolithiasis and acute sinusitis, in the placebo group an influenza-like illness. All these AEs were resolved without consequences.

**Based on 21 862 volunteers data (who received at least 1 dose).
No one of registered SAEs was associated with vaccination.
Most post-vaccinal systemic and local reactions (93-96%) were mild.**

Conclusions



Interim analysis of Sputnik V phase 3 trial in participants aged 18 years or older showed:

- Vaccine is effective in preventing symptomatic COVID-19 cases with 91.6% efficacy after day 21 from the Dose 1.
- Vaccine induces robust humoral and cellular immune response.
- Vaccine has a good safety profile.
- More than 8 million doses of Sputnik V have already been administered to the public
- Vaccine has EUA in 62 countries.

Sputnik V Safety Profile To Date

Sputnik V Safety Profile

Summary of the safety profile

The safety assessment was carried out in the framework of three clinical studies of the safety, tolerability and immunogenicity of the Sputnik V vaccine for the prevention of the new coronavirus infection (COVID-19), in healthy male and female volunteers and in healthy volunteers of 60 years and older. Safety assessments in these studies were performed in a similar manner and included assessment of AE incidence, vital signs, the results of instrumental studies, physical examination, and laboratory parameters (full blood count, biochemical blood test and urinalysis).

Adverse events specific to the vaccine use identified in clinical trials of the Sputnik V vaccine, as well as studies of other vaccines based on of a similar technological platform, can be predominantly mild or moderate, can develop in the first or second days after vaccination and are resolved within 3 consecutive days. The following short-term general reactions: short-term flu-like syndrome, characterized by chills, fever, arthralgia, myalgia, asthenia, general malaise, headache and local (soreness at the injection site, hyperemia, swelling) may develop more often than others.

The prescription of non-steroidal anti-inflammatory drugs (NSAIDs) is recommended for fever after vaccination. Such reactions as nausea, dyspepsia, decreased appetite, and sometimes an increase in regional lymph nodes can occur less frequently. Some patients may develop allergic reactions, a short-term increase in the level of hepatic transaminases, creatinine and creatine phosphokinase in the blood serum.

Most of the adverse events reported in clinical studies resolved without consequences. Laboratory abnormalities of immunological parameters had no clinical significance and did not require additional diagnostic procedures and therapy.

Description	Group 1 (IP) N = 14964		Group 2 (Placebo) N = 4902		Total N = 19866		P value
	N	%	N	%	N	%	
Any PT	6670	44.6	1328	27.1	7998	40.3	<0.001
<i>General disorders and injection site reactions (12035 AE episodes)</i>							
Influenza-like illness	3667	24.5	524	10.7	4191	21.1	<0.001
Reaction at injection site	3273	21.9	205	4.2	3478	17.5	<0.001
Hyperthermia	823	5.5	135	2.8	958	4.8	<0.001
Asthenia	477	3.2	139	2.8	616	3.1	0.217
Chills	131	0.9	26	0.5	157	0.8	0.018
Pyrexia	124	0.8	6	0.1	130	0.7	<0.001
Sensation of fever	77	0.5	27	0.6	104	0.5	0.760
Chest pain	67	0.4	11	0.2	78	0.4	0.030
Hyperhidrosis	65	0.4	15	0.3	80	0.4	0.218
Malaise	53	0.4	12	0.2	65	0.3	0.244
Disorder of the regulation of the autonomic nervous system	36	0.2	6	0.1	42	0.2	0.118
Organ system total	6006	40.1	916	18.7	6922	34.8	<0.001
<i>Nervous system disorders (1276 AE episodes)</i>							
Headache	705	4.7	244	5.0	949	4.8	0.448
Impaired sense of taste	26	0.2	9	0.2	35	0.2	0.887
Doubtfulness	25	0.2	6	0.1	31	0.2	0.492
Organ system total	855	5.7	278	5.7	1133	5.7	0.911
<i>Respiratory, chest, and mediastinal disorders (1018 AE events)</i>							
Oropharyngeal pain	142	0.9	43	0.9	185	0.9	0.650
Rhinorrhea	139	0.9	58	1.2	197	1.0	0.119
Cough	133	0.9	48	1.0	181	0.9	0.563
Nasal congestion	110	0.7	42	0.9	152	0.8	0.396
Parosmia	43	0.3	26	0.5	69	0.3	0.012
Nasopharyngitis	34	0.2	13	0.3	47	0.2	0.635
Shortness of breath (30%);	25	0.2	9	0.2	34	0.2	0.808
Organ system total	578	3.9	226	4.6	804	4.0	0.021
<i>Muscular, skeletal, and connective tissue disorders (671 AE episodes)</i>							
Myalgia	263	1.8	45	0.9	308	1.6	<0.001
Arthralgia	101	0.7	25	0.5	126	0.6	0.207
Musculoskeletal pain	86	0.6	16	0.3	102	0.5	0.035
Pain on the back side	32	0.2	9	0.2	41	0.2	0.685
Organ system total	502	3.4	106	2.2	608	3.1	<0.001
<i>Vascular disorders (655 AE episodes)</i>							
Hypertension	286	1.9	70	1.4	356	1.8	0.027
dizziness	118	0.8	49	1.0	167	0.8	0.160
Hypotension	55	0.4	11	0.2	66	0.3	0.131
Hypertensive crisis	15	0.1	3	0.1	18	0.1	0.588
Organ system total	474	3.2	134	2.7	608	3.1	0.126

Sputnik V Safety Profile

<i>Gastrointestinal disorders (487 AE episodes)</i>							
Nausea	91	0.6	24	0.5	115	0.6	0.342
Dyspepsia	71	0.5	22	0.4	93	0.5	0.819
Diarrhea	69	0.5	20	0.4	89	0.4	0.629
Stomachache	40	0.3	15	0.3	55	0.3	0.655
Abdominal discomfort	29	0.2	3	0.1	32	0.2	0.062
Organ system total	351	2.3	92	1.9	443	2.2	0.054
<i>Heart disorders (180 AE episodes)</i>							
Tachyarrhythmia	83	0.6	17	0.3	100	0.5	0.074
Angina pectoris	43	0.3	7	0.1	50	0.3	0.080
Organ system total	138	0.9	28	0.6	166	0.8	0.019
<i>Vision disorders (69 episodes of AE)</i>							
Decreased visual acuity	89	0.6	19	0.4	108	0.5	0.087
Visual disturbance	22	0.1	5	0.1	27	0.1	0.458
Organ system total	50	0.3	17	0.3	67	0.3	0.894
<i>Injury, intoxication and complications of procedures (63 episodes of AE)</i>							
Poisoning	39	0.3	5	0.1	44	0.2	0.040
Organ system total	48	0.3	8	0.2	56	0.3	0.071
<i>Immune system disorders (61 AE episodes)</i>							
Hypersensitivity	19	0.1	4	0.1	23	0.1	0.628
Organ system total	46	0.3	14	0.3	60	0.3	0.809
<i>Infections and invasions (64 episodes of AE)</i>							
Oral herpes	16	0.1	5	0.1	21	0.1	0.927
Organ system total	39	0.3	16	0.3	55	0.3	0.447
<i>Metabolic and nutritional disorders</i>							
Decreased appetite	29	0.2	4	0.1	33	0.2	0.107
Organ system total	35	0.2	4	0.1	39	0.2	0.039
<i>Skin and subcutaneous tissue disorders (47 episodes of AE)</i>							
Rash	15	0.1	7	0.1	22	0.1	0.437
Organ system total	32	0.2	12	0.2	44	0.2	0.689
<i>Disorders of the blood and lymphatic system (24 episodes of AE)⁵</i>							
Organ system total	22	0.1	2	0.0	24	0.1	0.093
<i>Hearing and labyrinth disorders (22 episodes of AE)⁶</i>							
Organ system total	18	0.1	2	0.0	20	0.1	0.192
<i>Kidney and urinary tract disorders (24 episodes of AE)</i>							
Organ system total	18	0.1	6	0.1	24	0.1	0.971
Notes:							
4. The findings are presented as the number of subjects with reported AEs and the percentage of the safety population in a given group.							
5. Enlarged lymph nodes, lymphadenopathy							
6. Noise in ears							

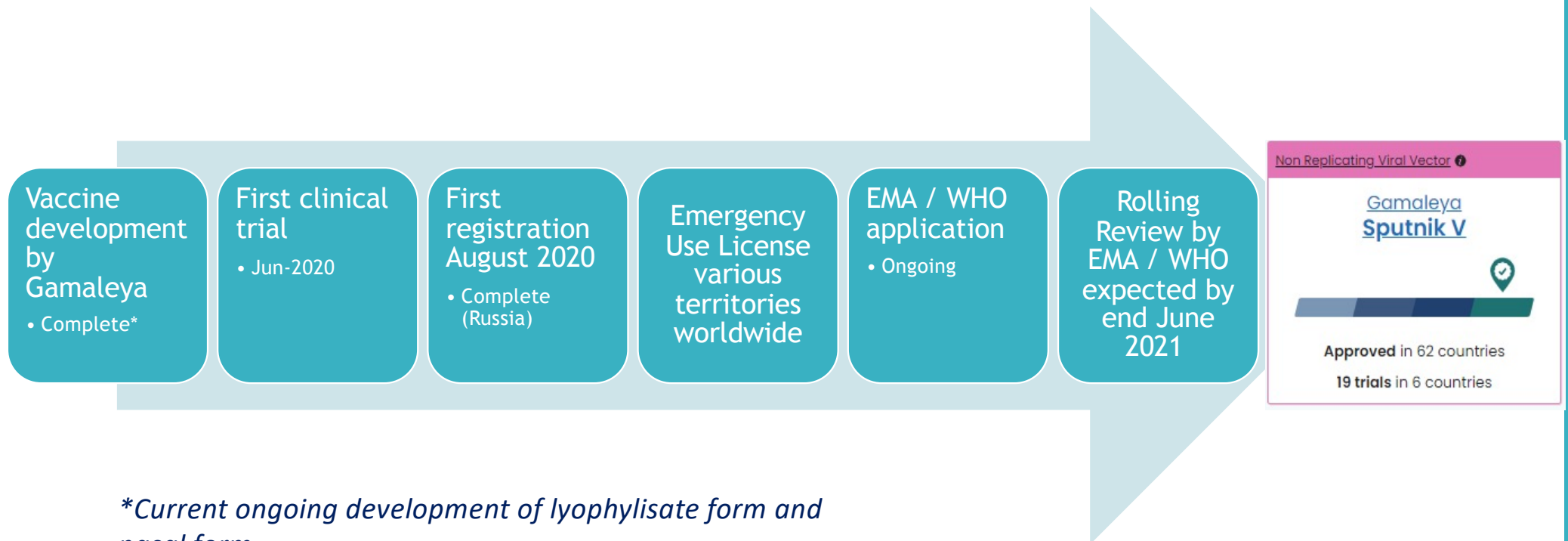


Global Pharmacovigilance System for Sputnik V

Key Safety Data of SPUTNIK-V Vaccine

- Key safety data are based on the following study:
 - Randomized Double-Blind Placebo Controlled Clinical Trial of Efficacy, Immunogenicity and Safety of the Gam-COVID-Vac Vaccine against the SARS -CoV-2 Infection (The Lancet 2021 Feb 20)
 - 21963 subjects were randomized in a ratio of 3:1 vaccine group / placebo group.
 - Safety Analysis - 19,866 volunteers (14964 vaccine / 4902 placebo).
 - A total of 16,795 AEs were registered during the study
 - 6670 (44%) vaccine
 - 1328 (27%) placebo
- RMP was developed by Gamaleya according to Eurasian Union & Russian Federation Requirements
- Global RMP was developed according to EMA's requirements by Inpharmatis

Sputnik Roadmap



**Current ongoing development of lyophilisate form and nasal form*

Challenges with RMP Development

- Market entry from Russian Federation
- Eurasian Union GVP requirements are very similar to European GVP requirements
- Many on-going Clinical Trials around the world, including with another vaccine
- Many Emergency Use Authorizations in the world
- Many CMOs around the world for Sputnik V
- Data derived from other vaccines / PRAC recommendations should be considered (e.g., thrombosis events)
- Daily received new information from the market that requires urgent processing, centralization, analysis and conclusions requiring urgent RMP update
- Different RMP or RMP-like expectations (format, frequency) globally

Our Conclusions and Recommendations

- RMP for COVID-19 vaccines is a “live” document, that must be updated on almost monthly basis
- Global RMP must be managed according to the highest regulatory standards despite possible deviations in expectations of various Regulators
- Safety profile and measures for risk management must be reviewed on daily basis and RMP is not the best document for the management of such task
- Guidance from EMA, WHO and other Regulators is highly appreciated
- Harmonisation of safety data with other vaccine manufacturers is needed



Thank you for your attention

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Industry Experience and Perspective

**Jiayi Wang
(Sinovac)**



Covid-19 Vaccines Risk Management Planning: Stakeholders Experiences and Perspectives

Jiayi Wang PV Supervisor

科兴控股生物技术有限公司
SINOVAC BIOTECH LTD.

2021年5月20日星期四

RMP Experiences

- ◆ SINOVAC COVID-19 vaccine obtained Conditional Marketing Authorization in China on 5th February 2021 and obtained EUA in many Countries/Regions worldwide, as of now.
- ◆ SINOVAC is in the process of answering the Second List of Questions focusing on RMP for Emergency Use Listing (EUL).
- ◆ SINOVAC has submitted RMP to EMA for Obtaining an EU marketing authorization.

AEFI Collection in Countries/Regions outside China

- ◆ Sign Pharmacovigilance Agreements with local agents or MOH/DOH
Usually take a couple of days. Not in a timely manner.
- ◆ AEFI reporting with CIOMs Form (Serious and Non-serious)
Time consuming with huge volume of reports under mass vaccination
Changed to Excel Spreadsheet for Non-serious AEFI
- ◆ AEFI reporting from Countries/Regions with immature PV system
Not available. Need to figure out a way to get more AEFI information

SINO VAC 科兴

为人类消除疾病提供疫苗
Supply Vaccines to Eliminate Human Diseases



官方微信号



让中国儿童使用国际水平的疫苗 让世界儿童使用中国生产的疫苗

科兴以“为人类消除疾病提供疫苗”为使命，致力于人用疫苗及其相关产品的研究、开发、生产和销售，为我国乃至全球的疾病预防控制提供服务。

Round table

Panelists

- Petra Doerr (WHO)
- Shanthi Pal (WHO)
- Nora Dellepiane (former WHO PQ)
- Emil Cochino (EMA)
- Helaine Carneiro Capucho (Brazil)
- Juan Roldan (Chile)
- Mojisola Christianah Adeyeye (Nigeria)
- Corinne Jouquelet-Royer (IFPMA)
- Alexander Precioso (DCVMN)

Moderator

Katharina Hartmann

Q&A curator

Gabrielle Breugelmans

Summary and conclusions

Shanti Pal (WHO)

Jakob Cramer (COVAX)

**Summary &
conclusions**

Thank you