SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA's Vaccine Authorisation Process

09 September 2021

SAHPRA's Governing Acts

Medicines & Related Substances Act of 1965

- **Efficient, effective and ethical assessment and regulation** of health products that meet defined standards of quality, safety, efficacy and performance;
- **Transparent, fair, objective and timeous assessment** and registration;
- In executing its functions, the Authority may enter into agreements to **co-operate** with any regulatory authority in order to achieve the objects of this Act.

Hazardous Substances Act Act 15 of 1973

- Within the Medicines Act, "medical device" means any **instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article contemplated in the Hazardous Substances Act**, 1973 (Act No. 15 of 1973).
- The Hazardous Substances Act (HSA) provides for the **efficient, effective and ethical evaluation** and registration of non-ionising radiation emitting devices and radioactive nuclides.

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SAHPRA'S MANDATE

MONITOR | EVALUATE | REGULATE | INSPECT | REGISTER | CONTROL

ROLE OF THE CEO

REGULATORY DECISIONS

Based on technical assessment by internal and contracted experts in consultation with the expert committee members

APPEAL REVIEW

As set out in Section 24 (A) of the Medicine and Related Substances Act

APPLICANT WITH FAILED APPEAL RESERVES THE RIGHT TO APPEAL TO THE MINISTER IN WRITING WITHIN 30 DAYS UPON PAYMENT OF PRESCRIBED FEE

REGULATION 48 PROVIDES HOW THE APPEAL COMMITTEE CAN BE APPOINTED AND THE PROCEDURES THAT COULD BE FOLLOWED.

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Governance Framework

1 PFMA Schedule 3A Public Entity

- Autonomous entity
- Operates independently

2 Entity of National Department of Health

- Previously Medicines Control Council within the National Department of Health.
- 4th year of operation as a schedule 3A public entity

3 Governance structures in place

- Accountable and reports to the Minister of Health and Parliament through the SAHPRA board
- The board is appointed by the Minister
- The board has a governance and strategic oversight role

4 Mandate: Safety, Quality, Efficacy and Performance

- Regulates all health products for human and animals use

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SAHPRA process & procedures align with international regulators

- The regulatory requirements applied by SAHPRA are consistent and harmonized with those of other regulators
- Alignment and Reliance on the WHO Prequalification and Emergency Use Listing
- International Coalition of Medicines Regulatory Authorities (ICMRA) and WHO
  - forum to support strategic coordination and international cooperation among global medicine regulatory authorities
  - Members include, SAHPRA (SA), USFDA (USA), TGA (Australia), Health Canada (Canada), EMA(Europe), NAFDAC (Nigeria), ANVISA (Brazil) to name a few
- SAHPRA's role spans three critical areas

1. QUALITY
2. SAFETY
3. EFFICACY

- Post market surveillance is a critical part of oversight of the products along the value chain

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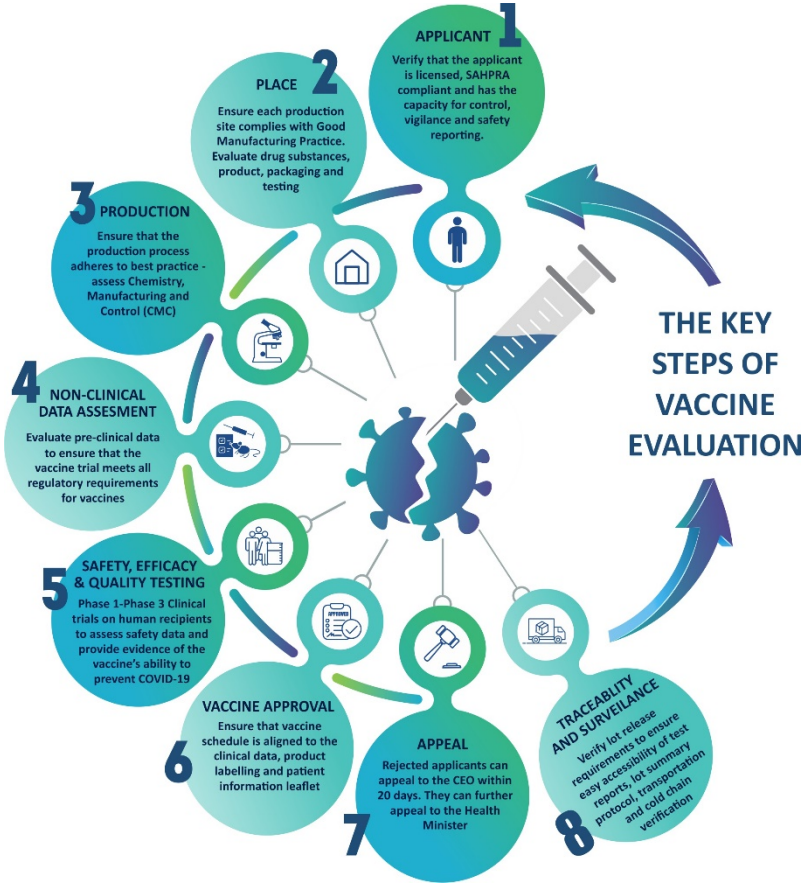
Vaccines Authorisation Process

Key steps of COVID-19 vaccine assessment



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PLACE 2

Ensure each production site complies with Good Manufacturing Practice. Evaluate drug substances, product, packaging and testing

Assessment of CGMP

Compliance of Good Manufacturing Practice

Sites producing drug substance (DS), drug product(DP), filling, packing, testing

NOTE

- **Inspections performed at sites that are not GMP certified must be executed by an authority SAHPRA aligns with**
- **SAHPRA is a member of WHO Pharmaceuticals Inspections Cooperation (PICS). Thus, other regulators can rely on the inspection outcome by SAHPRA**
- **SAHPRA has an upcoming PICS audit in 2021**

THE KEY ASPECTS OF VACCINE EVALUATION

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Assessment of CMC

CHEMISTRY | MANUFACTURING | CONTROL

FOCUS ON HOW DRUG SUBSTANCE AND DRUG PRODUCT ARE:

- Manufactured
- Characterized
- Impurities are monitored and controlled
- Control tests and limits are justified within specified limits
- Test methods are used
- Tests are validated
- Standards are referenced and used
- Packaged – packing materials and stability

THE KEY ASPECTS OF VACCINE EVALUATION

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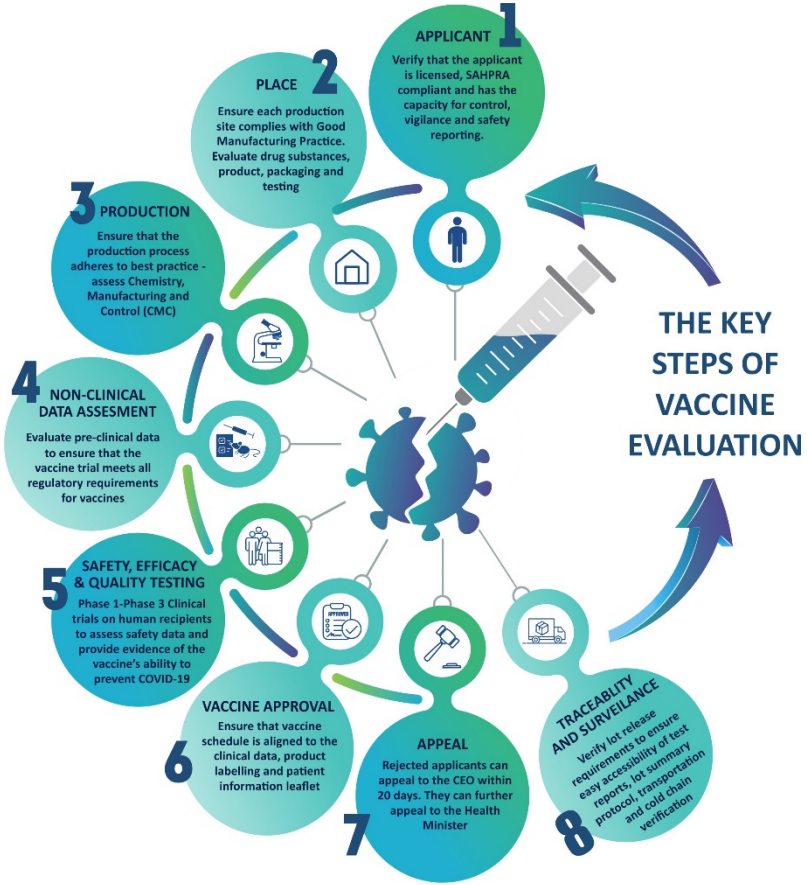
Key Steps of COVID-19 Vaccine Assessment



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Clinical Studies Assessment

5 SAFETY, EFFICACY & QUALITY TESTING

Phase 1-Phase 3 Clinical trials on human recipients to assess safety data and provide evidence of the vaccine's ability to prevent COVID-19

THE KEY ASPECTS OF VACCINE EVALUATION

ASSESSMENT OF SAFETY DATA

- Requires an adequate number of vaccine recipients and monitoring for a sufficiently long time
- Safety is monitored across all three phases of clinical trials

ASSESSMENT OF EFFICACY DATA

- Requires robust evidence of the vaccine's ability to prevent infection/reduce disease severity from well-conducted phase 3 clinical trials in humans
- Clinical data does not have to be generated in SA only
- SAHPRA may require data considering the local disease burden or disease epidemiology i.e in case of COVID-19 SAHPRA required efficacy against variants of concern

ASSESSMENT OF RISK MANAGEMENT PLAN

- Applicant's ability to record and report side effects
- In the case of COVID-19, assessment of efficacy against emerging variants of concerns is critical

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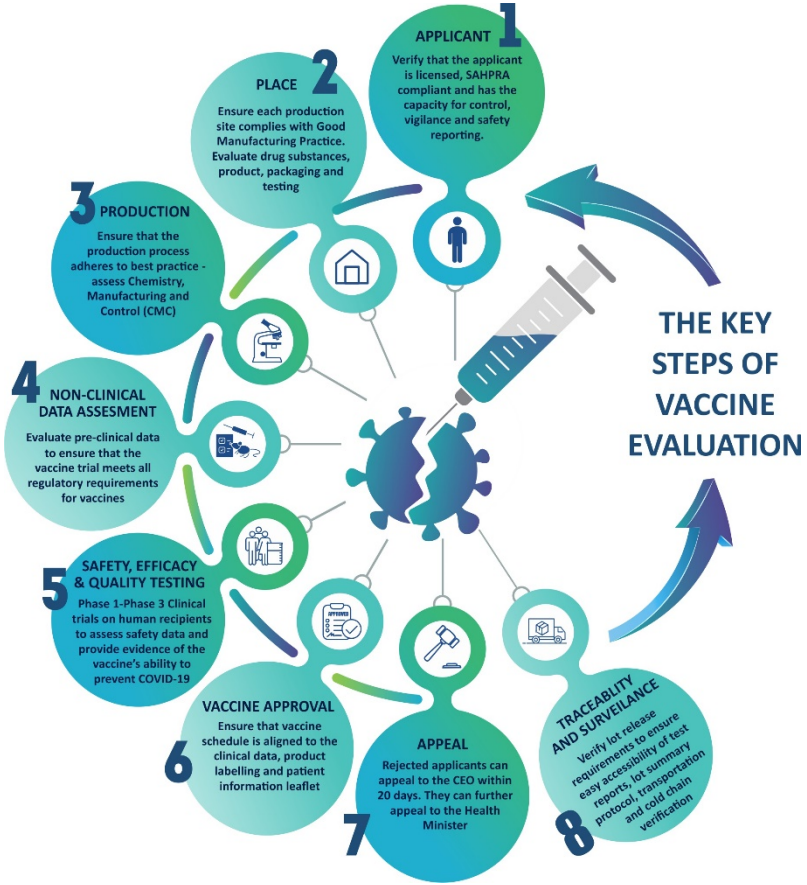
Key Steps of COVID-19 Vaccine Assessment



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THE KEY ASPECTS OF VACCINE EVALUATION

TRACEABILITY AND SURVEILANCE

LOT RELEASE TESTING

- Lot release is part of the regulation of vaccines and involves the independent assessment of each individual lot of a licensed vaccine before it is released onto the market
- Conducted by the SA National Control Lab for Biological products
- SAHPRA contracted lab to provide lot release testing for all locally manufactured and imported vaccines
- The WHO Guidelines for Independent Lot Release of Vaccines by Regulatory Authorities describe the role and responsibilities of a NCL:
    - NCLs support regulatory authorities
    - Control the quality of medicinal (biological) products available on the market
    - Monitor manufacturing process of each lot of imported vaccine
    - Monitor manufacturing process of each lot of locally manufactured vaccine
- Accreditation
    - SANAS ISO 17025:2017
    - GMP licenced (SAHPRA)
    - WHO approved

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COVID-19 Vaccines Updates

Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process

19 August 2021

	Manufacturer / WHO EUL holder	Name of Vaccine	NRA of Record	Platform	EOI accepted	Pre-submission meeting held	Dossier accepted for review*	Status of assessment**	Decision date***
1.	BioNTech Manufacturing GmbH	BNT162b2/COMIRNATY Tozinameran (INN)	EMA	Nucleoside modified mNRA	✓	✓	✓	Finalized: Additional sites: – Baxter Oncology GmbH Germany (DP) – Novartis Switzerland – Mibe (Dermapharm) Germany (DP) Diluent suppliers: – Pfizer Perth, AustraliaFresenius Kabi, USA	31/12/2020 30/06/2021 08/07/2021 16/07/2021 18/062021
			USFDA				✓	Finalized: – Pharmacia & Upjohn, Kalamazoo (DP)PGS McPherson (DP)	16/07/2021 16/07/2021
2.	AstraZeneca, AB	AZD1222 Vaxzevria	EMA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Core data finalized	16 April 2021
							✓	Finalized: Additional sites: – SK-Catalent – Wuxi (DS) – Chemo Spain – Amylin Ohio US (DP)	 16 April 2021 30 April 2021 04 June 2021 23 July 2021
3.		AZD1222 Vaxzevria	MFDS KOREA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	15 Feb 2021
4.		AZD1222 Vaxzevria	Japan MHLW/PMDA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	09 July 2021
5.		AZD1222 Vaxzevria	Australia TGA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	09 July 2021
6.									
7.	Serum Institute of India Pvt. Ltd	Covishield (ChAdOx1_nCoV-19)	DCGI	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	15 Feb 2021

Status of COVID-19 vaccines within WHO EUL/PQ Evaluation process

19 August 2021

	Manufacturer / WHO EUL holder	Name of Vaccine	NRA of Record	Platform	EOI accepted	Pre-submission meeting held	Dossier accepted for review*	Status of assessment**	Decision date***
8.	Janssen–Cilag International NV	Ad26.COV2.S	EMA	Recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored vaccine encoding the (SARS-CoV-2) Spike (S) protein	✓	✓	✓	Core data finalized (US +NL sites)	12 March 2021
							Additional sites: - Merck, Durham, UK (DS) - Merck, West Point/PA (DP)	Finalized – Aspen RSA (DP) – Catalent Agnani Italy (DP) - Future submission - Future submission	-25 June 2021 - 02 July 2021 - As submitted - As submitted
9.	Moderna Biotech	mRNA-1273	EMA	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)		✓	✓	Finalized	30 April 2021
			USFDA	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)	✓	✓	✓	Finalized ModernaTx. Norwood (DS) - Catalent Indiana, LLC (DP) - Lonza Biologics, Inc. Portsmouth, USA (DS) - Baxter, Bloomington, USA (DP)	06 August 2021
10.	Sinopharm / BIBP[3] Beijing Institute of Biological Products Co., Ltd. (BIBP)	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV)	NMPA	Inactivated, produced in Vero cells	✓	✓	✓	Finalized	07 May 2021
11.	sinovac Sinovac Life Sciences Co., Ltd. Sinovac Life Sciences Co., Ltd.	COVID-19 Vaccine (Vero Cell), Inactivated/ Coronavac™	NMPA	Inactivated, produced in Vero cells	✓	✓	✓	Finalized	01 June 2021
12.	THE GAMALEYA NATIONAL CENTER	Sputnik V	Russian NRA	Human Adenovirus Vector-based Covid-19 vaccine	Additional information submitted	Several meetings have been and continue to be held.	"Rolling" submission incomplete.	On hold, awaiting completion of rolling submission	Anticipated date will be set once all data is submitted and follow-up of inspection observations completed.
13.	BHARAT BIOTECH Bharat Biotech, India	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)/ COVAXIN	DCGI	Whole-Virion Inactivated Vero Cell	✓	✓	Rolling data started 06 July 2021	Ongoing	To be confirmed
14.	Sinopharm / WIBP[2]	Inactivated SARS-CoV-2 Vaccine (Vero Cell)	NMPA	Inactivated, produced in Vero cells	✓	✓	Rolling data started 23 July 2021	Ongoing	To be confirmed
15.	康希诺生物 CanSinoBIO	Ad5-nCoV	NMPA	Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector)	✓	✓	Rolling data started 09 August 2021		
16.	NOVAVAX	NVX-CoV2373/Covovax	EMA	Recombinant nanoparticle prefusion spike protein formulated with Matrix M™ adjuvant.	✓	✓	Rolling data starting in August 2021		
17.	SANOFI	CoV2 preS dTM-AS03 vaccine	EMA	Recombinant, adjuvanted	✓	✓	Rolling data started 30 July 2021		
18.	SERUM INSTITUTE OF INDIA PVT. LTD.	NVX-CoV2373/Covovax	DCGI	Recombinant nanoparticle prefusion spike protein formulated with Matrix-M™ adjuvant.	✓	10 August 2021	Rolling data starting in August 2021		

Status of COVID-19 vaccines within WHO EUL/PQ Evaluation process

19 August 2021

	Manufacturer / WHO EUL holder	Name of Vaccine	NRA of Record	Platform	EOI accepted	Pre-submission meeting held	Dossier accepted for review*	Status of assessment**	Decision date***
19.	Clover Biopharmaceuticals	SCB-2019	NMPA	Novel recombinant SARS-CoV-2 Spike (S)-Trimer fusion protein	✓	Being planned			
20.	CUREVAC	Zorecimeran (INN) concentrate and solvent for dispersion for injection; Company code: CVnCoV/CV07050101	EMA	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)	✓	Planned for Q4 of 2021, at request of the applicant.			
21.	Vector State Research Centre of Viralogy and Biotechnology	EpiVacCorona	Russian NRA	Peptide antigen	Letter received not EOI. Reply sent on 15/01/2021				
22.	Zhifei Longcom, China	Recombinant Novel Coronavirus Vaccine (CHO Cell)	NMPA	Recombinant protein subunit	Response to 2nd EOI sent 29 Jan 2021. Additional information requested.				
23.	IMBCAMS, China	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)	NMPA	Inactivated	Not accepted, still under initial development				
24.	BioCubaFarma - Cuba	Soberana 01, Soberana 02 Soberana Plus Abdala	CECMED	SARS-CoV-2 spike protein conjugated chemically to meningococcal B or tetanus toxoid or Aluminum	Awaiting information on strategy and timelines for submission.				

1. Beijing Institute of Biological Products Co-Ltd
2. Wuhan Institute of Biological Products Co Ltd

* Dossier Submission dates: more than one date is possible because of the rolling submission approach. Dossier is accepted after screening of received submission.

**Status of assessment: 1. Under screening; 2. Under assessment; 3. Waiting responses from the applicant. 4. Risk-benefit decision 5. Final decision made

*** Anticipated decision date: this is only an estimate because it depends on when all the data is submitted under rolling submission and when all the responses to the assessors' questions are submitted.

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Pre-Submission Meetings between SAHPRA and Applicants

Vaccine	Applicant	Date	Outcome
J&J Ad-26	Janssen	4/11/ 2020	Submission of a rolling review application (Rolling review Part 1)
AZ/ RPharm	RPharm/AZ	15/12/2020	Rpharm-Russian Manufacturer
	RPharm	18/01/2020	Establish Rpharm local Intend for S21 and rolling submission
AZ/SII-ChadOX	NDoH	31/12/2020	Section 21 NDoH granted 22 Jan 2021
Pfizer/BioNtec Comirnaty mRNA	Pfizer	7/01/2021 03/02/2021	Submission for Reliance review application Section 21 application 04/02/2021
Sputnik V Ad-26 and Ad-5	Lamar Pharmaceuticals	11/02/2021 18/02/2021	Applicant to provide details of vaccine and available data, Applicant to submit Section 21 and rolling review for registration 23/02/2021
Sinovac CoronaVac (Vera-cell)	Numulox/Curanto Pharma	18/02/2021	Intend to submit Section 21
Sputnik V Ad-26 and Ad-5	Dr Reddy (Pty) Ltd	08/04/2021	Proceed with submission of application (A submission to be made as rolling review submission)

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Pre-Submission Meetings between SAHPRA and Applicants cont…

Vaccine	Applicant	Date	Outcome
UB-612 Multitope Peptide-Based Vaccine (MPV) Against COVID-19	Vaxxinity	16/04/2021	Will establish local presence of Vaxxinity. Data up to phase II available; phase 3 India commenced in March 2021. Intend for EUL WHO mid 2021
Coronavac (Vera-cell)	Solace	16/04/2021	Applicant not licensed for Pharmaceuticals and will apply for SAHPRA license. Applicant required to gain more knowledge and information of their product
Covaxint	Bharat Biotech Limited (Usembe Healthcare)	05/05/2021	A submission to me made for a rolling review
Sinopharm	LHC Pharmaceutical	11/06/2021	Submitted application subsequently
Sputnik V Ad-26 and Ad-5	Mbabala Biotech	11/06/2021	Contract with RDIF requested
ZIfivax	Advance Medicals/Bliss Pharma	14/06/2021	Proceed with submission of application
Moderna	Tautomer (Pty) Ltd	22/06/2021	Intention for booster-No stock of Moderna for 2021
Sputnik V Ad-26 and Ad-5	E Trade Health Solutions (Pty) Ltd	03/07/2021	E-Trade brought in MC PHARMA as Applicant for duplicate of Sputnik V

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SAHPRA COVID-19 Vaccine Applications and Approvals

Section 21 for	Applicant	Application Date	Status
Sputnik V	Dr Reddys	30/04/2021	Sequence 0002 submitted on 08 June 2021 outstanding sequences of data still awaited from the applicant. Review of the submitted information in progress
Sinopharm	LHC	22/06/2021	Rolling Review submission cGMP review report - 12/07/ 2021 Technical screening queries -15/07/2021 (Information in Chinese e.t.c and request for rolling review submission plan 1st review report – 23/08/2021 1st review report - 19/08/2021.
Sinopharm	MC pharma	08/07/2021	Rolling Review submission cGMP review report - 06/08/ 2021 1st review report - 23/08/2021.

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COVID-19 Safety Report

The overall safety monitoring of vaccines – Reporting

Tools for reporting

- Med Safety App
- E-Reporting portal on SAHPRA Website
- Paper-Based system
  - Captured into Vigilance Hub – Back office of Med Safety App
  - Captured at district, provincial, National or SAHPRA
  - Vigilance Hub is accessible by both SAHPRA & NDoH
  - Data on Vigilance Hub feeds directly into VigiFlow system

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The overall safety monitoring of vaccines

- In 2017, The National Immunisation Safety Expert Committee (NISEC) was appointed
- NISEC is a non-statutory standing Ministerial appointed Expert Committee responsible for:
  - Review and assessment of all reported serious and severe adverse events following immunisation (AEFIs)
  - Review of individual serious and unusual AEFIs
  - Perform causality assessment of AEFIs
  - Provide feedback on the causality assessment outcome to relevant stakeholders e.g. SAHPRA
  - Submit recommendations to National Department of Health who also engages with the serious AEFIs reporters

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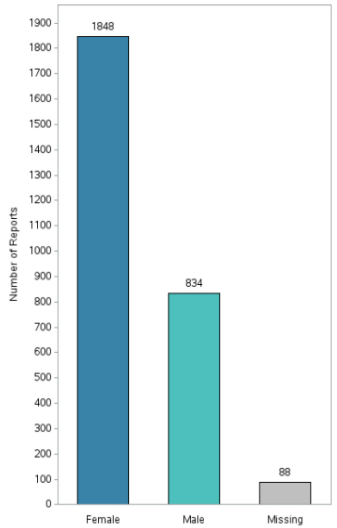
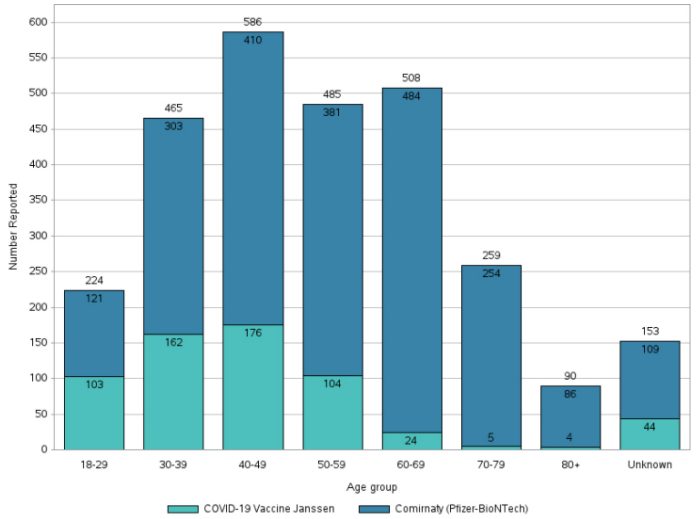
Data reported on microsite

http://aefi-reporting.sahpra.org.za/index.html

Adverse Events Following Immunisation (AEFIs) Reports Distributed By Gender



Number Of Adverse Events Following Immunisation (AEFIs) Reports Distributed By Age And Vaccine Dose



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AEFI Data Analysis

Vaccine name	# of ICSRs	# of fatalities	Total Vaccinations	Prevalence of death
Comirnaty	2148	76	9 798 502*	0,77/100 000
COVID-19 Vaccine Janssen	622	10	2 367 541*	0,42/100 000
Total	277**0**	86	12 166 043*	0,71/100 000

*9 798 502 = 6 629 517 1st Dose + 3 168 985 2nd Dose
*2 367 541 = National roll-out only
It should be noted that all the AEFIs reported under the Sisonke Phase 3b study are not included in this analysis
Data up to 31 August 2021
ICRS: individual case reports

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NISEC Causality Assessment

Cases with NISEC	Death cases	Other cases	Total number of cases
Cases causality assessed	40	107	147 (121 COVID-19 vaccines)
Follow-up cases	15	21	36 (All for COVID-19 vaccines)
Cases under review	31	13	44 (36 for COVID-19 vaccines)

Causality assessed	Death cases	Other cases	Total number of cases
Comirnaty	35	41	**76**
J&J Vaccine	5	40	45

Outcome of death cases

- 34 cases are co-incidental
- 6 insufficient information provided

http://aefi-reporting.sahpra.org.za/index.html

Other cases under assessment

- Myocarditis/pericarditis
- Capillary leak syndrome
- Guillain-Barre Syndrome
- Vascular disorders etc

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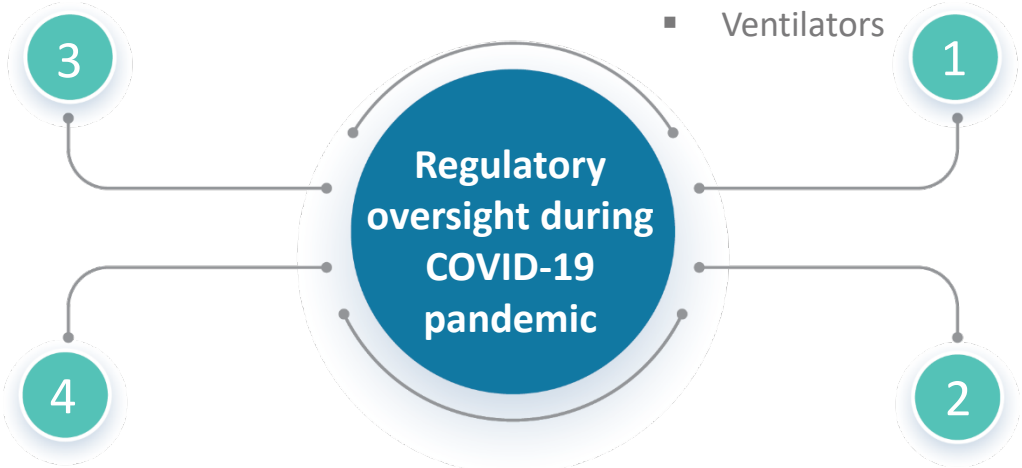
SAHPRA's role extends beyond COVID-19 vaccines

S21 AUTHORISATION FOR NEW REPURPOSED THERAPIES

- Dexamethasone
- Tocilizumab

MEDICAL DEVICES AND IVDs

- Molecular PCR SARs-COV-2 tests
- Antibody and Antigen tests
- PPE used in high risk settings
- Ventilators



AUTHORISATION OF VACCINES

COVID-19 Vaccines

- Astra Zeneca
- Pfizer
- Janssen
- Sinovac

CLINICAL TRIALS

- COVID-19 therapies
- COVID-19 vaccines

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THANK YOU