SAFETY DATA EXCHANGE AGREEMENT

This Safety data Exchange Agreement (SDEA) is entered

Between

- **Rwanda Food & Drugs Authority**, established by Law **N° 003/2018 0f 09/02/2018** of RWANDA, and having its registered office at NYARUTARAMA PLAZA, KG 9 Avenue, KIGALI-RWANDA, which expression shall unless repugnant to the context or meaning there of shall mean and include its successors and assigns (hereinafter referred as "RWANDA FDA"); of One Part

and

- **SERUM INSTITUTE OF INDIA PVT. LTD.** a company incorporated under the Companies Act, 1956, and having its registered office at 212/2, Off Soli Poonawalla Road, Hadapsar, Pune - 411028, India, which expression shall unless repugnant to the context or meaning thereof shall mean and include its successors and assigns (hereinafter referred as "SIIPL"); of Other Part;

RWANDA FDA and SIIPL also may be referred to herein individually as a "Party" or collectively as the "Parties."

RECITALS

WHEREAS SIIPL, is currently manufacturing the pharmaceutical products for further distribution in RWANDA (Territory) as detailed in Annexure A. (Products).

AND WHEREAS both the Parties intend to ensure the compliance with worldwide regulatory requirements for reporting pharmacovigilance data on "the Product(s)"

WHEREFORE, intending to be legally bound, the Parties here to agree as follows:

1. Purpose

The purpose of this SDEA is to describe the procedures and to define the responsibilities between RWANDA FDA and SIIPL through the Pharmacovigilance Unit of SIIPL to ensure that pharmacovigilance (PV) data reporting comply with the requirements for "the Products" as detailed in Annexure A, as per the current regulatory authority regulations and guidelines.

The procedures herein are explicitly subordinate to any current laws, rules, and regulations in the Territory.

Each Party warrants that it has a pharmacovigilance system in place before signing this SDEA.

2. Scope

The Products are currently manufactured by SIIPL and distributed by RWANDA BIOMEDICAL CENTRE.

The present SDEA shall apply to the Products: -

- All spontaneous Adverse Event (AE) reports forwarded to any employee of RWANDA FDA or SIIPL or to their affiliates/partners thereof, including medical representatives, All put together referred hereinafter as Representatives) by Health Authorities or consumers,

- Other PV data such as reports of misuse, medication error, overdose, abuse, interactions, vaccination failure or lack of therapeutic effect, suspicion of transmission of infectious agent, exposure during pregnancy or breast feeding or any request for safety information reported to RWANDA FDA or SIIPL,

- All serious adverse events (SAEs) from post-marketing surveillance studies (PMS) reported to RWANDA FDA or SIIPL,

- All information required for Periodic Safety Update Reports or other summary/aggregated safety reports,

- All other information requested by Regulatory Authorities (RAs) worldwide,

- Any identified safety concern,

Should the above conditions change, the Parties will ensure that the procedures and the responsibilities for handling PV data are defined sufficiently for the Parties to meet applicable RA regulations and guidelines.

If one of the Parties enters into a Contract with a Research Organization (CRO) the CRO must follow the requirements of the present SDEA as if the CRO was party to this Agreement and the Party engaging such CRO shall ensure that CRO executes necessary documents / agreements to this effect.

3. Term

All obligations of the Parties under this SDEA shall take effect, from the date of the last execution by the Party and shall continue in effect for a period of five (5) years unless mutually extended by a further written agreement of the Parties.

4. Contact persons

The contact persons in each company for handling AE reports and Pharmacovigilance actions identify below:

" RWANDA FDA"	"SIIPL"
NTIRENGANYA LAZARE Division Manager for Pharmacovigilance and Safety Monitoring Address: Kigali /Rwanda Tel: + 250 788 771 663 Email: Intirenganya@rwandafda.gov.rw (RUDASIGWA Janvier Medical Advisor/ Any other PV related personnel Address: Kigali/Rwanda Tel: +250788491595 Fax: Email: jrudasigwa@rwandafda.gov.rw	Mr. Dinesh Kumar Sood Director-Quality Assurance Serum Institute of India Pvt. Ltd. 212/2, Off Soli Poonawalla Road, Hadapsar, Pune 411028, India Tel: ++91-20-26602113 Email: pharmacovigilance@seruminstitute.com, dineshksood@seruminstitute.com Dr. Prasad Kulkarni Medical Director Serum Institute of India Pvt. Ltd. 212/2, Off Soli Poonawalla Road, Hadapsar, Pune 411028, India Tel: ++91-20-26602384 Email: pharmacovigilance@seruminstitute.com, drpsk@seruminstitute.com

5. Terminology

The definitions of terms are in accordance with the ICH.

- **Adverse Event (AE):** any untoward medical occurrence in a patient or clinical investigation subject administered a Product and which does not necessarily have to have a causal relationship with this treatment.
- *An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of the Product, whether or not considered related to the Product.*
- **Averse Drug Reaction (ADR):** all noxious and unintended responses to the Product related to any dose should be considered ADRs.
- **CCDS:** document prepared by the marketing authorization holder containing, in addition to safety information, material relating to indications, dosage, pharmacology and other information concerning the Product.
- **CIOMS:** Council for International Organizations of Medical Sciences
- **Date of first receipt:** any Representative of either RWANDA FDA, **SIIPL** or a third party such as a CRO should consider the date of reception of AE as the first date of reception. The date of first receipt will be considered as Day0 for the calculation of transmission and submission timeframes.
- **Pharmacovigilance data:** includes all serious and non-serious safety reports from spontaneous notifications irrespective of the source:
  - Adverse events,
  - Pregnancy, Breastfeeding reports (with or without associated AE)
  - Lack of efficacy / vaccine failure,
  - Overdose, abuse (with or without associated AE)
  - Misuse or medication error (with or without associated AE)

- Interaction
- Suspected transmission of an infectious agent via medicinal product.

- **The Product**: in this document "**the Product(s)**" means products as per Annexure A

- **Serious Adverse Event (SAE):** any **untoward** medical **occurrence that at any dose of the Product:**
  - Results in death
  - Is Life threatening,
  - Requires in-patient hospitalization or prolongation of existing hospitalization,
  - Results in persistent or significant disability / incapacity,
  - Results in Congenital anomaly / birth defect,
  - Medical and scientific judgment should be exercised in deciding whether expedite reporting is appropriate in other situations, such as important medical events that may not be immediately life threatening or result in death or hospitalization, but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These cases should also usually be considered as SAEs.

The term ***"life threatening"*** refers to an event in which the patient was at risk of death at the time of the event, and it does not refer to an event, which hypothetically might have caused death if it were more severe.

- **SADR:** Serious Adverse Drug Reaction
- **Territory**: RWANDA BIOMEDICAL CENTRE distributes the product in RWANDA
- **Unexpected Adverse Reaction**: any adverse reaction, the nature, or severity of which is not consistent with the applicable product information i.e. SPC (Summary of Product Characteristics) or Investigator's Brochure.

6. EXCHANGE OF SINGLE CASE REPORTS INFORMATION

6.1 SIIPL to RWANDA FDA
These will be part of the annual PSURs and/or as per the periodicity required by long as it is after the cutoff date (March 31) of SIIPL. However, if any batch is withdrawn or suspended, it will be immediately notified by **SIIPL** to RWANDA FDA".

6.2 RWANDA FDA **to SIIPL**
RWANDA FDA shall provide **SIIPL** with all AEs, reported with the product, according to the following timelines:
- **All SAEs** within 3 business or 5 calendar days.
- **All Non-Serious** AEs and other PV data within 15 calendar days.

6.3 Format of exchanged documents
Pharmacovigilance reporting form/ source document will be used for all cases which will be informed by RWANDA FDA to **SIIPL** (see CIOMS form in annexure 2)

6.4 Follow-up Information
It is RWANDA FDA's responsibility in RWANDA. Nevertheless, whatever additional information is required by SIIPL, RWANDA FDA will provide it.

6.5 Medical Assessment of SAEs

SIIPL shall be responsible for the medical assessment of all SAEs and AEs for the purpose of reporting to the local regulatory authorities.

SIIPL shall insert a sentence at the end of the narrative of AE specifying the medical assessment by the company.

6.6 Submission to Regulatory Authorities

RWANDA FDA will collect and report all AEs to SIIPL. SIIPL will do the further follow up and submissions to local / national regulatory authorities as applicable.

6.7 Record retention

Each party shall be responsible for filing and archiving of AE source data and related documentation according to applicable regulation or company procedures.

Source data of AEs and other documents related to the scope of this agreement may be requested by **SIIPL** to RWANDA FDA and shall be forwarded upon request.

7. Responsibilities for PV Activities in (country) for the Product

Description	RWANDA FDA	SIIPL
Local responsibility for PV	X	
Collection and & Notification to **SIIPL** of SAE & AE reports occurring in RWANDA	X	
Processing of SAE & AE occurring in RWANDA		X
Follow-up SAE & AE reports occurring in RWANDA	X	
Medical assessment of SAEs		X
Record retention & archiving of PV data in RWANDA	X	
Log all AE reports occurring in RWANDA in a database with individual case ID	X	
Reference Safety database		X
Notification to **SIIPL** of Product Technical Complaints associated with AE occurring in RWANDA	X	
PSUR Production		X
Info about regulatory status, ongoing clinical trials & patient exposure in RWANDA	X	
Notification of Regulatory action / pending action / medico legal case in RWANDA	X	
Notification of any significant change in drug Safety Regulation in RWANDA	X	
Standard Reference Document (CCDS) (see point 13)		X
Amendment to this SDEA	X	X

8. Reference Safety Database

SIIPL shall hold and maintain the worldwide central safety database for the Product, into which it shall enter information for AEs received from RWANDA FDA as well as from **SIIPL** or other party.

9. Product technical complaints (PTC)

PTC should be reported by RWANDA FDA to the Quality Assurance (QA) group of **SIIPL**.
In addition to the usual AE case management process, all PTC's associated with PV data should also be sent directly to the QA Group of SIIPL.

10.Periodic Reports

10.1 Periodic Safety Update Reports (PSURs)

SIIPL will write the Periodic Safety Update Reports (PSURs) in English according to the ICH E2C guideline and in-line with international requirements.
SIIPL will contact RWANDA FDA in advance of the data lock point specifying the information required to write the PSUR. RWANDA FDA will provide such information to **SIIPL** within 35 calendar days of the data lock point.

11.Signal detection/identification, safety issues and crisis management

Each party will notify the other party as soon as possible (no more than 7 days) of any regulatory action or pending action that might result in a change in the product benefit risk balance, such as product suspension, product recall, labeling change for a safety reason.
In the case of a Regulatory Authority question is forwarded to RWANDA FDA, the answer will be consolidated by both **SIIPL** & RWANDA FDA Pharmacovigilance departments.
If RWANDA FDA has a medical-legal case report, or if a complaint is lodged against RWANDA FDA, or if a case goes to court, SIIPL should be informed accordingly.

12.Risk Management Plan

RWANDA FDA shall inform **SIIPL** of any specific request from local Health Authorities regarding local Risk Management Planning (RMP) for the product, in order to initiate communication with the Health Authorities and take into account such a requirement into the product Risk Management Plan, if appropriate. **SIIPL** shall inform RWANDA FDA of the Product RMP release / revision and provide copy upon request.

13.Regulatory Authorities and reporting responsibilities

RWANDA BIOMEDICAL CENTRE shall be responsible for submitting all required safety information to the RAs. This shall include expeditable SAEs and EAs and all other safety information required by the RAs.

All safety documents submitted to RA by RWANDABIOMEDICAL CENTRE may be requested by **SIIPL** and shall be sent upon request and vice versa.
RWANDA FDA must inform **SIIPL** of any significant change in Drug Safety Regulation in its territory that may affect this SDEA.

14. Standard reference documents, product information

SIIPL shall be responsible for the content, amendments and updates of the Company Core Data Sheet (CCDS) for the product, following the **SIIPL** procedures.
In case of any proposed changes to the labeling, **SIIPL** shall notify RWANDA FDA in writing with justification information.
In order to assess the information of each spontaneous report, the reference document will be the last version of the CCDS.

15. Miscellaneous

15.1 Confidentiality / Disclosure
Both Parties should consider all safety data as confidential.

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15.2 Amendments to this SDEA
All sections and appendices of this SDEA may be modified through written consent of the Parties as necessary to ensure that each Party (**SIIPL** and RWANDA FDA is able to comply with current worldwide RA requirements.
Should the conditions change; the Parties will ensure that the procedures and the responsibilities for handling AEs are defined sufficiently for the Parties to meet applicable RA regulations and guidelines. The Parties agree that this SDEA might be updated accordingly.

15.3 Data privacy Amendments to this SDEA
RWANDA FDA shall abide with the provisions of any applicable law regarding privacy, protection. In that respect, RWANDA FDA shall not send full identification (name, address) of patients and reporters to **SIIPL**.

"RWANDA FDA" REPRESENTATIVE

By:	Digitally signed by Rwanda FDA (Ag DG) Date: 2021.04.20 22:14:13 +02'00'	By:	
Name:	**Dr. Charles KARANGWA**	Name:	
Title:	Ag. Director General	Title:	
Date:	20/04/2021	Date:	
Place:	Kigali, Rwanda	Place:	

"SIIPL" REPRESENTATIVE

By:		By:	
Name:	**Mr. Sumit Gupta**	Name:	**Dr. Chetanraj Bhamare**
Title:	Senior Manager - QA	Title:	Safety Physician
Date:	21.04.2021	Date:	21/04/2021
Place:	Pune, India	Place:	Pune, India

Serum Institute Of India Pvt. Ltd. ★ Pune-411 028. INDIA ★

Annexure A:

Product list

Sr No.	Generic name	Brand Name	Date of Registration/ Marketing Authorisation in (country)	Registration/ Marketing Authorisation No	Validity of Registration/ Marketing Authorisation
1.		COVISHIELD			
2.					
3.					

Annexure B:

CIOMS FORM

CIOMS FORM

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE Years	3. SEX	4-6 REACTION ONSET Day	Month	Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20 DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)	19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		
	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOWUP	