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SIGNATURE			
DATE	02/07/2018	03/07/2018	03/07/2018

DEPARTMENT : PHARMACOVIGILANCE

SOP TITLE : STANDARD OPERATING PROCEDURE FOR THE ACTIVE PHARMACOVIGILANCE PLAN (RECEIPT, HANDLING, EVALUATION & REPORTING OF ADVERSE EVENTS.)

1. PURPOSE:-

The purpose of this SOP is to describe the process for Receipt, Handling, Evaluation and reporting adverse events.

2. SCOPE:-

This procedure applies for the process required for the collection, collation, analysis for all human products manufactured in BIO-MED (P) LTD.

3. RESPONSIBILITY:-

3.1 Marketing Executives are responsible for submitting the AEFI report within time frame duration.

3.2 Zonal Heads are responsible for direct coordination with their designated zonal marketing executives & directly co - ordinate with PV officer In-charge.

3.3 Zonal heads are also responsible for investigation of ADR/SADR Reports

3.4 Pharmacovigilance officer In-charge are responsible for analysis of AEFI which provide the unique identification Number for each case to review the investigation report.

3.5 QA In- Charge & QC In- charge are responsible for investigation of case study as per their concern.

4. GUIDELINES:-

4.1 All the event (expected or unexpected) report shall be submitted within 15 calendar days to licensing Authority.

4.2 All the serious adverse event (expected or unexpected) report shall be submitted within 15 calendar days to licensing Authority initial receipt of the information by the applicant.

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4.3 All serious ADRs/AEs must be reported to the regularity authority/NCC-PvPI, IPC within 30 days of initial receipt of the information by the MAHs.

4.4 The report of the AEFI observed shall be quarterly submitted to CDSCO along report and action taken report for all Products wise.

5. ABBREVIATION:-

ADR - Adverse Drug Reaction.

AE - Adverse Event

AEFI - Adverse Event Following Immunization.

IMP - Investigation Medicinal product

PV - Pharmacovigilance

SADR - Serious adverse Drug reaction

SAE - Serious Adverse Event

SUSAR - Suspected Unexpected Serious Adverse reaction

6. Procedure:

6.1. DEFINITION: Consequently, AEs can be classified into different categories-

6.1.1. **Adverse Event**: Any untoward medical occurrence (including a symptom /disease or an abnormal laboratory finding) during treatment with a pharmaceutical product in a patient or a human volunteer that does not necessarily have a relationship with the treatment being given.

6.1.2 **Adverse Drug Reaction:** A response which is noxious and unintended response related to IMP which occurs at any doses normally used in humans for prophylaxis or therapy of disease or for modification of physiological function.

6.1.3 **Serious Adverse drug reaction/Serious Adverse Event :** An AE or ADR that is associated with:

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- Results in death.
- Life threatening.
- Results in permanent disability.
- Requires hospitalization or prolongation of existing hospitalization.
- Requires intervention to prevent permanent impairment/damage.

6.1.4 **Suspected Serious Adverse Reaction**:- An Adverse reaction that is classed in nature as serious, which is consistent with the information about the medicinal product in question set out.

6.1.5 **Suspected Unexpected Serious Drug Reaction:** - An Adverse reaction that is categorized in nature as serious and which is not consistent with the information about the medicinal product in question set out.

6.1.6 **AEFI**: - Any untoward medical occurrence which follows immunization and which does not necessarily have a casual relationship with the use of vaccine .The adverse event may be any unfavorable or unintended sign, an abnormal laboratory finding, a symptom or a disease.

- **Vaccine Reaction**:- An event caused by active component / other component of the vaccine. Example – High grade fever, anaphylaxis.

- **Program Error**:- An event caused by an error in vaccine (preparation, handling, administration). Example- Bacterial abscess.

- **Coincidental Reaction**:- An event that occurs after immunization but is not caused by vaccine. Example – Pneumonia.

- **Injection Reaction:-** An event caused by anxiety or pain from the injection itself rather than vaccine. Example- Fainting spell.

- **Unknown**:- The cause of event can't be determined. Example- does not fit in any of the above four types.

6.1.7 **Cluster**: - Two or more cases of the same event or similar events, related in time, geography and the vaccine administered.

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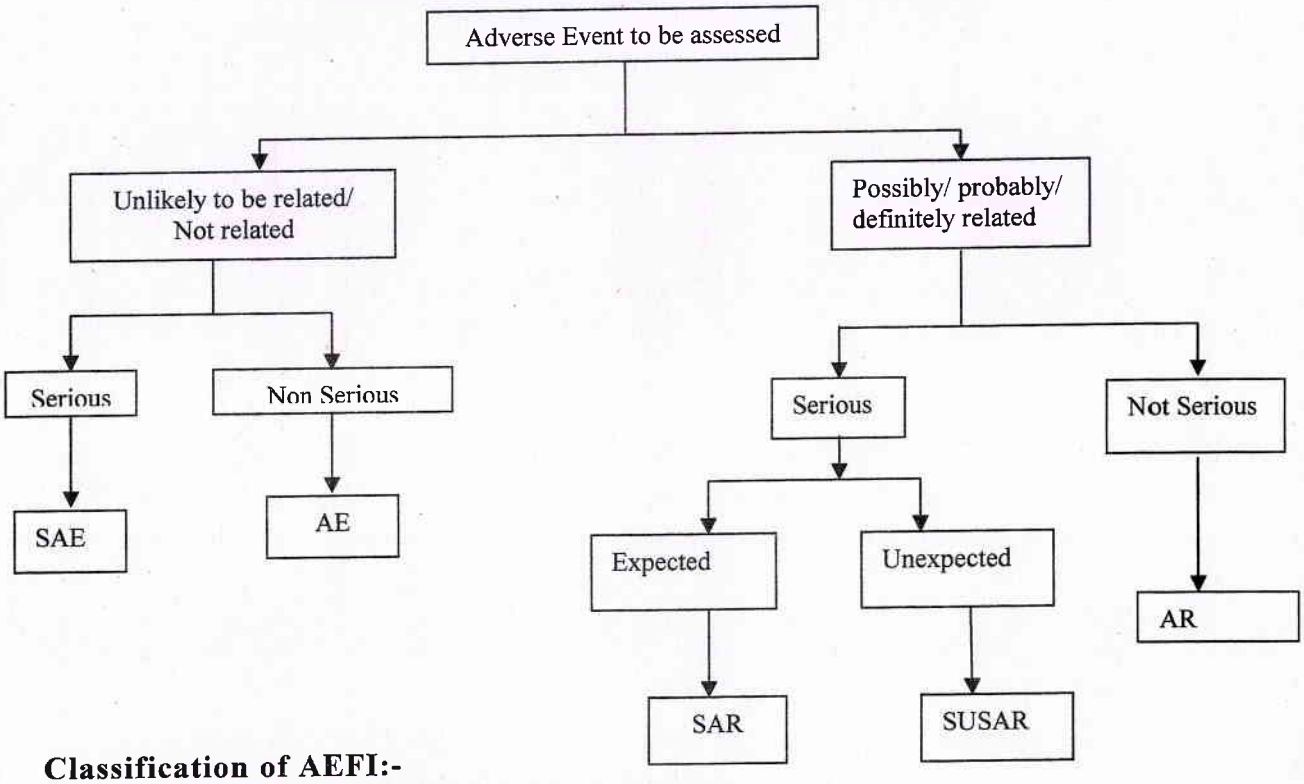
6.1.8 **Side Effects**:- Any intended effect of pharmaceutical product or IMP occurring at normal dosage which is related to the pharmacological properties of the drug.

CLASSIFICATION OF ADVERSE EVENTS



Classification of AEFI:-
AEFI CAN BE CLASSIFIED INTO 5 TYPES:

a. Vaccine Reaction.
b. Program error.
c. Coincidental Reaction.
d. Injection reaction.
e. Unknown

6.2. Active Pharmacovigilance Plan

6.2.1. **Channels of reporting AEFI:** it is essential that the marketing executives identify and report all serious and non – serious adverse events. There are two channels of reporting AEFIs:

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SIGNATURE	Shalini	Divyansh	HK
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6.2.1.1. Monthly routine reporting:-

This includes reporting of Post Marketing surveillance report of all vaccines .If there is no any side effects observed in the month the report shall be submitted into BM/PV/F/008B.This information is collected and complied by medical executives in monthly reporting formats, these includes:

a. Pain.
b. Pruritus/Itching.
c. Fever.
d. Redness
e. Headache.

6.2.1.2. Immediate Notification of serious AEFI/Side effect:-

The serious AEFI is defined as "ANY UNTOWARD MEDICAL OCCURANCE" that result in death, hospitalization or prolongation of hospitalization, significant disability, incapacity, life threating. All serious AEFI are to be immediately notified by marketing executive & notify the case by quickest means of communication e.g. telephone, messenger etc. This includes:

a. Death.
b. Severe local pain
c. Seizures.
d. Life Threatening.
e. Hospitalization/Prolonged
f. Disability
g. Congenital Anomaly
h. Required intervention to prevent permanent impairment/damage.
i. Other.
If any Side effects are observed, the same shall be reported immediately to PV Department.

6.2.2. Process of reporting AEFI:-

Serious events are needed to be immediately investigated, managed and reported on standardized AEFI formats. All the serious events should be reported within 24 hours of events.

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6.2.2.1. On receipt of information about any other AEFI, the marketing executive should report the same in the monthly reporting form (AEFI format). The AEFI ID shall be allotted by Pharmacovigilance department, it shall be in terms of AEFI/PV/XXX/YY, where AEFI is Adverse Event Following Immunization, PV is Pharmacovigilance, XXX- Tracking No starts from 001 and YY indicates the current year.

6.2.3. Collection of data:-

6.2.3.1. Marketing executives visits to primary health center/ medical institutions/ Govt. Depots/ District Hospitals.

6.2.3.2. Entire distribution/ sales and marketing network of Bio – Med (P) Ltd. is divided into 4 zones (East, West, North, South) and each zone has respective zonal head.

6.2.3.3. If there is any serious event observed during visit. The FIR should be filled and copy of the same shall be sent to Bio – Med Pvt. Ltd. within 24 hours of the event report. Except serious events, all the events are reported monthly.

6.2.4. Investigation of AEFI:-

6.2.4.1. If the reported AEFI is an event that needs investigation. The marketing executive inform to the Bio – Med Pvt. Ltd. by telephone or fax immediately.

6.2.4.2. At times, lab testing is required to confirm or rule out the suspected cause. In such cases the incriminated vial of vaccine(if available) used to administer the vaccine should be collected and sent under cold chain to Bio – Med Pvt. Ltd & internal investigation need to be proceed.

6.2.4.3. If the event is due to programmatic error, action should be taken to correct wrong practices.

6.2.4.4. On receipt of FIR from marketing executive that warrant investigation, the zonal head of the concern area should initiate an investigation.

6.2.4.5. On basis of investigation, a root cause is found and the corrective action is taken.

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6.2.5. In case of export, the reports of the events are received through the mail.

6.3. Causality assessment:-

Decision	Description	Classification
Not Related	Temporal relationship of the onset of events, relative to the administration of the product, is not reasonable or due to some another cause can itself explain the occurrence of the event.	AE
Unlikely to be related	Temporal relationship of the onset of events, relative to the administration of the product is unlikely but cannot be ruled out.	AE
Possibly related	Temporal relationship of the onset of events, relative to the administration of the product, is reasonable and the event could have occurred due to another, equally likely cause.	AR
Probably related	Temporal relationship of the onset of events, relative to the administration of the product, is reasonable and the event Is more likely explained because of administration of drug than by any other cause.	AR
Definitely related	Temporal relationship of the onset of events, relative to the administration of the product, is reasonable and there is no other cause to explain the event or a re – challenge is positive.	AR

6.4. In both cases, Event is expected or unexpected, Analyze the causality & seriousness of event.

Causality assessment

1. Not related
2. Unlikely to be related
3. Possibly related
4. Probably related
5. Definitely related

Seriousness

1. Result in Death
2. Life threatening
3. Disability
4. Requires Hospitalization
5. Congenital anomaly/Birth defect

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6.5. AEFI During Clinical Trial:

6.5.1. As with other vaccines, in rare cases anaphylactic shock may occur in susceptible individual. The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis. The vaccines should remain under observation for not less than 30 minutes for possibility of occurrence of rapid allergic reactions. Hydrocortisone and antihistaminic should also be available in addition supportive measures such as oxygen inhalation.

6.5.2. In case of pain anti inflammatory drug should be prescribed by the doctor.

6.5.3. Id fever occurs, and then antipyretic drug should be given to the volunteer as per the prescription of the doctor.

6.5.4. All the adverse events should be informed to PI/ COPI etc.

6.5.5. If there is a serious adverse event observed during clinical trial, then PI along with Pharmacovigilance officer in-charge should be informed to DCG (I).

7. REFERENCE:-

Pharmacovigilance Guidance Document for Marketing Authorization Holders of Pharmaceutical Products 2018, Version: 1.0.

8. DOCUMENTATION:-

8.1. BM/PV/ANX/001/A Side Effects reporting Form.

8.2. BM/PV/ANX/001B AEFI Reporting Form.

9. IMPLEMENTATION:-

9.1. Develop/ modify relevant SOPs if applicable.

9.2. Trained the staff if applicable.

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BIO-MED
PRIVATE LIMITED

Format No. : BM/PV/ANX/001A
Revision No. : 04
SOP Ref. No. : BM/PV/001
Effective date : 03/07/2018
To be reviewed : 03/07/2020
Replaces revision : 03

VACCINE SIDE EFFECT REPORTING FORM

Patient details

Patient name: **Gender:** **Age:**

Health information

Reason of the taking Drug/Vaccine (disease/symptoms) :

Drug/ Vaccine advised by : Doctor □ Pharmacist □ Friend□ Self□

Details of the Person reporting the Side Effects :

Name :

Address :

Telephone : Email :

Details of vaccine taken :

Name of Drug/vaccine (write vaccine & diluent details in separate rows)	Quantity taken & dose no. (zero/ first/ second etc. As applicable)	Name of manufacturer	Batch/ lot no.	Expiry date	Date of Administration/vaccination

Dosage form : Liquid □ /Oral Liquid □ Other □

About the side effect -

When did the Side Effect start ? ☐ Side effect is still continuing (Yes/No)

When did the Side Effect stop ? ☐

Relationship to Drug/Vaccine: 1 = Not related, 2 = Unlikely, 3 = Possible, 4 = Probably, 5 = Definitely, 6 = Not Assessable.

Other Drug/Vaccine administered at the same time? No□ Yes□ if yes, specify below.

Vaccine	Manufacturer	Batch No.	Route/Site	No. of previous Doses

Kindly mark all the side effects in appropriate boxes .Please use this form for the side effects occurred from the date of administration /vaccination.

S. No	Parameter	Grade	DAY Details after administration/vaccination of Drug/vaccine	Date of resolution & Relationship to drug/vaccine

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			D-	D-	D-	D-	D-	D-	D-	
Local adverse events (at the injection site)										
1	**Pain**	**None**	□	□	□	□	□	□	□	
		Mild	□	□	□	□	□	□	□	
		Moderate	□	□	□	□	□	□	□	
		Severe	□	□	□	□	□	□	□	
None: Absent; **Mild**: Minor reaction to touch; **Moderate**: Painful to touch; **Severe**: Spontaneously painful										
2	**Pruritus/Itching**	**None**	□	□	□	□	□	□	□	
		Mild	□	□	□	□	□	□	□	
		Moderate	□	□	□	□	□	□	□	
		Severe	□	□	□	□	□	□	□	
None: Absent; **Mild:** Itching localized to injection site and relieved spontaneously or within <48 hours of treatment; **Moderate:** Itching beyond injection site, not generalized or localized and requiring >48 hours of treatment; **Severe:** itching causing inability to perform usual social & functional activities										
3	**Fever**	**None**	□	□	□	□	□	□	□	
		Mild	□	□	□	□	□	□	□	
		Moderate	□	□	□	□	□	□	□	
		Severe	□	□	□	□	□	□	□	
		Life Threatening	□	□	□	□	□	□	□	
None: Absent; **Mild:**38.0 – 38.4°C (100.4 – 101.1°F); **Moderate:** 38.5 -38.9°C (101.2 – 102.0°F); **Severe:** 39 - 40°C (102.1 - 104°F); **Life Threatening:** >40°C (>104°F)										
4	**Redness**	**None**	□	□	□	□	□	□	□	
		Mild	□	□	□	□	□	□	□	
		Moderate	□	□	□	□	□	□	□	
		Severe	□	□	□	□	□	□	□	
None: Absent; **Mild**: Localized skin erruption; **Moderate**: Diffuse skin eruption from body surface area ; **Severe**: Generalized skin erruption involving >50% from the body surface area.										
5	**Headache**	**None**	□	□	□	□	□	□	□	
		Mild	□	□	□	□	□	□	□	
		Moderate	□	□	□	□	□	□	□	
		Severe	□	□	□	□	□	□	□	
None: Absent; **Mild**: No interference with daily activity; **Moderate**: Some interference with daily activity; **Severe**: Significant interference and prevents daily activity (Non Bearable).										

Other than mentioned above (Please specify)

Describe treatment used (if any) for any of the above reported events (brand/ generic name of medications and the course of treatments):

_____

_____

_____

_____

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*Outcome measures: 1 = Recovered, 2 = Recovered with sequelae, 3 = Event continuing without treatment, 4 = Event continuing and controlled with treatment, 5 = Event continuing and not controlled with treatment, 6 = Unknown ,7 =Death

Reporter Name:-
Signature and date:_____

Reviewed by : _____
Signature and date
(Pharmacovigilance Department)

Remarks : _____

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PRIVATE LIMITED

Format No. : BM/PV/ANX/001B
SOP Ref. : BM/PV/001
Revision No. : 04
Effective Date : 03/07/2018
To be reviewed : 03/07/2020
Replaces Revision : 03

AEFI CASE REPORTING FORM

AEFI REPORTING ID : _____ (TO BE ALOTTED BY BIOMED)

(To be submitted within 24 hours of case notification)

State	**District**
Block/ Ward	**Village/ Urban Area**
Address of the Site:	
Notified by (Name):	Designation (please circle): health worker/ government doctor/ private practitioner/ community/ media/ others (specify)
Date: __ __/ __ __/ __ __ __ __	_____ _____
Contact phone number (with STD code):	

Patient Name:																		
Age/ Date of Birth:									Sex			Male			Female			

Father's Name/ Husband Name																			
Complete Residential Address of the case with landmarks (Street name, house number, village, block, tehsil, Pin No. etc.)																			
P	**I**	**N**	**-**							**P**	**H**	**O**	**N**	**E**	**-**				

Date of vaccination	D	D	M	M	Y	Y	Y	Y	Time of vaccination	H	H	M	M	(AM	PM)
Address of session site: Place of vaccination :Govt Health Facility/Outreach/Private Health facility/others															
Date of First Symptom	D	D	M	M	Y	Y	Y	Y	Time of First Symptom	H	H	M	M	(AM	PM)

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Details of vaccine, diluents & Vitamin A given to the patient on day of event

Name of vaccines received (write vaccine & diluent details in separate rows)	Dose no. (zero/ first/ second etc. as applicable)	Name of manufacturer	Batch/ lot no.	Mfg. date	Expiry date	Date of opening of vial	Time of opening the vial (for reconstituted vaccine)	No. of OTHER beneficiaries who received vaccine from the SAME vial in this session

Details of hospitalization:

Hospitalization: No/Yes (date)	D	D	M	M	Y	Y	Y	Y	Time of Hospitalization	H	H	M	M	a. m.	p. m.

Name and address of hospital (if hospitalized): _____

_____

_____

Current Status (encircle)	**Death/ Still Hospitalized/ Recovered & Discharged/ Left Against Medical Advice (LAMA)/Recovered completely and discharged/Not Hospitalized.**														
If Died, Date of Death	D	D	M	M	Y	Y	Y	Y	Time of Death	H	H	M	M	(AM	PM)

Post mortem done? (*encircle*)	Yes**/ No/ Planned on (Date) _____	If Yes, Date _____ Time _____

Describe AEFI (signs and symptoms):

_____

_____

_____

_____

Suspected adverse event(s) (tick at least one):

☐ Severe local reaction ☐ Seizures

○ *>3 days* ○ *febrile*

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○ *Beyond nearest joint* ○ *afebrile*

☐ Abscess ☐ Sepsis ☐ Encephalopathy ☐ Toxic Shock Syndrome

☐ Thrombocytopenia ☐ Anaphylaxis ☐ Intussusception

☐ Fever ≥ 39 °C (102 °F) ☐ Hypotonic hypo-responsive episode (HHE)

☐ Acute flaccid paralysis ☐ Sudden Unexplained death syndrome.

☐ Death due to any reason other than above – specify _____

_____

☐ Hospitalization due to any reason other than above – specify _____

_____

☐ Disability ☐ Cluster – is this case part of a cluster? Yes/ no/ unknown

If yes, no of other cases in the cluster_____ (use separate form for each case in a cluster)

Signature and Date of reporting/ verifying person: - _____ **Email Id:** _____

Proposed date of investigation: - ____/____/_____

Review By :
(Sign/Date)
Notes/ Comments: _____

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