STANDARD OPERATING PROCEDURE	
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Title: Search & Review of Global Medical Literature & Digital Media to Identify Adverse events & Safety Data	**Effective Date:**
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1. OBJECTIVE:

To define procedures for the collections, review, selection, documentation and record keeping of literature retrieved from global literature database, local scientific journals (as per regulatory requirement), SDEA Partners and Digital media for screening and collections of ICSR's and detection of new safety signals or emerging safety issues. The aim is to identify ICSR's and significant new information from safety studies (clinical, non-clinical and epidemiological) that is not already covered by the current product labeling. Review of Literature and Digital Media is also an important part of aggregate report, risk management plan, and signal management activity.

2. SCOPE:

This procedure is applicable to all members of ..... who are involved in literature/digital media search and review related to medicinal products. It describes search strategies, methods for identification of safety concerns, documentation and record keeping of the entire process. This SOP shall be used by all relevant personnel of ..... to ensure that literature search process is consistnt and of high standards.

3. RESPONSIBILITY:

a. Pharmacovigilance Department:

Responsible to perform global medical literature and digital media search and classify search results to get AE's and products safety information.

Preparation, distribution, retrieval and destruction of this SOP.

b. Pharmacovigilance Officer In-charge (PvOI):

Review and Approval of the output in form of AEs and products safety information.

Review, training and effective implementation of this SOP.

c. Third Party

A third party e.g. client/vendor may be assigned to take over responsibilities for specific processes described in the related documents.

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4. ACCOUNTABILITY:

Pharmacovigilance Officer Incharge.

5. PROCEDURES

a. Setting Up And Updating Literature Search Alerts

i. Literature monitoring activity needs to be performed whenever ..... receives new marketing authorization, PvOI/ Department Head or designate person shall ensure that search alerts are set-up on Pubmed/relevant literature database to identify ICSRs and articles of interest for aggregate reports, risk management activities and signal management activities for all of the ..... products. Literature monitoring is to continue while the authorization is active and for a period following cessation of authorization depending on the pharmacological properties of medicinal product and its marketing status.

ii. Literature search strategies shall be set up by designated person.Set up of search criteria has to be accessed control and cannot be changed by anyone but the designated person.Whenever a literature search strategy is required to be generated/changed it has to be approved and signed by PvOIand/or Department Head. (Refer to Annexure -I).

iii. Additional searches may also be added if a new safety issue is raised that needs to be closely monitored, e.g. a safety issue that needs to be monitored from an aggregate report or signal management activity.

b. Review of "Literature Article" in Literature Search Alerts

Worldwide literature review shall be done at least monthly for all …… products in India market and for products registered out of India shall be done as recommended locally using PubMed/ relevant literature database. Monthly/weekly alert emails will be received to the predefined oneemail account of the designated person. Each literature article shall be reviewed for identification of ICSR's and other safety concerns. After the review, each shall be classified as either:

- ICSR's for which cases shall be processed as per …….. SOP and recorded in the AE Tracker.
- Articles of interest for aggregate report and signal management activity.
- Not selected.

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c. Selection of ICSR's:

i. For selecting a Literature article as an ICSR, the literature should have four minimum criteria for case creation – at least one identifiable reporter, one single identifiable patient, at least one suspected adverse reaction and at least one suspect medicinal product.

ii. Selection of cases for ICSR's shall be based on the above points and the possibility that the event may be attributed with use of the suspected medicinal product. This may not always be apparent in the authors' text but should be judged while reviewing the article.

iii. Articles can be excluded as ICSR based on one of the following criteria - medicinal product name, active substance name, pharmaceutical form, batch number or route of administration not consistent with ..... product. Also when the primary source country or country of origin of the adverse reaction can demonstrate that in that country the suspected medicinal product has never been supplied or placed on the market or that the product is not a travel medicine (e.g., anti-malarial medicinal product).

iv. Exceptions are articles which describe misuse of a product or the preparation of an extemporaneous product (e.g. making solutions from solid dose forms) shall be included as ICSR.

v. In the absence of a specified product source and/or brand name, ownership of the product shall be assumed for articles about the active substance.All ICSRs shall be checked for expedited reporting as per the applicable regulatory requirements during initial review of literature.All selected ICSR's shall be processed as per procedure outlined in the SOP.

vi. Selection of articles of interest for aggregate report and signal management activity

Any data which is not an ICSR, but contains significant new safety information from safety studies (clinical, non-clinical and epidemiological) that is not already covered by the current product labeling shall be collected for review/discussion for aggregate report and signal management purposes.

vii. Types of literature shall not be considered as an article of interest

These are:

- Efficacy studies with no significant safety issues
- In vitro studies, where the clinical relevance is unclear
- Non-Pharmacovigilance-related articles e.g. epidemiological / cost-effectiveness studies
- Mechanism of action studies

d. Data Entry Notes

For the ICSR's described in the worldwide scientific literature, the clock for reporting to Competent Authorities starts (day 0) with awareness of a publication containing the four minimum elements of safety information by any personnel of ..... including medical representatives or any organization having a contractual arrangement with ..... to provide a Pharmacovigilance literature service, including contractors hired by ..... service providers. If an ICSR is found during scientific review of the abstract - the day 0 for the report should be the date the search which generated the abstract was conducted.

e. Medical Review of Selected ICSR's

All selected ICSRs by literature reviewer will be further confirmed by Medical reviewer for selection as ICSR and documented.

f. Quality Control

For the not selected literature articles, 10% of articles shall be chosen randomly and reviewed for quality check by medical reviewer. If any single ICSR is identified from it then all remaining articles shall be reviewed by literature reviewer.

g. Ordering Full Papers/Publications

It may be considered necessary to order the full paper if there is insufficient data available in the abstract to validate the case.

h. Follow up

The need to follow up on information provided in literature articles with the author may be required to gain necessary information for case assessment. Correspondent author of the article shall be considered as a point of contact in such situations. The follow up shall be done by medical reviewer or designee.

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i. Information on Suspected Adverse Reactions from the Internet or Digital Media

i. Internet or digital media under the management or responsibility of ..... shall be regularly screened (at least once in week) for identification of potential reports of suspected adverse reactions.

ii. Reports/queries received via ..... websites shall be screened for the collection of reports of suspected adverse reactions.If a report of suspected adverse reaction received/screened from in any non-company sponsored digital medium, the report shall be assessed to determine whether it qualifies for reporting.

Unsolicited cases of suspected adverse reactions from the internet or digital media shall be handled as spontaneous reports.

iii. In relation to cases from the internet or digital media, the identifiability of the reporter refers to the existence of a real person, that is, it is possible to verify the contact details of the reporter (e.g., an email address under a valid format has been provided).If the country of the primary source is missing, the country where the information was received, or where the review took place, shall be used as the primary source country.

iv. Potential valid ICSR‘s shall be reported to the competent authority within the appropriate reporting timeframe based on the date the information was posted on the internet site/digital medium.

j. Record Keeping

The PvOI/ Department Head shall maintain records of the search string/strategy. The literature hits received from the Pubmed/literature database shall be archived in a separate folderwith the reason of selection or non-selection of each hit. All relevant literature articles, form as source documents for ICSR‘s and/ or for signal management shall be archived for 10 years. Other material, after due risk assessment can be destroyed after 5 years.

6. DISTRIBUTION:

Not Applicable

7. REFERENCE:

Not Applicable

8. ANNEXURES:

S.No.	Title	Annexure No.	Format No.
1.	Literature search strategies	I	
2.	Flowchart of literature monitoring process	II	

9. ABBREVIATIONS:

AE	:Adverse Event
ICSR	:Individual Case Safety Report
PV	:Pharmacovigilance
PvOI	:Pharmacovigilance Officer In-charge
SDEA	:Safety Data Exchange Agreement
SOP	:Standard Operating Procedure

10. REVISION HISTORY

Revision No.	Effective Date	Reason for Revision	Change Control No.
01		NEW SOP	NIL

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ANNEXURE I

LITERATURE SEARCH STRATEGIES

Search strategies shall be set up for each ..... product to generate new articles added to Pubmed on a monthly basis, as follows:

- ✓ **Search String # 1**: Generic names of all ..... products
- ✓ **Search String # 2**: (Adverse event) or (Adverse drug reaction) or (Lack of efficacy) or (Pregnancy) or (Drug abuse) or (Medication error) etc.
- ✓ **Search String # 3**: Combination of Search String # 1 & Search String # 2

Search String # 3 shall be set for automated weekly email alerts in to the inbox of the designated personnel.

Points to be considered while setting a search on pubmed:

1. The search shall be made based on the generic name rather than the brand name.
2. Unless medically relevant, the search shall not be based on a particular salt or specific compound for an active ingredient.

When alternate names or spellings of the drug are possible the same shall be used in the search build up.

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ANNEXURE II

FLOWCHART OF LITERATURE MONITORING PROCESS