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Aggregate Reporting and Regulatory Requirements

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Abstract

Aggregate report preparation represents one of the most time and resource intensive pharmacovigilance regulatory requirements. Pharmacovigilance is defined as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem". The aggregate report plays an important role in the safety assessment of drugs; it is also known as periodic reporting and cumulative safety information. The main purpose of aggregate study is to compile safety information for a drug over an extended period of time. The aggregate report is required to be submitted to various regulatory agencies to comply with regulatory requirements. The periodic reports play a significant part in the drugs risk-benefit assessment and involve collective case analysis in the database, tracking of regulatory action, literature search etc. The benefit of aggregate reporting is that it gives wider perspective of the drug's safety profile. The present work highlight the types of aggregate report, format and presentation of PSUR, PBRER, PADER and DSUR the timeline, and the key form of aggregate report to be presented for different regulatory authorities.

Keywords: Case safety report, Risk-Benefit evaluation, PSUR, PBRER, PADER, DSUR.

INTRODUCTION

Aggregate reports are the reports that emphasize on evaluation of safety profile and benefit risk and do not focus much on individual cases. Aggregate report is the process that reviews the cumulative safety information from a wide range of sources, on a periodic basis and submits the findings to regulators worldwide. The aggregate report examines and summarizes all existing safety experience with a medicinal product. Report includes benefit-risk assessment of Adverse Drug Reaction (ADR) and the Serious Adverse Event (SAE, Pregnancy reports. The aggregate safety reports are presented to regulators as soon as the medicine is marketed anywhere in the world and enables understanding of risk and benefit profile of the product over a period of time. Preapproval aggregate report contains Investigational New Drug (IND) report in United States and annual safety report in Europe. The post approval aggregate report is Periodic Benefit Risk Evaluation Report (PBRER), Periodic Adverse Drug Experience Report (PADER), and Periodic Safety Update Report (PSUR). The safety evaluation of medicinal product can be achieved by aggregate report and submitting it to various regulatory agency. Primary goal of overall report is to periodically to measure the medicinal products safety experience worldwide.

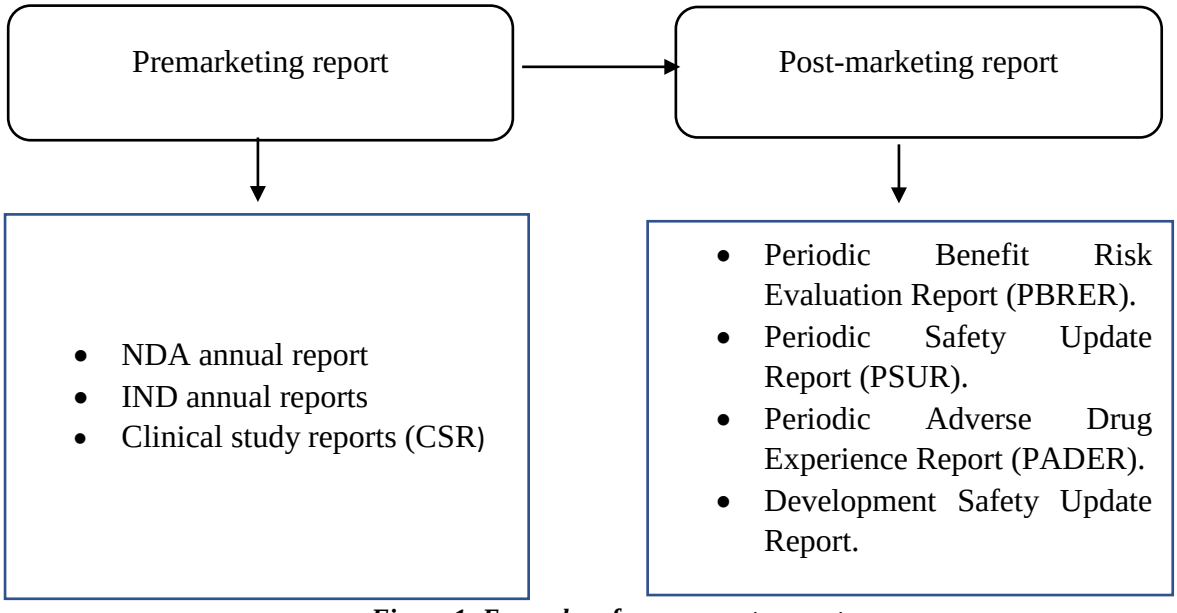

Figure 1: Examples of an aggregate report

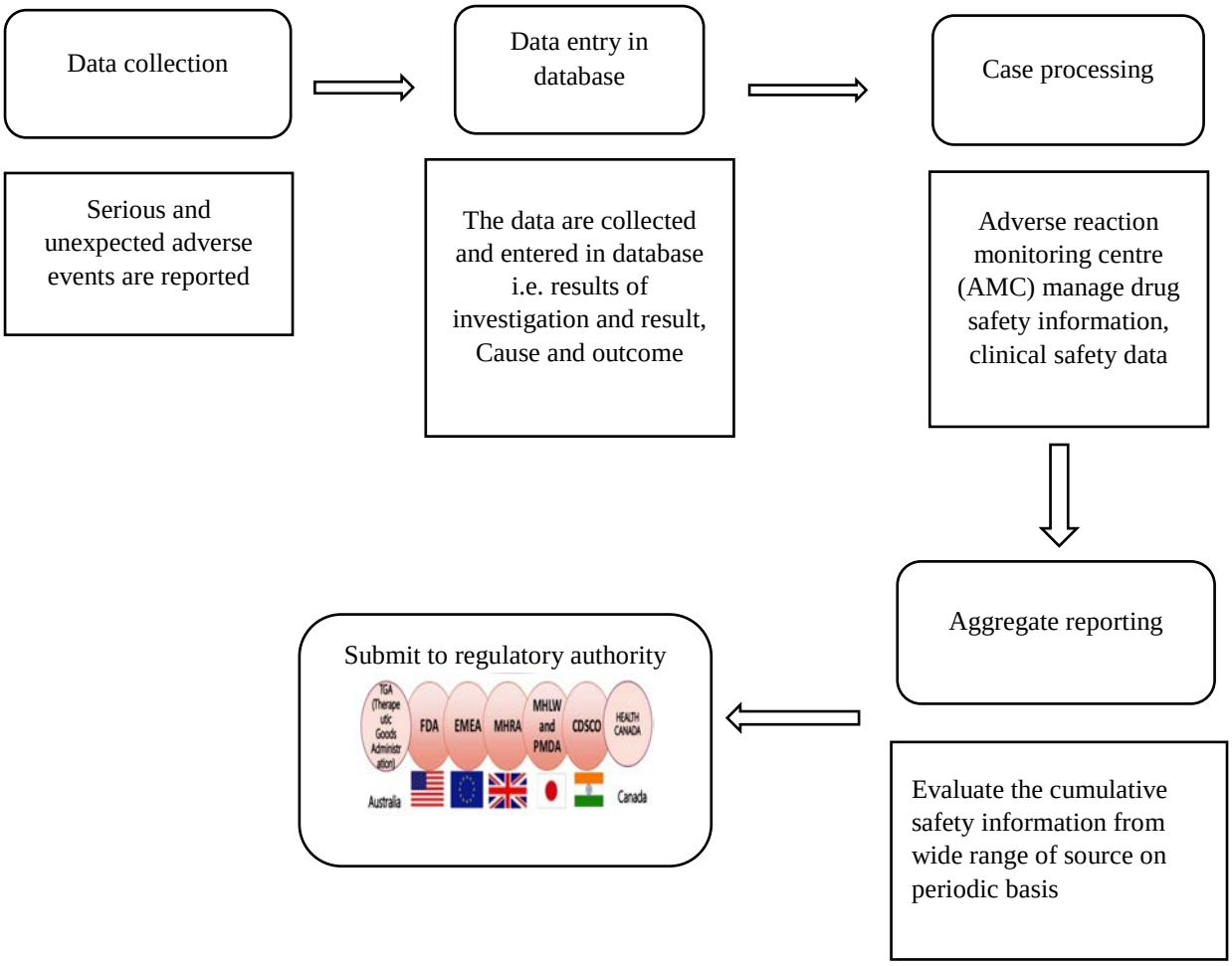

Figure 2: Pharmacovigilance process

DISCUSSION

Periodic Safety Update Report (PSUR)

Upon approval and market introduction of the new drug, Clinical security should be supervised carefully. Regular Periodic safety update reports (PSUR) shall be provided by candidates by: [1]

a) Report information from a suitable source
b) Relates contact of patient information.
c) Review the status of market authorisation in various countries.
d) The product data should be changed to enhance the use of the product

PSUR represent an acceptable and practical mechanism for conducting an overall safety evaluation and for summarising interval safety data. It covers ongoing safety issue and helps marketing authorization holder for conducting the efficient analysis of safety information on the consistent basis. PSUR include an update on developing or urgent safety issues. Throughout the development period, based on the limited number of patients involved in the trial the safety and efficacy of the substance are measured. Regulatory authorities and Marketing authorisation holder are sharing responsibilities in marketed drug surveillance. The comprehend safety of an active substance; the MAH should monitor the product continuously after launching the product during the first year on the market. Detailed assessment of the drugs benefit risk ratio is not possible for individual case report. Thus, periodic review of the safety report was obtained globally cumulatively. This grows very important in order to analyse the product's benefit risk.

PSUR should define the studies that are schedules and performed to study security problems. All dosage form, formulation, indication of new drug should be contained in the single PSUR. All appropriate clinical, non-clinical security information should be given in Periodic Safety Update Report, global MAH status, product approval, removal or launch status must be given during the reporting interval and cumulative information must be submitted on severe, unlisted Adverse Drug Reaction. PSUR should concentrate on Adverse Drug Reaction (ADR) and whether modification needs to be made to the product reference safety data to optimize the product use. There is no suggested particular methodology for presenting specific Adverse Drug Reaction patterns; attention should be provided to existing such a rise in ADR frequency and its impact on the safety of general product.

Table 1: Format and presentation of PSUR [1]

Title page	The title page includes data on the medical product name, approval date of the new drug, marketing date of the holder name and address of the new drug marketing authorization, authorized medical product indication.
Introduction	The PSUR contains the information about medical product pharmacokinetic, efficacy, dosage form, formulation and report of the approved indication and population.
Worldwide marketing authorization status	PSUR contains details of the country where the product approved currently with the date of approval, date of marketing and reason should be given if any product was withdrawn in any country with reasons
Steps taken for safety purposes in the reporting interval	Actions related to the investigational uses - Summary of planned and ongoing studies; Activity related to investigational use - Regulatory authorities work toward the safety studies
Changes in the safety data reference	The part of PSUR contain any change in reference safety information such changes associated with a warning, precaution, adverse drug reaction, overdose, interaction, and contraindication.
Assessed patient exposure	This part of PSUR contain individual patient information when exposed to the product in a clinical trial, cumulatively and patient exposure from marketing experience
Individual case history	General consideration To determine the safety information of the marketed product marketing authorization holder the normal medical and science journals should be monitored The case accessible as line listing The type of cases included in line listing are: All severe and non-serious unlisted literature and notified reaction All serious reaction from regulatory authorities and from studies or named-patient. Presentation of line listing Cases should be tabularized by figure system (typical structure system arrangement system).
Summary of significant findings in the reporting period	This section contains the finding from completed clinical trials, finding from ongoing clinical trials, finding from literature or independent studies
Signal assessment and risk evaluation	WHO defines the safe signal as the data outlined in a necessary causal link between an adverse case and a medication. The strength of the safety signal is determined by several factors of adverse effect. The safety signal detected from a wide range of bases such as experimental studies and systematic literature.
Overall safety evaluation	The pharmaceutical companies should demonstrate the benefit and the risk of the medical products during the marketing authorization process
Conclusion	This part of PSUR should contain the safety outline of the medical product and the essential action taken by Marketing authorisation holder.
Appendix	The appendix contains copy of marketing authorization, line listing of an individual case safety report

Table 2: Format and presentation of PADER [2]

Title page	This section includes the name of the pharmacovigilance report author, reviewer and person and also contain molecule name along with strength, formulation
Cover letter	This includes a number of serious expected, non-serious unexpected and non-serious expected cases received during the reporting interval
Introduction	Includes an overview of the product, reporting interval, authorisation information.
Summary and evaluation of the report's data	Details of safety problem recognized and evaluation of the reporting period of 15 days finding.
Discussion and action taken for safety reasons	Information about the labelling changes, studies initiated and submitted, drug safety recommendation from FDA
Appendices	Table of the frequency of adverse event occurrence of from the reporting period

Periodic Adverse Drug Experience Report (PADER)

Periodic Adverse Drug experience report (PADER) are presented regularly in post-marketing safety report in the United State PADER should be presented on a periodical basis for the first three years after approval of drug in the United States and annually thereafter. The PADER objective is to provide summary data with an assessment of an approved drug product's benefit risk profile. All new data from adequate sources should be reported, such data should be related to patient interaction to the medicine, any significant safety-related variations should be reported, opportunities should be created periodically for a comprehensive safety review and changes to the authorized medicine label should be produced to optimize product use.(2)

The information which obtained from commercial marketing experience, post marketing clinical investigation, a report in scientific literature, the unpublished scientific article should be reviewed by the marketing authorization holder. When shifting PSUR to PBRER unless there is a change in the Data Lock Point (DLP) reporting frequency, the marketing authorisation holder can proceed without altering the new waiver application and if there are any changes to the DLP, marketing authorization holder must submit a new waiver request and a one-time PADER request. For a specific item, the PSUR reporting cycle is three years.

Table 3: Format and presentation of PBRER [3]

Section	Significance
Title page	It contains the label of the medical product, the description number, the name and address of the Marketing authorisation holder, the global birth date with the name of the nation, the report date.
Introduction	This section contains international birth date with reporting interval, route of administration pharmacokinetic action, dose and administrative route.
The worldwide marketing approval status	Contains cumulative data from all nations and marketing regulatory decisions linked to indication and authorized dose.
The action was taken in the reporting interval for safety reason	Important safety measures made during the reporting interval
Changes to reference safety information	The changes in contraindication, precaution, warning, ADR or interaction made during the reporting period in Company Core Data Sheet CCDS and Reference safety information (RSI) should be mentioned
Estimated exposure and use patterns	This section contains size and population exposed to the medicinal product, Include information on cumulative subject exposure in a clinical trial and cumulative and interval patient exposure from marketing experience
Data in summary tabulation	It includes cumulative summary tabulation of SAEs from clinical trial and post-marketing data source
Summaries of important clinical trial results during the reporting time	It includes the findings from the clinical trial supported by MAHs that are usable during investigating period, such as information from completed, continuing clinical studies, brief -term read up of new safety data relating to combination therapy with fixed doses.
Finding from non-interventional studies	Evidence acquired for the active substance during the marketing authorization holder reporting supported non-interventional research.
Non-clinical data	This section contains information from in vivo, in vitro non-clinical studies
Literature	Literature article published during the reporting interval like pregnancy outcome, use in the paediatric population
Benefit evaluation	Includes information on important efficacy information, newly identified information
Conclusion	A summary on the conclusion concerning the new information arose by the time of interval reporting and the consequence on risk and benefit of product, any changes in the reference safety data should be mentioned
Appendices	Contain summary tabulation, a listing of post-authorization interventional, non-interventional studies reference safety information.

Periodic Benefit Risk Evaluation Report (PBRER)

The ICH E2C(R2) guideline, periodic benefit-risk assessment report (PBRER) is regarded to serve as a standard norm for Periodic Benefit-Risk Evaluation Report evaluation monitoring on distributed products between ICH regions. The ICH E2C(R2) guidance launched the new concepts related to the development of the traditional Periodic Safety Update Report (PSUR) from the safety sequence report to an overall benefit-risk study. It altered the focus to aggregate data assessment from individual case safety reports. Moreover, the expanded range improved the need for data to be integrated into the report.(3)

The regular safety update report provides detailed data on the drug safety of the approved drug product. The risk assessment of a medical product is more essential than its overall benefit. The " Periodic Benefit -Risk Evaluation Report (PBRER) emphasizes risk-benefit ratio''

The PBRER should therefore inculde information on benefits and safety, as well as the reference data for report. In general, havingone reference data is not viable for the marketing authorisation holder

- Includes benefit-risk evaluation
- Common to all ICH region
- Provide information on all generics, product licensed in one country only

All new safety and efficacy evidence should be reported in the appropriate unit of PBRER. The efficacy or information on efficiency available from the International Birth Date (IBD), the date of the first world marketing approval or the Developmental Inetrnational Birth Date (DIBD), the date of the first authorisation for conducting the clinical trial from which the new safety information is available. Clinical drug development continues after marketing approval, data from post-marketing research or clinical trials should be included in PBRER.

The objective of PBRER is to present products overall benefit-risk profile and to present investigation of new information on risk of drugs, comprehensive and concise of a medical product. The PBRER must comprise new evidence related to a medical product that existed during the reporting interval by the marketing authorization holder, in the situation of collective information by

- Specific original safety data that might influence the medical product's benefit risk profile.
- Any fresh efficacy data acquired during throughout the reporting period.
- Evaluating the information obtained by the marketing authorization holder is same as earlier data of medical product risk-benefit profile.
- For approved indication benefit-risk are evaluated, when new safety information has emerged
- The PBRER should include suggested measures for optimizing the risk-benefit profile

For a portion of the other documents such as DSUR, the PBRER content of several parts can be used as a

modular approach basis such as PSUR requires one research for active product, irrespective of its market approval for different formulations or dosage forms or separate indication.

Development Safety Update Report (DSUR)

The Development Safety Update Report is prevalent for regular reporting or reporting of drugs being marketed under research in the ICH region. Regulator considers that the U.S and EU submit DSUR annually, which would fulfil the regional and national requirements. The Development safety Update Report (DSUR) is an annual report, U.S. Investigation New Drug Application (IND) and the EU yearly Safety description is a common standard for periodic reporting on the drug being developed. DSUR provides data on promoted drugs under additional study. The outcome of the evaluation is an investigational drugs security profile. Regulators consider the current specific investigation, change in manufacture, and complete progress position and strategies should be submitted to the national and regional law regulation in the form of the periodic report. DSUR's structure, design and duration emphasize the significance of a basic standard report in encouraging accuracy and effectiveness.[4]

Objectives

- The safety information of the annual review is presented in a complete, throughout the period of reporting for drugs beneath the study
- The data obtained at the time of reporting period should be in concurrence with the previous investigational drug safety.
- The potential risks which are identified should be in summarized based on the current understanding and management.
- The clinical investigation and study result should be updated

The safety issues which are revealed throughout the reporting period should discourse in the DSUR. The DSUR must be summarized and offer the data to the controllers and sponsor that the risk outlines of investigational medicine is adequately observed.

Table 4: Format and Presentation of DSUR [5]

Title page	The DSUR title page should contain the following data
	• Development Safety Update Report number (reports should be numbered sequentially) • Drugs for investigation • Duration of reporting • Date of report • Name and address of the sponsor • Declaration of confidentiality and • Unblinded data is included in the DSUR.
Executive summary	This chapter should include a concise overview of the report's significant data. It should serve as a "stand-alone'' document for submitting to ethics boards and other decision makers in conjunction with the title page. The following information should be included in the summary of the executive: • Introduction: version of report and duration of reporting • Research or investigational drug: Pharmacokinetic action, type, dosage form, mechanism of action, estimated exposure to consecutive clinical studies • Authorization for marketing (yes/no) if yes, country number • Overall safety evaluation summary • Summary of significant problems (based on DSUR section 15) • Action taken for safety detail including substantial Investigation Brochure modification. • Conclusion All parts should be fulfilled; this should be indicated if no data is accessible.
Table of content	Introduction This chapter should include reporting period and reporting sequence • Brief medication description, example, Class of therapy, mechanism of action, administration route, drug formulation • Whether the study includes a single clinical trial or a development program. Also, this chapter should notice the scope of the studies covered by the study, example, all investigative drug trials or indication-specific tests. • A short description of the studied symptoms and demographics • A short description and explanation of any excluded information (example where written contract with a partner business do not provide for the exchange of all security data).
Status of market authorisation worldwide	• Only when a product marketing request has been filed in one or more countries or region this section should be completed. • Where available, cumulative information should be provided, usually in the form of a table showing each application status • For this table, the content and format are the same as for PSURs as outlined in ICH E2C.

Table 5: Overview of format for PBRER and DSUR

DSUR	PBRER
Title page Executive summary Table of contents 1. Introduction 2. Market authorisation world wide 3. Update of action taken during the safety reporting period 4. Changes to safety information reference 5. Status of ongoing and completed clinical trial during reporting period 6. Exposure estimation 6.1 Cumulative clinical trial patient exposure (phase IV) 6.2 Exposure of patient 7. Presentation of clinical trial safety data 7.1 General consideration 7.2 Listing of serious Adverse Reaction (SARs) 7.3 Tabulation of summary overview 7.4 Deaths during the period of reporting 7.5 Subjects that have dropped out in the reporting interval in connection with any adverse event 8. Important clinical trial findings during the reporting period 8.1 Tests conducted and any provisional analyses 8.2 Continuous or ongoing clinical trial 8.3 Other therapeutic use of the research drug 8.4 new combination therapy safety information. 9. Related non-interventional studies findings 10. Related results from other studies 11. Additional information 11.1 Non clinical information 11.2 Long term monitoring 11.3 Literature 12. Other information 12.1 Significant changes in production 12.2 Lack of effectiveness 12.3 Changes to the protocol in Phase I 13. Information on late-breaking 14. Evaluation of overall safety 14.1 Risk assessment 14.2 Considerations of benefit-risk 14.3 Conclusion 15. Summary of important risk DSUR annex	Title page Executive summary Table of contents 1. Introduction 2. Market authorisation world wide 3. Actions taken at the safety reporting interval. 4. Changes to safety information reference 4.1 Estimated pattern of exposure and use 4.2 In clinical trial, cumulative subject exposure 4.3 Cumulative and interval marketing experience patient exposure 5. Summary data tabulation 5.1 Information on the reference 5.2 Cumulative summary tabulations of clinical trial serious adverse event 5.3 Cumulative and frequency overview post-marketing data source tabulation 6. Summaries of important clinical trial findings during the reporting period 6.1 Clinical trial completion 6.2 Continuous or ongoing clinical trial 6.3 Long term monitoring 6.4 Other medicinal product therapeutic use 7. New fixed combination therapy safety data 8. Non- interventional studies finding 9. Other clinical trial and source information 10. Non clinical information 11. Literature 12. Other periodic report 13. Lacking effectiveness in controlled clinical trials 14. Information on late breaking 15. Signal overview: new, continuous or closed 16. Signal and risk assessment 16.1 summary of safety issue 16.2 Signal assessment 16.3 Risk evaluation 16.4 Risk characterisation 16.5 Risk minimization effectiveness 17 Benefit valuation 18 Integrated benefit-risk analysis for indications approved 19 Appendices of Conclusion and action

Table 6: Overview of Format for PSUR and PADER

PSUR
Title page Executive Summary Contents of the periodic safety update report 1. Introduction 2. Worldwide registration status 3. Actions are taken in the reporting interval for safety reasons 4. Changes to reference safety information 5. Estimated exposure 5.1. Cumulative subject exposure in clinical trials 5.2. Cumulative and interval patient exposure from post-registration experience 6. Data in summary tabulations 6.1. Reference information 6.2. Cumulative summary tabulations of serious adverse events from clinical trials 6.3. Cumulative and interval summary tabulations from post-registration safety data sources 7. Summaries of significant findings from clinical trials during the reporting interval

7.1. Completed clinical trials
7.2. Ongoing clinical trials
7.3. Long-term follow-up
7.4. Other therapeutic use of medicinal product, vaccine, tuberculin (if applicable)
8. Findings from non-interventional studies
9. Information from other clinical trials and sources Annex 12 to Pharmacovigilance Procedure (item 1 of chapter 3 of part V)
9.1. Other clinical trials
9.2. Medication errors relating to medicinal product, vaccine, tuberculin
10. Non-clinical data
11. Literature
12. Other periodic safety update reports
13. Lack of efficacy in controlled clinical trials
14. Late-breaking information
15. Overview of signals (new, ongoing or closed)
16. Signal and risk evaluation
16.1. Summaries of safety concerns
16.2. Signal evaluation
16.3. Evaluation of risks and new information
16.4. Characterisation of risks
16.5. Effectiveness of risk minimisation (if applicable)
17. Benefit evaluation
17.1. Important baseline efficacy and effectiveness information
17.2. Newly identified information on efficacy and effectiveness
17..3. Characterisation of benefits
18. Integrated benefit-risk analysis for registered indications
18.1. Benefit-risk context (medical need and important alternatives)
18.2. Benefit-risk analysis evaluation
19. Conclusions and actions
20. Appendices to the periodic safety update report

PADER

Title page
Cover letter
1. Introduction
2. Summary and analysis of report's data
3. Discussion of safety related actions
4. Appendixes

Reporting to USFDA

The substance for marketing in the USA must submit PADER as an overall report. The marketing authorisation holder should evaluate all ADR information found after a source such as post-marketing epidemiological study or surveillance survey, scientific literature reports, profitable selling practice, post-approval clinical study.[6]

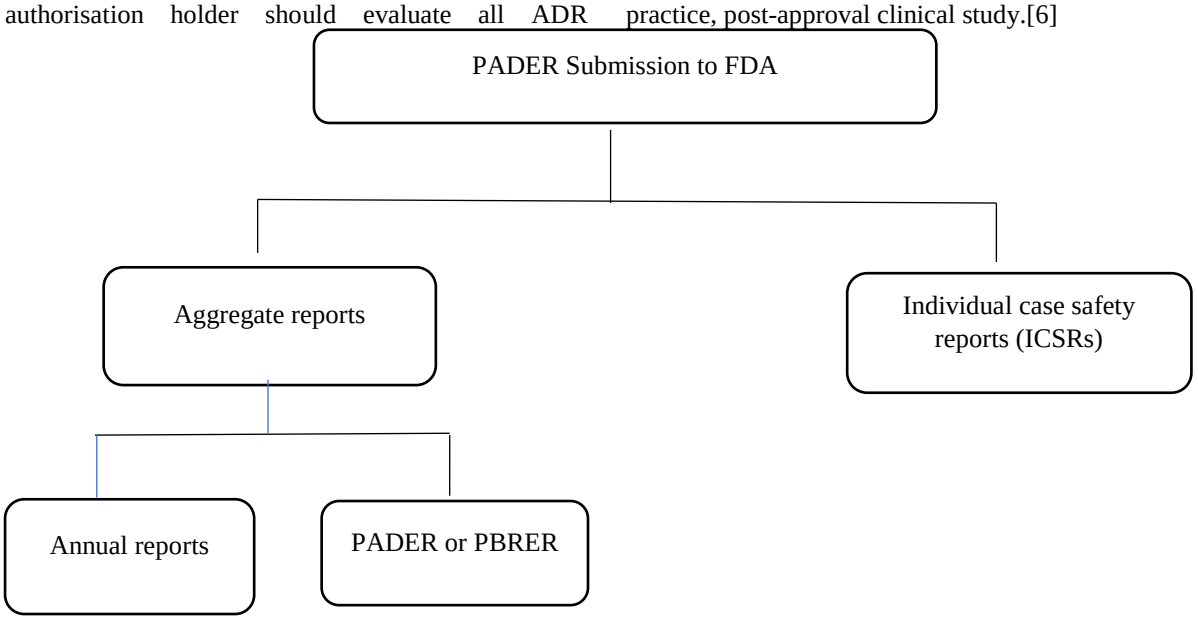

Figure 3: Submission of PADER to FDA

Marketing authorisation holder should send Periodic Adverse report on drug experience at first periodic interval of three years from the date of approval and of the request and then for regular period until the item is withdrawn. Post -marketing adverse drug report under 21 CFR 314.80 must be submitted.

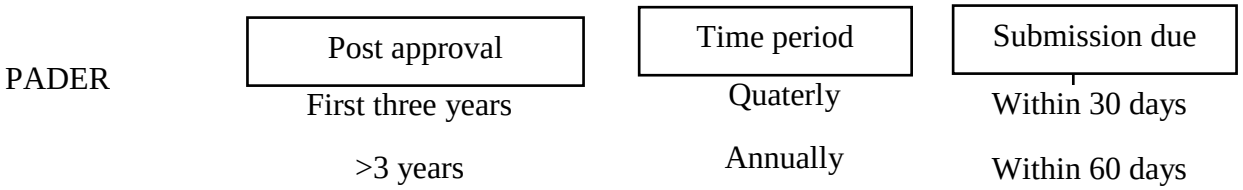

Figure 4: Timeline required for submission [6]

European Medicine Agency- European Union

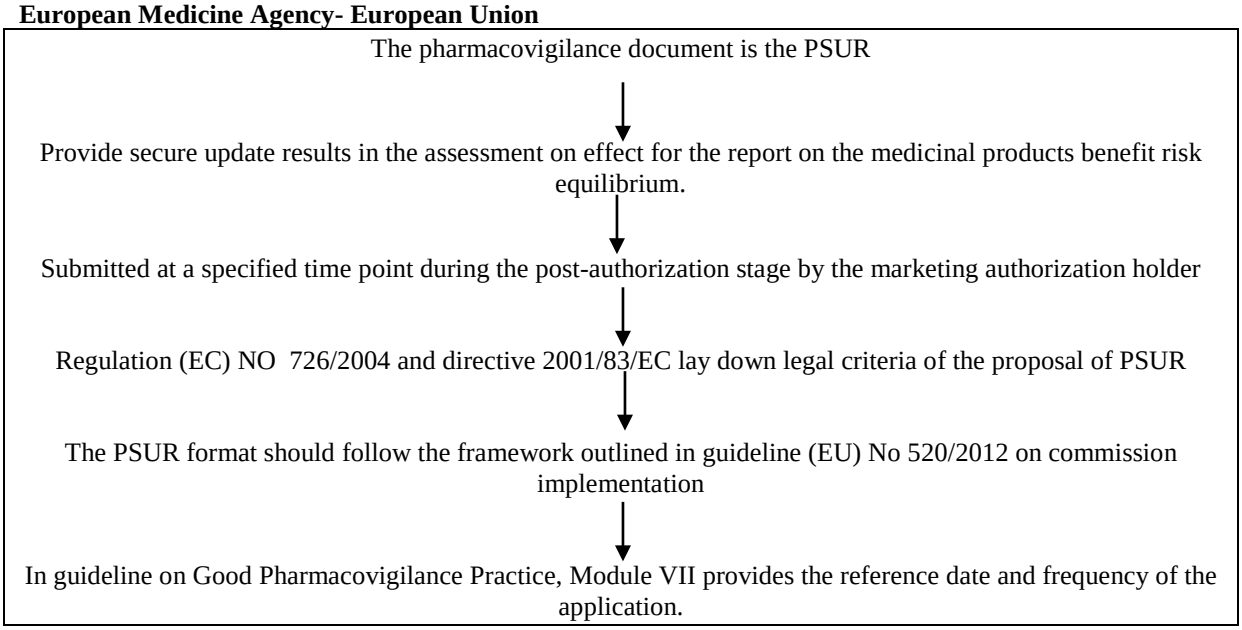

Figure 5: Submission of PSUR in EU [7]

Marketing authorization holder shall submit PSUR as detailed in the list of EU reference date (EURD). For each active substance/combination contained in it, the EURD list provides the following information

- PSUR submission frequency
- DLP
- Date for submission
- Requirement for generic, well-established use of PSUR, herbal product, homeopathic and traditional medicine.

MAH shall submit PSUR according to following submission schedule.

- After the item has been authorized (not marketed) at an interval of six months
- After the item has been launched on the marketplace, regular PSUR must originally be continuous for the two years.
- Subsequently for the next two years and then at an interval of 3 years.

India-CDSCO

The structure of PSUR In India, Periodic Safety Update Reports (PSURs) of drugs are needed to be presented to the office of Drugs Controller General India in accordance with the regulations of clause 4 of Schedule "Y" Drugs and Cosmetics Rules

The PSURs should be structured as per clause 4 subclause (v) of schedule "Y" which is as under and the report should be India specific

a) A title page

PSUR for the product, applicants name, the period covered by the report, date of approval of the new drug, approved indication, date of marketing of new drug and date of reporting

b) Introduction
c) Worldwide registration status
d) Actions are taken in the reporting interval for safety reasons
e) Changes to reference safety information
f) Assessed patient exposure
g) Individual case report or history presentation
h) Clinical studies
i) Other information
j) Overall safety assessment
k) Conclusion
l) Appendix providing material relating to indications, dosing, pharmacology and other related information

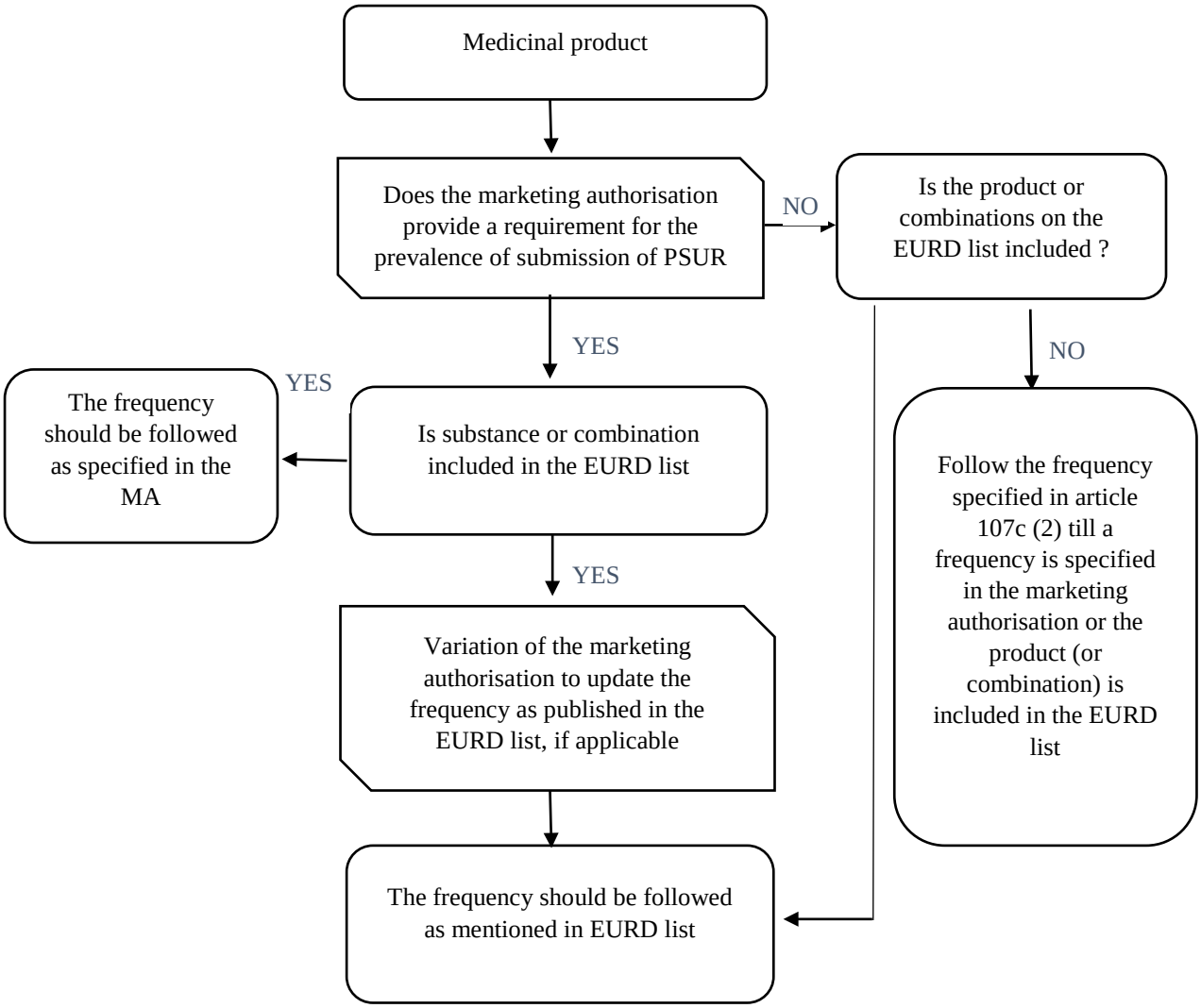

Figure 6: Concepts for submission of PSURs as a basic requirement [8]

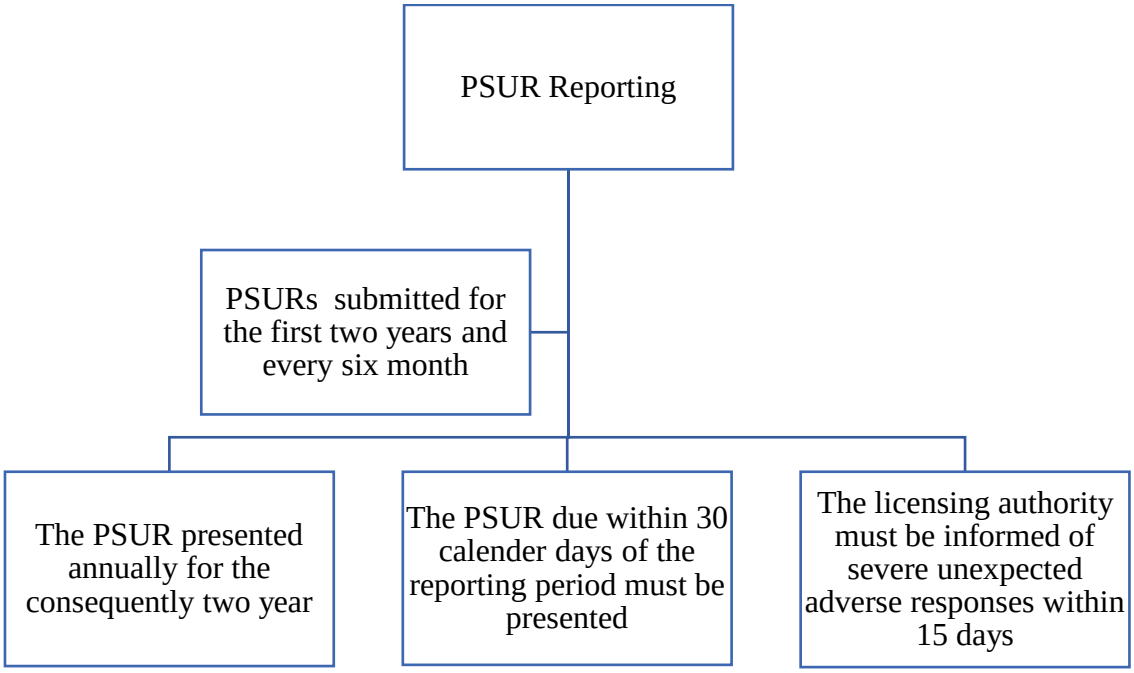

Figure 6: Timeline required for submission of PSUR in India [9]

Table 7: Regulatory Requirement for Submission of PSUR in different countries [10]

Regulatory requirement	USA	EU	India	Japan	Singapore
PV regulations	FD&C Act 1938; FDA Modernization Act 1997; FDAAA 2007; FDASIA 2012; 21 CFR	Regulation EC 726/2004; Directive 2010/84/EU; Regulation (EU) 1235/2010; EU Vol. 9A	Drugs and Cosmetics Act 1940; Drugs and Cosmetics Rules 1945 (Schedule Y)	Pharmaceutical Affairs Law; MHLW Ordinance No.135 of 2004; GVP and Good Post-Marketing Study Practice (GPSP)	Medicine Act Chapter 176, 1977
Periodic safety update reports	Every 3 months for the first 3 years.	Every 6 months for the first 2 years	Every 6 months for the first 2 years and then annually thereafter	Every 6 months for the first 2 years.	Every 6 months for the first 2 years.

Singapore – Health Science Authority (HAS)

PBRER preparation for regulatory officials is a regular pharmacovigilance activity described in the E2E rules of the International Council for Harmonization (ICH). The content and format guidelines for the PBRER can be found in the recent version of ICH Periodic Benefit- Risk Evaluation Report in the E2C(R2)

The PBRER report must be submitted by the registrant of a therapeutic product:

- For an early period of 2 year, at durations of 6 months either from date of the therapeutic product registration or its international birth date.
- Each year, over the next three years.

HSA may request in writing that PBRERs continue to be presented after the original 5 years of registration authorization if there are reasons for continuing the safety surveillance of the medicinal product on the market. The PBRER must also cover the time period from the last updated document and must be presented from the information lock point within 70 days (for PBRER coverage up to 12 months) or 90 days (for PBRER coverage up to 12 months).

Health Canada – Canada

The PBRER is a pharmacovigilance document that aims to provide a thorough, concise and critical analysis of current or existing product risk data and its value in authorized information to allow an evaluation of the product's general benefit -risk profile. ICH revised guidance E2C(R2) ensures that annual summary reports for marketed substance or medicine play the role of periodic benefit-risk evaluation reports by covering safety evaluation of all relevant information available to MAHs benefit -risk evaluation.

The objective of PBRER review in health Canada [11]

- An effect in the risk and benefit outline of the health products on current evaluation of all new and cumulative information.
- Firming up the link between risk assessment and actions taken to minimize risk.
- Assisting the lifecycle approach to product vigilance.
- Line-up product vigilance with international best practice.
- Reducing the problem on the industry that would result if MAHs were to have to produce PSUR for health Canada and PBRER for other jurisdiction.

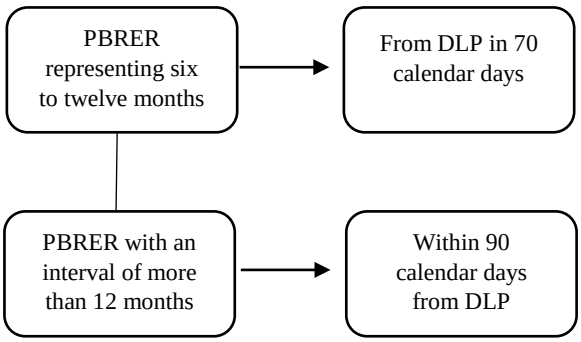

Figure 7: Timeline for submission of PBRER in Canada(11)

Japan -PMDA

Once a firm is approved to sell a drug in Japan, the safety of the product should be evaluated over a period of four, six or ten years of "re-examination", depending on the nature of the drug. In the early post-marketing stage, the operations that should take place as follow,

Table 8: PSUR submission in Japan [12]

Approval condition	6 months for the Early Post-marketing Phase Vigilance (EPPV).
Plan of post-approval study	PSUR Re-examination (4-10 years) after

Early Post-marketing phase vigilance

- To inquire medical organizations to use the medicines cautiously and to report severe Adverse Drug Reactions to pharmaceutical companies instantly if they occur
- To request suitable use and repeated ADR reporting for 6 months after delivery to medical organization.

Non-serious, but moderate in serious and unidentifiable, adverse responses must be recorded for 3 years every 6months and annually thereafter.[13]
The main purpose of performing EPPV is to ensure that the prescribers have received adequate information to promote warning, awareness of the suitable use of drug, and investigate simultaneous adverse effect and infectious disease to enforce the subsequent safety precautions and reduce the consequent health hazard

Australia-TGA

Australia Periodic Safety Update Report are needed for certain registered goods in accordance with Australian criteria and requirements for pharmacovigilance functions of sponsors drugs published by the Therapeutic Goods Administration. During the registration of the drug, PSURs are not needed for all drugs, only those to which this particular condition is applied. The reports shall at least fulfil the PSUR criteria as outlined in the guideline on Good Pharmacovigilance Practices (GVP) module VII -Periodic Safety Update report of European Medicines Agency
The Criteria set out in the guideline for good pharmacovigilance practice (GVP) module VII Periodic Safety Update Report should be met by Australia's Periodic Safety Update Report. Periodic safety report as follow.[14]

- Periodic Safety Update Report may be presented annually for at least 3 years from the registration date or may be presented separately for every 6 months
- The first Data Lock Point is either six months or one year from the approval date.

CONCLUSION

This can be only achieved by working and collaborating continuously with drug manufacturers to promote international harmonization of PV regulations and with the regulators worldwide.This can be only achieved by working and collaborating continuously with drug manufacturers to promote international harmonization of PV regulations and with the regulators worldwide.
Aggregate safety reports should submit to regulators for a period of the medicine that is marketed anywhere in the world and enables to understand the risk-benefit of product over the period of time. The new product is introduced in different markets. Reporting and using data on clinical protection information should be considered as part of persistence. Regulatory requirement for submission frequency and aggregate report content is not the same in all the countries. In order to avoid duplicating of effort, the important data should be submitted with constancy to regulatory authorities.

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