GUIDE FOR REQUESTING THE REPORT PHARMACOVIGILANCE

This document specifies the information that must be included in the request for a pharmacovigilance report, in accordance with Section 8.5 of the Mexican Official Standard NOM-220-SSA1-2016, "Installation and Operation of Pharmacovigilance" and its amendments, published in the Official Gazette of the Federation on September 30, 2020.

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1. INTRODUCTION

Article 376 of the General Health Law (LGS) establishes that, among other products, medications, narcotics, psychotropic substances, and products containing them require health registration. This health registration may only be granted by the Ministry of Health, and will be valid for five years and may be extended for equal periods at the request of the interested party.

The extension of registration renewals is the result of a reform approved by the Congress of the Union, which requires that every five years all medications sold in this country must guarantee their quality, safety, and efficacy to the health authority.

To this end, on February 21, 2017, the Ministry of Health published in the Official Gazette of the Federation (DOF) the ***Agreement announcing the procedures that may be requested in conjunction with the extension of the health registration, as well as the requirements for such application.*** The procedures for which the extension of the corresponding health registration may be requested in conjunction with the application are as follows

PROCEDURE	HOMOCLAVE	MODE
Application for Extension of Health Registration for Allopathic Medicines, Vaccines, Blood Derivatives, and Biomedicines.	COFEPRIS-04-023-TO	Modality A.- Extension of the Sanitary Registry of Allopathic Medicines, Vaccines, Blood Derivatives and Biomedicines of National Manufacture.
	COFEPRIS-04-023-B	Modality B.- Extension of the Health Registry of Allopathic Medicines, Vaccines, Blood Derivatives and Biomedicines of Foreign Manufacture.

The extensions of health registration referred to in procedure COFEPRIS-04-023-A, which are requested jointly with any of the procedures mentioned in the previously cited agreement, must be accompanied, in addition to the documents indicated for the latter, in the ***Agreement by which the formats of the procedures in charge of the Ministry of Health are made known,*** published in the DOF on September 2, 2015, the following documents:

I. Authorization, certificate and visit form duly completed for the extension procedure;

II. Original and two copies of the proof of payment of fees, in accordance with the Law Federal Rights, for the concept of the extension;

III. Certificate of Good Manufacturing Practices and Certificate of Pharmaceutical Product, from the drug manufacturer and the medicine manufacturer, respectively, or where applicable, the documentation that, in accordance with the applicable provisions, is equivalent to said certificates, and

IV. RECEIPT OF THE REQUEST FOR THE PHARMACOVIGILANCE REPORT TO THE NATIONAL CENTER OF PHARMACOVIGILANCE, WHICH MUST HAVE A DATE PRIOR TO THE REQUEST FOR THE PROCEDURE THAT INTENDED TO BE CARRIED OUT JOINTLY WITH THE REGISTRATION EXTENSION PROCEDURE SANITARY.

For applications for extensions of the health registration referred to in procedure COFEPRIS-04-023-B, in addition to the aforementioned documents, the document proving the legal representative domiciled in the United Mexican States must be submitted.

2. JUSTIFICATION

Based on the provisions established in the Regulation on Health Supplies, where Article 190-bis 1 establishes the requirements needed to obtain the extension of the sanitary registration of medicines, Section V specifies the administrative requirement regarding safety and requests that the application be accompanied ***by the pharmacovigilance report (IFV) of the medicine, in accordance with the terms of the applicable regulations.***

The holders of the health registry or their legal representatives in Mexico, supported by their pharmacovigilance units in compliance with health legislation, as well as in compliance with NOM-220-SSA1-2016, installation and operation of the

pharmacovigilance and its modifications, must request the pharmacovigilance report.

3. OBJECTIVE

Describe the necessary requirements to guide the holder of the health registration or the legal representative in Mexico in the preparation of the IFV application before the CNFV of
According to NOM-220-SSA1-2016, installation and operation of pharmacovigilance and its modifications.

3.1. SPECIFIC OBJECTIVES

- ÿ Describe the information required in each of the sections that make up the IFV application.
- ÿ Inform the submission times for the IFV application to the CNFV.
- ÿ Provide information on the documentation that must be attached to the IFV application.

4. GENERALITIES

This guide is based on the provisions of NOM-220-SSA1-2016, installation and operation of pharmacovigilance and its modifications, which contains the structure and timeframes established for the IFV request. Failure to comply with this, the regulatory authority has the power to reject the document and establish the necessary measures for its compliance.

5. PHARMACOVIGILANCE REPORT (PVR)

Based on the provisions of NOM-220-SSA1-2016, installation and operation of pharmacovigilance and its modifications, the IFV is the document issued by the CNFV based on the analysis of all the information contained in the Periodic Reports of
Security (RPS), Risk Management Plan (PMR), Suspected Notifications
Adverse Drug Reaction (ADR), Adverse Drug Reaction (ADR),

Adverse Event (AE), Event Supposedly Attributable to Vaccination or Immunization (ESAVI) or any safety issue related to the use of medications and vaccines, safety reports from clinical studies, and relevant national and international information.

6. GUIDELINES

The health registration holder or their legal representative who intends to renew their health registration in Mexico must prepare and submit a written request to the National Health Commission (CNFV) requesting the IFV. The request must include the following information:

1. The IFV application must be made through the Comprehensive Service Center (CIS) through free writing.

2. The IFV application is for sanitary registration, which must include all presentations and concentrations of the product as well as the regulatory status of each of them (including those not marketed).

3. The request for the pharmacovigilance report must be submitted in the language Spanish and in electronic format (USB/CD).

4. The requested annexes must be submitted in electronic format, PDF.

5. A simple copy of the health registration and information must be submitted as an annex. to prescribe a wide range of updated and current information.

6. When there is a transfer of rights to ownership of the product or a change in the company name, the corresponding acknowledgment issued by the CNFV must be attached, in addition to simple copies of both health registries.

7. When there is a change in the health registration number, in addition to clarifying this situation on the cover page of the document, simple copies of both health registrations must be included.

8. If information is missing for any of the sections that make up the IFV application, it is necessary to write the corresponding justification for the omission of said information within the same point.

7. SUBMISSION LETTER

The holder of the health registration or the legal representative must request the IFV by means of a free written document addressed to the Executive Director of Pharmacopoeia and Pharmacovigilance, which must be delivered through the (CIS), with the following information:

- ÿ Reason for the IFV request.
- ÿ Calendar days prior to the expiration of the health registration considered for the submission of the IFV application to the CNFV (240 to 360 days).
- ÿ Distinctive name of the medicine or vaccine.
- ÿ Generic name or generic name of the medicine or vaccine.
- ÿ Health registration number.
- ÿ Expiration date of the health registration.
- ÿ Tentative date of the extension request.
- ÿ Pharmaceutical form.
- ÿ Product presentations indicating the regulatory status of each one (including those not marketed).
- ÿ Total number of SRAM/ RAM/ ESAVI/ EA notifications sent to the CNFV in the period it covers.
- ÿ Complete data from the pharmacovigilance unit (updated with the CNFV):
  - ÿ Name of the person in charge.
  - ÿ Address.
  - ÿ Telephone number and extension (if applicable).
  - ÿ Email.

8. STRUCTURE

8.1 Cover.
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8.1 Cover.

The cover sheet of the pharmacovigilance report request must be submitted on letterhead by the health registration holder or his or her legal representative in Mexico, including the following:

- ÿ Generic name.
- ÿ Distinctive name.
- ÿ Pharmaceutical form and presentation(s).
- ÿ Health registration number with fraction.
- ÿ Time period covered by the IFV
- ÿ Number of notifications sent to the CNFV in the IFV period being carried out submitting.
- ÿ Complete data from the pharmacovigilance unit (updated with the CNFV):
  - ÿ Name and signature of the person responsible for pharmacovigilance.
  - ÿ Address.

ÿ Telephone number and extension (if applicable).

ÿ Email.

8.2 Information tables.

8.2.1. Periodic Safety Reports.

Example:

No	No. of RPS	Period covered	No. of CIS (when applicable)	Date of submission (when applicable)	Status	No. of patients exposed in Mexico
1	first semester	From dd/mm/yyyy until dd/mm/yyyy	xxxxxxxxxxxxxxx dd/mm/yyyy		Marketed / No marketed	
2						
3						

8.2.2 Risk Management Plans.

If you have PMR approval at the time of the IFV application, please provide the following information:

No no.	of CIS	Date of submission	Approval of code	Document type approval/annual report/final report	Security findings
1					
2					

8.2.3 Clinical Studies.

Only information on clinical studies, including bioequivalence studies, that are open, ongoing, or completed during the period covered by the IFV application should be included.

No.	No. of CIS	Date of submission	Study code	Title of the study
1				
2				
3				

8.2.4 Adverse reactions in the Mexican population.

8.2.4.1 Post-marketing (includes pharmacovigilance studies)

Information on ADRs, SRAMs, AEs, AEFIs or any other safety problem related to the use of the medicines must be included during the period covered by the request for the pharmacovigilance report.

Example:

	Period:	From dd/mm/yyyy to dd/mm/yyyy		
	RAM, SRAM, ESAVI or any other security related issues with the use of the medications	No. of bass	No. of non-serious Total	
SOC	Gastrointestinal			

PT	Diarrhea	1	52	53
PT	Vomit	1	0	1
Subtotal		2	52	54
SOC	Cardiovascular			
PT	Heart attack	5	16	21
Subtotal		5	16	21
SOC	Central nervous system			
PT	Headache	0	25	25
Subtotal		0	25	25
	Total	7	93	**100**

8.2.4.2 Clinical research

Only information on adverse events from clinical studies that are open, ongoing or completed, including bioequivalence studies, should be included during the period covered by the IFV application.

Example:

	EA	No. of bass	No. of no serious	Total
SOC	Gastrointestinal			
PT	Nausea	1	25	26
PT	Vomit	1	5	6
Subtotal		2	30	32
SOC	Cardiovascular			
PT	Arrhythmia	3	17	17
Subtotal		3	17	17
SOC	Central nervous system			
PT	Dizziness	0	25	25

Subtotal		0	25	25
	Total	5	72	**77**

8.2.5 Safety Tables

8.2.5.1 Actions related to marketed medicines or vaccines:

The following information must be provided. It is important to clarify that the health registration holder or his or her legal representative must conduct a search for the active ingredient in the main health surveillance agencies for the years of registration.

Action taken	Yes / No	Agency that took the action	Brief summary of the information
Denial of authorization of marketing			
Denial of extension or renewal of health registration			
Suspension of authorization of marketing recall			
Actions taken due to product quality problems			
Suspension of supply of medicine or vaccine by the health registration holder.			

8.2.5.2 Security alerts or communications.

The holder of the sanitary registration or his or her legal representative in Mexico must conduct a search for the active ingredient in all available years in the different regulatory agencies (mainly those with high sanitary surveillance).

Alert title or statement of security.	Name of the agency that issued the document	Date of publication	Place link of the publication.	Brief summary of the information

8.2.5.3 Presentation of new, ongoing and closed signals.

Only information on new, ongoing, and closed signals submitted during the IFV application period should be included.

DESCRIPTION OF THE SIGNAL	DATE OF DETECTION	STATE (NEW, IN PROGRESS, CLOSED)	DATE OF CLOSING (YEAH APPLY)	FOUNTAIN OF THE SIGN	REASON FOR THE EVALUATION AND SUMMARY OF THE INFORMATION IMPORTANT OF THE SIGNAL	METHOD OF EVALUATION OF THE SIGNAL	ACTIONS TAKEN OR PLANNED

8.2.5.4 Summary of security concerns.

The holder of the health registration or his or her legal representative in Mexico must inform about the significant risks associated with the use of his or her medication.

Security concerns	
Significant identified risks	Liver damage Drug-drug interaction Drug-food interaction Off-label uses

	Misuse Etc.
Significant potential risks	Acute myocardial infarction Teratogenicity
Missing information	Pediatric population Geriatric population Pregnancy Patients with liver failure

8.3 Annexes

ÿ Legible copies of the following documents in PDF format:

1. Copy of the acknowledgments issued by the CNFV regarding the RPS or of non-marketing letters and/or forms approved by the CNFV, from the last 5 years. For those medicines that do not require RPS submission, the corresponding RPS covers must be attached in PDF format.

2. Copy of clinical trial acknowledgments (authorization notice, notice of cancellation, suspension, discontinuation, and/or resumption of clinical trials, annual follow-up safety report, notice of completion of the clinical phase, or final safety report) from the last 5 years (when applicable).

3. Copy of the PMR approval letter or the last CIS admission slip.
(When applicable).

4. Copy of the acknowledgments of the reports of activities derived from the PMR. (When apply).

5. Simple copy of the health registration (updated and valid).

6. Simple copy of the updated and approved prescribing information (IPPA).

7. Copy of the acknowledgment of the transfer of rights letter issued by the CNFV (when apply).

9. APPLICATION TIME TO THE NATIONAL CENTER FOR Pharmacovigilance (CNFV)

The IFV application must be requested by the holder of the health registration or his legal representative through the Head of the pharmacovigilance unit to the National Pharmacovigilance Center based on the times established in sections **8.5.1** and **8.5.2** of *NOM-220-SSA1-2016,* installation and operation of pharmacovigilance and its modifications:

- From **240 to 360** calendar days prior to the expiration of your health registration.
- From **30 to 60** calendar days prior to the application associated with the modifications that result in the extension of the health registration.

For product extension requests whose health registration expires before September 18, 2018, submitting the Safety Report in Mexico (SMR) to the CNFV will be valid only once.

Registrations with an expiration date after September 18, 2018, must request the IFV from the CNFV in accordance with the time periods established in NOM-220-SSA1-2016 and its amendments, as indicated in these guidelines.

For medicines and vaccines that have a health registration and have not been marketed in the country and need to be extended, their non-marketing status must be confirmed within the same IFV application, with the applicable annexes.

10 REFERENCES

1. Official Journal of the Federation. Mexican Official Standard MODIFICATION NOM220-SSA1-2016, Installation and Operation of Pharmacovigilance. Available from: https://www.dof.gob.mx/nota_detalle.php?codigo=5601541&date 09/30/2020 of access

2. Official Journal of the Federation. Mexican Official Standard NOM-220-SSA1-2016, Pharmacovigilance Installation and Operation. Available from: http://www.dof.gob.mx/nota_detalle.php?codigo=5490830& access date 07/19/2017