Proposal for New Area/Project/Project Extension

For consideration of the Steering Committee

(Please submit to PANDRH Secretariat [PAHO])

Proposed title for the area/project	**Initiative of the National Regulatory Authorities for the joint evaluation of periodic safety update reports (PSURs), risk management plans (RMPs), and periodic benefit-risk evaluation reports (PBRERs)**
Proponent	Institute of Public Health of Chile National Health Surveillance Agency (ANVISA-Brazil) Health Canada
Objective and rationale (including reference to one or more objectives of the PANDRH Strategic Development Plan)	Objective Under Strategic Objective IV, the following objectives are proposed: ▪ Define and implement a strategy for the joint evaluation of Periodic Security Reports (PSUR) and Risk Management Plans (RMP) among the NRAs of the countries of the Americas region. ▪ Develop capacities and generate experience at the level of the national pharmacovigilance programs of the NRAs, in terms of critical information analysis of PSUR and RMP. ▪ Generate exchange of joint PSUR and RMP evaluations among the NRAs in order to promote the efficient and effective use of resources. Rationale: Pharmacovigilance programs in the Americas present major challenges in terms of operations and communication, directly affecting risk management associated with the use of medicines in health systems. The following limitations and critical factors are most closely linked to PSURs and RMPs: • Weak capacity, heterogeneity, availability, and stability of human resources devoted to pharmacovigilance • Increasing market penetration of drugs that pose serious challenges to safety analysis and monitoring • The volume of information contained in the documents, particularly PSURs • Underreporting, either due to lack of training or sensitization, or excessive workload • The growing potential for drug use not in accordance with NRA-approved uses • Excessive workload at many national pharmacovigilance centers • Overexposure of the population and of health workers to information on medicines that is biased, unprocessed, unassessed, or of a promotional nature • Weak leadership on the rational use of medicines

	• Incomplete vision of pharmacovigilance (limited to data gathering and reporting). • Interaction with the pharmaceutical industry and analysis of the respective documentation (PSURs, PBRERs, RMPs, etc.) It is therefore essential to construct information exchange and analysis systems that strengthen the integration of regulatory authorities, so that successful experiences in facing common challenges can be discussed in an environment of collaboration and mutual learning. Furthermore, the existing workload at the national centers justifies the search for cooperation initiatives aimed at strengthening activities and avoiding the duplication of efforts. An example in this regard is the critical and well-reasoned analysis of very long documents presented by marketing authorization holders, such as PSURs and RMPs, which are often almost identical among countries. One of the expected results of collaboration through this project is, therefore, for NRAs to benefit from critical joint evaluations that can at the same time serve as reference for other NRAs, favoring the implementation of the respective regulatory measures. Technical evaluation of the content of PSURs and RMPs similarly implies the transfer of knowledge in the form of practical exercises and enhanced local capacities. <u>Correspondence with the objectives of the Strategic Development Plan</u> This proposal corresponds to Strategic Objective IV: Promote the exchange of experiences and regulatory knowledge among NRAs within the Network and with NRAs outside PANDRH.
Scope (including points that should be addressed and opportunities for regulatory convergence)	<u>Points for consideration</u> a) Design of the strategy to develop capacities for the analysis of PSURs b) Validation of tools to be used in the activity (evaluation formats) c) Implementation of joint analysis, initially coordinated by Health Canada and other NRAs of the Region (ANVISA, ISP,CECMED) d) Creation of a repository of analytic reports e) Design of a strategy for crisis and routine communication <u>Opportunities for regulatory convergence</u> ▪ The Pharmacovigilance strengthening is a priority task in the Latin American; there is a growing interest of the participating countries in the evaluation of PSUS and RMP. The activities that have been carried out have been positively evaluated by the members of the Pharmacovigilance

	network. ▪ The project will allow the exchange and exploitation of the information generated from the evaluations among the NRAs to advance a gap that affects most countries and that can have a great impact on the safe use of medicines in health systems. ▪ The joint work of evaluation of PSUR and RMP Risk allow to reduce costs in time, in personnel; and to strengthen joint work in an area of harmonization. ▪ In August 2017, within the framework of the pharmacovigilance meeting held in Colombia, 12 countries expressed their interest to participate in joint evaluations of IPS and 13 countries expressed their interest to participate in joint evaluations of PGR.
General work plan and proposed timeframes	Proposed steps and timeframes: <u>Joint evaluation of PSUR:</u> The main points that will be part of the plan are related to: a) Design of strategy for the development of capacities for the joint evaluation of PSUR (May 2015). b) Development and validation of tools to be used in the activity (evaluation formats) (June 2015 - December 2015). c) Implement the joint evaluation strategy in the framework of pilot stages under the initial coordination of Health Canada (December 2015). d) Training in the use of the established tools and in the analysis of the data (April 2016). e) First pilot evaluation of an PSUR between Brazil and Chile (from January 2016 to May 2016) f) Review of the evaluations carried out by each of the countries by Health Canada (August-September 2016) g) Face-to-face meeting of follow-up and discussion of the results of the first evaluation, within the framework of the Pharmacovigilance meeting of the Americas in Panama. (October 2016) h) Second pilot evaluation of an PSUR between Cuba and Peru (from January 2017 to August 2017) i) Review of the evaluations carried out by each of the countries by Health Canada (November - December 2017) j) Third pilot evaluation of an PSUR between Brazil and Chile (from June 2017 to July 2017) k) Face-to-face meeting of follow-up and discussion of the results of the 2nd and 3rd evaluation of PSUR, within the framework of the Pharmacovigilance meeting of the Americas in Colombia. (August 2017)

	l) Review of the evaluations carried out by each of the countries by Health Canada (August-September 2016). m) Generation of a repository of IPS evaluation reports. (December 2017). n) Preparation of a PSUR evaluation procedure, including criteria for the selection of medicines to be evaluated and evaluation criteria (March 2018). o) Joint evaluation of PSUR among the 12 interested countries (January - December 2018) <u>Joint evaluation of RMP:</u> The main points that will be part of the plan are related to: a) Design of strategy for the development of capacities for the joint evaluation of RMP (August-December 2017). b) Development and validation of tools to be used in the activity (evaluation formats) (January - March 2018). c) First pilot evaluation of a RMP between Brazil and Chile (from March - May 2018). d) Review of the evaluations carried out by each of the countries by e) Review of the evaluations carried out by each of the countries by Health Canada (June 2018). f) Second pilot evaluation of a RMP between two interested countries (from June-August 2018). g) Review of the evaluations carried out by each of the countries by Health Canada (September 2018). h) Preparation of an evaluation procedure for RMP, including selection criteria for the drugs to be evaluated and evaluation criteria (September - October 2018). i) Face-to-face meeting to discuss the results of the process, within the framework of the Pharmacovigilance Meeting of the Americas in Chile (October 2018). j) Planning of the joint valuation of RMP among the interested countries.
Proposed project leader	Institute of Public Health of Chile National Health Surveillance Agency (ANVISA–Brazil) Health Canada
Proposed sources of expertise/ financing	Actions will be coordinated by experts from the countries, particularly from the three NRAs involved (Canada, Brazil, and Chile), with support from PAHO/WHO regional advisors. Resources will come from the NRAs and PAHO/WHO, with an initial annual budget of US$15,000 to facilitate on-site meetings. The contribution of the RNAs mainly involves the HR available to carry out the evaluation activities of the documents.
Relevant documents	▪ **Resolución N°381 de 20 de junio de 2012 de MINSAL** Aprueba Norma General Técnica sobre Sistema Nacional de

(national or international agencies)	Farmacovigilancia de Productos farmacéuticos de uso Humano (Norma Técnica N°140) ▪ **Resolución N°108 de 2013** Aprueba instructivo de farmacovigilancia para la elaboración de los informes periódicos de seguridad. ▪ **Resolución N°2741 de 2013** Modifica la Resolución Exenta N°108, de 14 de Enero de 2013, que aprueba el instructivo de farmacovigilancia para la elaboración de los informes periódicos de seguridad. ▪ Anexo 2: Guia para elaboração do Relatório Periódico de Farmacovigilância (Versão 1.2) ▪ ICH Harmonised Tripartite Guideline. Inical Safety Data Management: Periodic Safety Update Reports (PSUR) for Marketed Drugs. E2C(R1). Disponible en línea: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002780.pdf ▪ ICH Harmonised Tripartite Guideline. Periodic Benefit-Risk Evaluation Report (PBRER) E2C(R2). Disponible en línea: https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2C/E2C_R2_Step4.pdf ▪ CH Harmonised Tripartite Guideline. PHARMACOVIGILANCE PLANNING ▪ E2E https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2E/Step4/E2E_Guideline.pdf