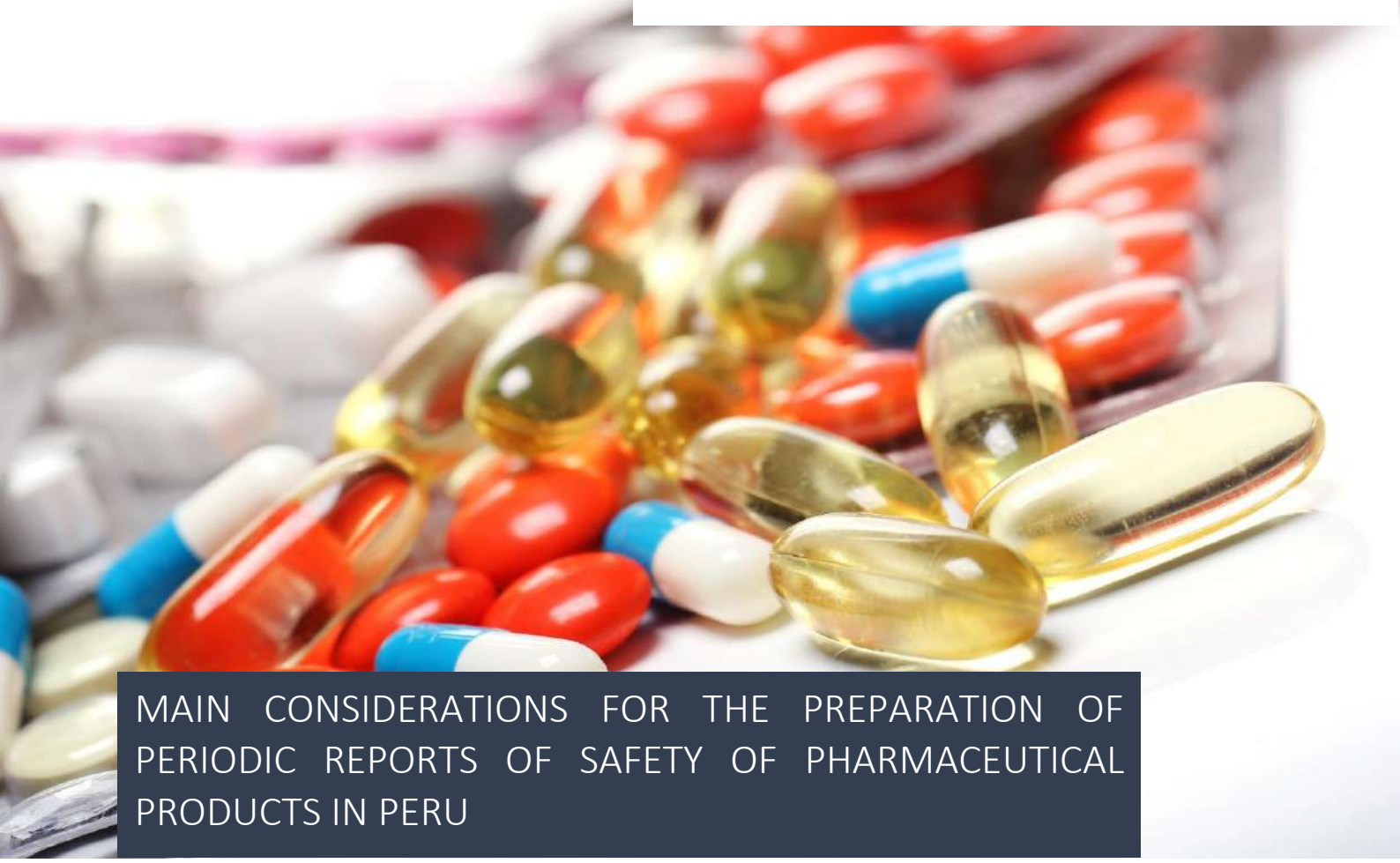

MAIN CONSIDERATIONS FOR THE PREPARATION OF PERIODIC REPORTS OF SAFETY OF PHARMACEUTICAL PRODUCTS IN PERU

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As part of the development of the pharmacovigilance system in Peru, since the publication of the Regulation for the Registration, Control and Sanitary Surveillance of Pharmaceutical Products, Medical Devices and Sanitary Products (Supreme Decree No. 016-2011-SA), the preparation and presentation of the Periodic Safety Report (IPS) for a pharmaceutical product from the date of its authorization in this country, during the time of its commercialization. In this regulation, Periodic Safety Reports are defined for the first time as a "*Document prepared by the holder of the sanitary registration, which contains updated information on the safety of a pharmaceutical product or medical device, information on suspected adverse reactions or adverse incidents of those that have been known in a reference period, as well as a scientific evaluation of the benefit-risk balance*".

Later in Peru, the Technical Document: Manual of Good Pharmacovigilance Practices was published through Ministerial Resolution No. 1053-2020-MINSA on December 13, 2020. It is in this document that more specific criteria and more precise definitions of the Periodic Safety Reports are proposed, as well as a format that describes in detail the structure for the preparation of this document.

In both documents issued, the Periodic Safety Report aims to carry out an assessment of the benefit/risk balance of the pharmaceutical product based on all the information accumulated on the product since the beginning of its development in the world.

For this, it is important to mention that according to the Manual of Good Pharmacovigilance Practices in Peru, the preparation of this report is carried out for all pharmaceutical products, with the exception of herbal medicines, galenic products, homeopathic products, diet products and sweeteners; but it is presented to the authority only in the following cases:

a) For pharmaceutical products requested by the National Medicines Authority (General Directorate of Medicines, Supplies and Drugs - DIGEMID).
b) For pharmaceutical products that correspond to present the risk management plan for the purposes of the sanitary registration.
c) For pharmaceutical products that the National Medicines Authority (General Directorate of Medicines, Supplies and Drugs -DIGEMID) requests the risk management plan for safety reasons.

Regarding point (a), some situations can be mentioned in which the authority could request the presentation of the Periodic Safety Report: serious or more frequently detected risks that affect public health and global alerts mainly related to the safety profile of the Pharmaceutical product registered in

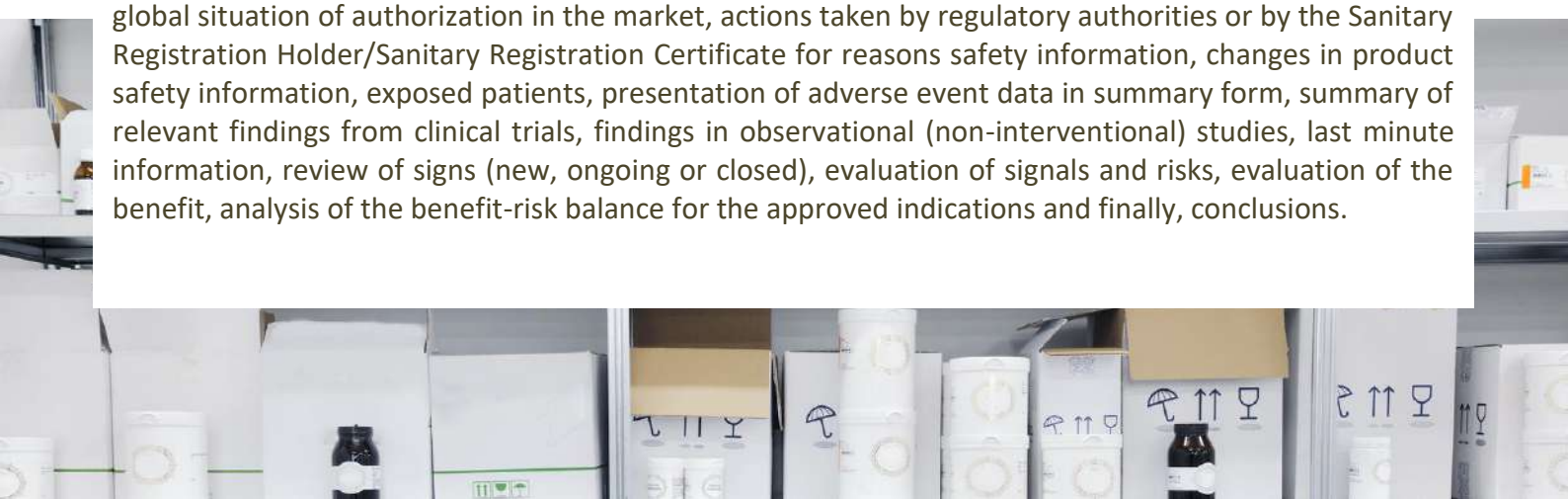
Regarding the periodicity with which this document should be prepared, we can refer to what is mentioned in the Manual of Good Pharmacovigilance Practices:

a) Every six (06) months during the first two (02) years, from the date of authorization of the pharmaceutical product in the country.
b) An annual report for the next three (03) years.
c) As of the sixth year, one report every five (05) years.

It should be noted that if the product has not yet been marketed in Peru, it must be taken into account that there is accumulated global information on the product, which can serve as a basis to start with its preparation and thus monitor the benefit/risk balance of the pharmaceutical product.

For its preparation, the structure presented in Annex 1 of the Manual of Good Pharmacovigilance Practices of Peru, mentioned above, must be followed. Thus, the Periodic Safety Report consists of the following sections:

Cover page, executive summary, index, list of tables, list of annexes, list of abbreviations, introduction, global situation of authorization in the market, actions taken by regulatory authorities or by the Sanitary Registration Holder/Sanitary Registration Certificate for reasons safety information, changes in product safety information, exposed patients, presentation of adverse event data in summary form, summary of relevant findings from clinical trials, findings in observational (non-interventional) studies, last minute information, review of signs (new, ongoing or closed), evaluation of signals and risks, evaluation of the benefit, analysis of the benefit-risk balance for the approved indications and finally, conclusions.



In addition to Peruvian regulations, the preparation of Periodic Safety Reports can be carried out according to the guidelines of the International Harmonization Conference (ICH E2C R2), which can be used for other countries in Latin America.

In summary, we can mention that the different sources of information that help us to prepare this type of documentation would include: clinical trials, post-authorization studies, scientific literature, spontaneous notifications, safety alerts and a database related to the safety of the pharmaceutical product under evaluation; in addition to the information obtained from the own pharmacovigilance system of the Sanitary Registration Holder/Sanitary Registration Certificate.

Likewise, to carry out the analysis of the benefit-risk balance, it is important to have the participation of different professionals with experience in the different points indicated; this in order to have a broader panorama of the evaluated information as well as the impact it would have on the target population.

All the points detailed above must be considered in the Periodic Safety Report and if there is no information regarding any of the points, the reason why such information is not available must be properly justified.

Another point to take into account are some general considerations referred to in the Manual of Good Pharmacovigilance Practices in Peru for the preparation and/or management of Periodic Safety Reports, such as:

- Maintain a record of all the Periodic Safety Reports prepared.
- Prepare a single Periodic Safety Report for the different concentrations of the same active ingredient and/or associations.
- That the person in charge of pharmacovigilance must review and approve the Periodic Safety Reports if they have been prepared by another company.
- Finally, in the face of a request by the authority for the presentation of a Periodic Safety Report for a certain pharmaceutical product, there is 90 days for its presentation and in general the presentation can be 90 days after the cut-off date of information (FCI).

Finally, in relation to the Periodic Safety Reports, we must bear in mind that the Holders of the Sanitary Registration/Certificate of the Peruvian Sanitary Registration must have progress and/or results regarding the preparation of these reports, even more so with the entry into force of the Manual of Good Pharmacovigilance Practices of this country.

In conclusion, the development of the Periodic Safety Reports for pharmaceutical products that are marketed in Peru will allow the Pharmacovigilance System of this country to be strengthened and, in turn, generate greater support for decision-making regarding the safety and proper use of a pharmaceutical product by the Peruvian population; since the results of the benefit/risk evaluation of a pharmaceutical product will be manifested mainly in modifications of the technical data sheet and its insert, thus maintaining the dynamism of its safety profile throughout its life cycle; finally contributing to the public health of Peru.

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