NEWSLETTER
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NEW SPANISH ROYAL DECREE ON OBSERVATIONAL STUDIES WITH MEDICINAL PRODUCTS FOR HUMAN USE

After a considerable time since the first news on the possible enactment of a new regulation on observational studies in Spain broke, the new Royal Decree 957/2020, of 3 November, regulating observational studies with medicinal products for human use, was published in the Spanish Official State Gazette (BOE), which will come into force on 2 January 2021.

This new Royal Decree, which repeals Order SAS/3470/2009, of 16 December, on the guidelines on post-authorisation studies of observational nature for medicinal product for human use (Order SAS), establishes the new legal framework for observational studies in Spain, and far from making irrelevant modifications, it introduces important new features that should be highlighted.

In this regard, with the main objective of simplifying, the regulatory and administrative burden that, since the approval of the Order SAS, it has been established that carrying out these studies entailed, the main changes that the new regime of observational studies introduces are the following:

a) Deletion of the classification of observational studies

Perhaps the most relevant (and undoubtedly most welcomed) new feature of the new Royal Decree is the deletion of the classification requirement for observational studies established by the previous Order SAS, which had been a real headache since its inception for both researchers and sponsors when it came to carrying out these studies, given the complexity and disproportionate bureaucratic burden that this entailed.

Therefore, as of 2 January 2021, the complex definitions contained in the Order SAS (the EPA-LA, the EPA-AS, the EPA-SP, the EPA-OD and the No-EPA), as well as the several special procedures provided for the processing of each of these, will no longer be in force and will therefore not apply.

The new Royal Decree establishes a single assessment procedure for all observational studies, even though it also provides for a transitional regime for the observational studies that have already been subject to a classification decision by the Spanish Agency of Medicines and Medical Devices (AEMPS) before 2 January 2021, which will not be governed by said Royal Decree and will be subject to the complex regime foreseen by the Order SAS.

b) Deletion of the obligation to hold a prior authorisation

In the same vein of simplification, the requirement to obtain prior authorisation from the AEMPS for carrying out observational studies has been deleted. This also has important effects with regard to

substantial modifications to the protocol, which no longer need to be authorised beforehand, although they will have to be assessed by an Ethics Committee for Research on Medicinal Products (CEIm).

Therefore, the new requirements to start an observational study are limited to the favourable opinion of a CEIm (which will be unique, binding and recognised throughout the national territory) and the agreement with the centre where the participating subjects are treated. It should also be taken into consideration that, for observational studies that are carried out with medicinal products that are to be monitored prospectively, the competent authorities of the Autonomous Communities may subject these studies to additional requirements, which will have to be justified by criteria of feasibility and relevance, and not by aspects already assessed by the CEIm.

As a consequence of the above, the Coordination Committee for Post-Authorisation Studies is also abolished, as its tasks now overlap with the functions of the CEIm.

c) Introduction of patient support programmes (PSPs)

Another important change introduced by the new Royal Decree is the legal recognition, for the first time in the Spanish legal system, of patient support programmes, which the Royal Decree itself conceives as any organised system in which a marketing authorisation holder receives and collects information from individual subjects related to the use of their medicinal products.

As it was already laid down in one of our previous newsletters (in Spanish), the development of PSPs has been a common practice in Spain, having seen a significant growth in recent years, due to several factors, such as the growing empowerment of patients and their new characteristics, the economic advantages that these represent for the National Health System and the increase in patient adherence that this type of programme seems to achieve.

However, this new Royal Decree provides that PSPs that foresee the registration of information on the use of medicinal products through planned contacts with patients may only be carried out in the context of a protocol which includes, as its objective, one of those provided for in the Royal Decree for this purpose.

Consequently, from now own, before launching any patient support programme in Spain, it will be necessary to carry out an assessment to establish whether the specific PSP is included within the scope of this Royal Decree or not.

d) Economic aspects

The limitation on the remuneration for healthcare professionals to the compensation for the time spent and expenses incurred is maintained, but a mention is added to the possible compensation that participants may receive, if any, and it is also established that all the economic aspects related to the study must be included in the contract that might be signed and in the documentation that should be included in the application to be submitted to a CEIm for assessment.

The Royal Decree also provides for the possible exemption of any applicable fees for observational studies that might be deemed non-commercial clinical research, which requires that the pharmaceutical industry does not participate in such studies.

e) Informed consent

With regard to informed consent, while the need to obtain the informed consent from patients when the observational study involves interviewing participating subjects is maintained, an exception to this principle is added, as it is established that informed consent may be waived provided that three cumulative conditions are met:

(i) The CEIm considers that the observational study has an important social value;

(ii) The conduct of the study is not feasible or practicable without such a waiver; and

(iii) The conduct of the study entails minimal risks for participants.

f) Guarantees of transparency, information and monitoring

In terms of transparency, the publication of information on observational studies in the Spanish Register of Clinical Studies is established, as already provided for in Royal Decree 1090/2015 of 4 December, which regulates clinical trials with medical products, the Ethics Committees for Research with Medicinal Products and the Spanish Register of Clinical Studies. This publication will be compulsory for observational studies with medicinal products that are to be monitored prospectively, and must be carried out independently to the obligation to publish the results of the study, both positive and negative, and preferably in scientific journals.

The communications to be made in the context of monitoring are also amended, establishing the obligation to communicate to the AEMPS the information resulting from the study that could involve a change in the risk-benefit balance of a medicinal product.

g) Reporting of suspected adverse reactions

The reporting system for suspected adverse reactions has also been modified because of the implications of Royal Decree 577/2013, of 26 July, which regulates the pharmacovigilance of medicinal products for human use, establishing the reporting of suspected adverse reactions by healthcare professionals to the Spanish Pharmacovigilance System and the reporting to the health authorities in the cases in which the protocol has stipulated that such suspicions must be systematically recorded by the healthcare professionals and transmitted to the sponsor, within a legally established time limit depending on the severity of the case.

h) Filling of study documentation

Finally, in relation to the filling of study documents, the need to maintain a master file with all essential documentation that has to allow the supervision of the execution of the observational study and the quality of the data obtained is maintained, but the remaining provisions on the specific documents that should be included in the master file and the filling conditions have been deleted, and will be further developed by future guidelines issued by the AEMPS.

Héctor Jausàs, Partner at Fieldfisher JAUSAS
Life Sciences Department
hector.jausas@fieldfisher.com

Gemma Colomer, Senior Associate at Fieldfisher JAUSAS
Life Sciences Department
gemma.colomer@fieldfisher.com