

## **CLINICAL RESEARCH IN SPAIN**

I would like to begin by thanking you for taking a few minutes of your time to read this article. In today's society, time is a very valuable commodity, and it is not unusual to hear the following, expressed in one way or another: "When a person gives you their time, they are giving you something they will never get back", so I would like to thank you sincerely for your time and hope that you find what I have to say to be of interest. The topic chosen on this occasion is clinical research in Spain, and I will focus on giving a general outline of the main characteristics of research in this country and an overview of the applicable regulations, and the reasons why Spain is a good place to do research.

Spain is a country with a population of approximately 48,146,134 inhabitants (July 2015), distributed over the following age groups: 0-14 years, 15.45%; 15-24 years, 45.57%; 25-54 years, 11.67%; and over 65 years of age, 17.75%. The mean life expectancy is 81.57 years. The country covers an area of 498,980 square kilometers (4,964 sq. kilometers of coastline) and borders Andorra (63 km), France (646 km), Gibraltar, UK (1.2 km), Portugal (1.224 km), and Morocco (Ceuta and Melilla) (18.5 km). Tourists are attracted by our climate and our gastronomy and both tourists and the local population enjoy our rich cultural heritage. The climate is temperate, with hot summers and cold winters in the interior of the country, while on the coastlines, summers are moderately warm and sometimes cloudy and cool and cloudy in winter.

Spain is one of the countries with the best healthcare systems: in 2014, healthcare expenditure was approximately 9% of GDP, there are about 4.95 doctors for every 1,000 inhabitants, more than 3,000 primary care centers ([Ministry of Health](#)), more than 10,100 doctor's offices, and around 790 hospitals (public and private). In February 2016, according to the Spanish Agency of Medicinal Products and Healthcare Devices (AEMPS, in Spanish), over 800 clinical trials were ongoing in Spain, quite a considerable number if you take into account that about 15,000 trials were ongoing in the entire European Union during the same period. Some of the many advantages fostering the performance of clinical trials in Spain include the increasing commitment of physicians and healthcare personnel to clinical research, legislation that protects patients' rights while easing the approval processes for setting up new studies, and the diverse opportunities to perform different types of studies, thanks to our varied climate, demographics, and nutritional and pathological characteristics.

## **REGULATIONS FOR THE CONDUCT OF CLINICAL TRIALS IN SPAIN**

The regulations applicable to all Phase I to IV studies with drugs that have not yet been granted marketing authorization have recently been revised and updated. These reworkings are reflected in the new Royal Decree 1090/2015, of December 2015, the main aim of which is to adapt progressively to the new European Clinical Trials Regulation EU No 536/2014. The various definitions that appear in Regulation 536/2014 are incorporated in Royal Decree 1090/2015, including the definitions of "clinical trial" which cover clinical trials, observational studies and low-intervention clinical trials.

Significant differences between the old and the new directives:

Previous directive:

- A clinical trial application was submitted to each of the Member States where the trial was to be conducted.
- Documentation for multicenter trials had to be submitted to all participating ethics committees.
- Hard copies of all documents were required.
- The timeframes for submission of the project were short.
- Patient representation was poorly defined.
- Full fees for evaluation were required by all ethics committees.
- Specific agreement templates were required for each site.
- Translation from English was required by many ethics committees.

New Royal Decree 1090/2015:

- The clinical trial submission is made in only one of the participating Member States.
- Study documentation is submitted to only one of the new Medicinal Research Ethics Committees (MREC).
- There are no timeframes for the submission of projects.
- No members of the MREC may be involved in the study.
- A single fee will be paid for evaluation.
- Single agreement template.
- The protocol may be submitted in English (with a summary in Spanish).

Specified timeframes for setting up a clinical trial in Spain and the steps to follow are now as follows:

- Submission of study documents (including the protocol) to the Spanish authorities (AEMPS). The AEMPS has up to 2 months to respond in favor of or against the proposed study.
- Submission of the study to the Medicinal Research Ethics Committee (MREC). This can be made at the same time as the AEMPS submission. Response will be received within a maximum of 2 months. Just 1 MREC is required under the new Royal Decree.
- Negotiation of agreements with participating sites: according to the new directive, negotiation with the participating sites can start at the time that the study is submitted to the AEMPS and the chosen MREC, allowing very significant time savings. Timeframes in this case vary among sites, but generally the period between starting negotiations and signature of the agreement is no longer than 2-3 months.
- To summarize, with the new Royal Decree, Spain not only harmonizes with the European directive, it also effectively smooths out the procedures required for setting up clinical trials, so that the period between submitting a study and actually initiating it can be as short as 2-3 months - which you will agree are excellent timeframes.

## **POST-APPROVAL STUDIES AND APPLICABLE REGULATIONS**

Post-approval studies are studies performed with drugs that have received approval for marketing. Spanish legislation clearly specifies that these studies cannot be used for marketing or promotional purposes.

Post-approval studies are performed for various reasons: some are performed at the behest of the health authority to study new drugs as they are launched on the marketplace and their use and outcomes in patients outside the setting of a controlled clinical trial, others are sponsored on the initiative of the pharmaceutical industry itself, responding to a need to collect information on the sociodemographic characteristics of patients, standard clinical practices, incidence and prevalence of a certain disease, etc. These, in essence, are studies which provide useful data for the health authorities, the industry, doctors and patients.

The regulations governing these types of study in Spain are set down in Order SAS 3470/2009, that followed on from Order 7302/2004, specifying the requirements for the conduct of post-approval studies, and in Royal Decree 1344/2007 on Pharmacovigilance.

The timeframes for setting up a post-approval study and the actions and waiting periods can be summarized as follows:

- Classification of the study by the AEMPS (maximum 1 month).
- Submission of the study to the applicable ethics committees (these 2 steps can be performed simultaneously) (maximum 1 month).
- Agreement signed with the participating site (times vary depending on whether the site is private or public, and on the autonomous community where the site is located. The process does not usually take more than 2-3 months).
- If the study is prospective, it must be submitted to the responsible authorities in the autonomous communities where the study is to be performed. (This is done in parallel with the AEMPS classification. Maximum 3 months).
- Final step! The AEMPS is informed whenever the favorable opinion of the first ethics committee is received. The final protocol and all appendices must be submitted to the AEMPS.
- The total time between starting the regulatory process and starting the study is 3-4 months maximum.

Thank you again for taking the time to read this information, which I hope you found interesting.



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