CAIBER: a Spanish platform to support clinical trials

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Clinical trials are the most rigorous type of scientific study; in the field of pharmacology, they allows us to determine or confirm the clinical, pharmacological or other pharmacodynamic effects of drugs and / or to identify adverse reactions, and to study the absorption, distribution, metabolism and elimination of one or more drugs being researched, in order to determine their levels of safety and / or efficacy[1]. A clinical trial is the accepted standard for generating scientific evidence, due to the controlled, objective and reproducible method used to measure the effects and safety of an intervention[2].

All clinical trials must be designed, conducted and reported in accordance with the rules of good clinical practice, and the research must ensure respect for the rights, safety and wellbeing of trial subjects, which should prevail over interests of science and society[3,4]. A study of these characteristics, without neglecting ethical principles (Declaration of Helsinki[5], Oviedo Convention[6]) or the law governing clinical trials[7], is a complex and expensive endeavour.

During the last two decades there have been numerous so-called "commercial" clinical trials, i.e. trials promoted by the pharmaceutical industry and biotechnology enterprises, to register and market new drugs, medical products, prosthetics or devices. In contrast, very few physicians or nurses have been supported with the funds and means needed to perform clinical trials that provide answers to their own research questions, arising from clinical practice and care of patients attended at the emergency department or hospitalized, because they lacked commercial interest[8,9].

The reality is that a large proportion of such possible clinical trials, called independent or non-commercial, were never performed due to lack of resources, whether tangible (human resources and materials, funding) or intangible (coordination, experience, training, information, communication).

When a clinician embarks on the adventure of a clinical trial, he/she not only acquires responsibilities as a researcher, but also those of a promotor3. In practice, this may involve performing more than 70 tasks related to preparation and submission of all the trial documentation, obtaining authorization and participant consent, organizing contracts and insurance, organizing the medication or any other type of intervention, clinical management, monitoring, management of data and analysis, elaborating reports, management of adverse events, etc.

To ensure patient safety and data quality in any clinical trial, whether commercial or independent, the principal investigator must not only be experienced, but also have received adequate training in ethical principles and international consensus standards. We have to remember that the actions undertaken in a clinical trial (if successful) will not only impact on the subjects participating in it, but also the entire population who in the future may use the drug or medical device that has been marketed as a result of all the previous research work.

In one descriptive analysis - the result of compiling inspection reports at 10 research centers - deviations from clinical trial protocol were detected in some hospitals with a long tradition of research, due mostly to lack of support in carrying out these tasks and lack of training in good clinical practice.

But who has been responsible so far for this

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training? Who has helped health professionals carry out their research ideas? Public Health Administrations, with some exceptions, have provided limited support. However, in recent years the effort has not been solely in the hands of the pharmaceutical Industry[11]. A large part of daily work in departments of clinical pharmacology has focused on offering this support and training to colleagues. Clinical research ethics committee members have also provided support for independent investigators regarding procedures to follow in order to obtain relevant authorizations. Some health research foundations have organized workshops and created discussion forums, which have allowed professionals to be informed about regulatory changes. The autonomous communities and the Spanish Agency of Medicines and Health Products have also contributed by publicizing the mandatory ethical and legal aspects through official web pages[12] and running courses on good clinical practice, both for researchers and inspectors.

But one of the most outstanding efforts in recent years occurred in 2008, thanks to the constitution, originating from the "Instituto de Salud Carlos III (ISCIII)" and setting up CAIBER (Consortium for Support of Biomedical Research Network), aimed at promoting multicenter randomized trials, mainly independent.

Support for independent research through CAIBER

CAIBER is the Spanish platform for clinical trials, with its own legal basis, created by an ISCIII resolution of March 12, 2008, with a public call to compete for grants from the Strategic Action in Healthcare within the framework of the National Plan of R + D + I 2008-2011[13]. It comprises forty Central Units of Clinical Research and Clinical Trials (UCICEC) distributed in health centers of established research excellence in 16 autonomous communities (Table 1). The objective was to strengthen the structure of the units specifically developing clinical trials without commercial interest and thus make a significant contribution to the translation of the knowledge generated to daily clinical practice. The staff of these Central Units (UCICEC) comprising CAIBER is hired specifically to meet the requirements of projects presented by hospital researchers, who combine their attending and research activity.

These units provide the infrastructure and common services for prospective randomized clinical trials (in areas such as prevention, diagnosis, treatment and / or services) by clinical research groups, in order to promote citizen health and wellbeing. The services offered are varied and depend on each project and available resources. CAIBER not only provides the necessary financial support of projects through calls for public or private funding. The staff of each Central Unit, recruited or contracted, have experience in clinical research and offer methodological advice on the management of authorizations, insurance, contracts, monitoring, pharmacovigilance, study coordination, medical and nursing support, training, data management, adequacy of medication etc., i.e. all that is needed to cover the different stages of the trial, from conception to publication and dissemination of the results. In addition, the network allows a rapid increase in critical mass of re-

Table 1. Central Units of Clinical Research and Clinical Trials (UCICEC)

Autonomous Community	Center
Andalucía	Hospital Carlos Haya
	Hospital Reina Sofía
	Hospital Virgen de Las Nieves
	Hospital Virgen Ddel Rocío
Aragón	Instituto Aragonés de Ciencias de la Salud
Asturias	Hospital Universitario Central de Asturias
Baleares	Hospital Son Espases
Canarias	Hospital Universitario de Canarias
Cantabria	Hospital Marqués de Valdecilla
Castilla-La Mancha	Complejo Hospital General de Albacete
Castilla y León	Hospital Universitario de Salamanca
Cataluña	Fundación IDIBELL
	Fundación Instituto de Inv. Dr. Josep Trueta
	Fundación Instituto de Investigación Vall d'Hebron (UCIEC-VH)
	Fundación Instituto Inv. Germans Trias i Pujol
	Hospital Clínic de Barcelona
	Hospital de la Santa Creu y Sant Pau
	IDIAP Jordi Gol
	Instituto Inv. Biomédica de Lleida. Fundación Dr. Pifarre (IRBLLEIDA)
	Instituto Municipal de Investigación Médica
Com. Valenciana	Hospital Clínico Universitario de Valencia
	Instituto de Investigación Sanitaria La Fe
Extremadura	Centro de Investigación Clínica del Área de Badajoz
Galicia	Complejo Hospit. Universitario de Santiago
	Complejo Hospitalario Universitario A Coruña
Madrid	Agencia Pedro Lain Entralgo
	Fundación Jiménez Díaz
	Hospital 12 de Octubre
	Hospital Clínico San Carlos
	Hospital de la Princesa
	Hospital Gregorio Marañón
	Hospital La Paz
	Hospital Puerta de Hierro
	Hospital Ramón y Cajal
Murcia	Hospital Virgen de la Arrixaca
Navarra	Clínica Universitaria de Navarra
País Vasco	Ambulatorio de Deusto
	Hospital de Cruces
	Hospital de Txagorritxu
	Hospital Donostia

searchers and patient volume required for the trial. It is assumed that the achievement of objectives within set times will in turn result in faster translation of knowledge.

On 15 November 2010, the first convocatory calling for research project applications (Primer Programa Intramuros CAIBER 2010) was announced; 357 projects were presented from the 40 units comprising the platform. These projects will be reviewed by respected evaluators preferably from foreign centers of agencies, and supervised by a technical evaluation committee at ISCIII appointed for that purpose. Each application will be reviewed by at least two experts with accredited scientific-technical expertise, on a confidential basis. The reviewers will issue a report, mainly taking into account: a) the history and current status of the research issue, b) the need to perform the investigation, c) the objectives of the study and working hypothesis d) planning and scheduling of the trial, e) sample selection and size, f) the methodology and statistical analysis, and g) the plan on exploitation of the results, applicability to clinical practice, and expected direct impact on the patients affected.

Additionally, the management of CAIBER will establish a strategic priority rating according to its existing priorities, assess the requirements and need for the study as well as its impact and health return on investment, in order to adapt those clinical trials positively evaluated from the scientific and technical standpoint to the capabilities of the consortium. For this reason, there is no predefined limitation of subject area or UCICEC. The deadline for project submission has now passed; after reviewing initial applications, none have been submitted by emergency medicine health professionals. CAIBER plans to issue new calls for research project applications on an annual basis and we would appeal to these professionals to participate with clinical trials consistent with any of the research lines of priority within the subject areas (Table 2) published in the general rules[13].

In summary, CAIBER is at the service of researchers, representing an opportunity to undertake multicenter clinical trials conceived by professionals of our health services, thus fostering more independent and higher quality clinical knowledge. The platform is there: it only remains for clinicians, and logically that includes emergency professionals, to take advantage and use it.

Table 2. Scientific-technical areas of high priority

Thematic areas
– Cancer.
– Diabetes and obesity.
– Neurological diseases.
– Mental.
– Infectious.
– Respiratory.
– Cardiovascular.
– Chronic and inflammatory diseases of the locomotor system.
Transversal areas
– Primary care.
– Pediatrics.
– Phase I Units.
– Non-pharmacological intervention.
– Training.
– International Programs.
– Advanced therapies.
– Ageing.

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