Informed consent in clinical research with drugs in Spain: Perspective of clinical trials committee members

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Summary. A survey among members of 16 Clinical Trials Committees and the Clinical Trials Evaluation Team of the Spanish Ministry of Health was carried out to discover their opinions about the procedure used to obtain informed consent in clinical research with drugs.

The responses of the 111 persons surveyed indicate that 97% consider that informed consent should be obtained before the patient is included in the trial, that it must “always” be in writing (68%), and that the consent form must previously have been approved by the Clinical Trials Committee (87%). The minimum information to be provided to the patient must be read by and later supplied to the subject (76%), and for at least 90% of the members surveyed it must “always” include: an invitation to participate in the clinical trial, information about the purpose, predictable benefits and risks of the trial, the statement that participation is voluntary and that refusal to participate would not imply loss of usual medical care, and that the trial was approved by the Clinical Trials Committee.

Only 33% of those surveyed considered that the study design should “always” be described to the patient.

In order to find out what the general outlook on this issue is in Spain, it is necessary to perform studies among medical investigators and patients.

Key words: Informed Consent, Clinical Trials Committee, Clinical Research, Ethics, Spain

The legislation effective in Spain since 1982 [1], which refers to all clinical trials (Phases I to IV) with medicines, requires prior approval of the protocol by a Clinical Trials Committee, and subsequent approval by the Ministry of Health (M.O.H.). This process means that there is a stricter control for Clinical Trials (CT) in Spain than in many other countries [2]. The Clinical Trials Committees of hospitals are constituted by physicians from various specialties, pharmacists and, when available, a biostatistician [1]. Their functions are similar to those of Ethics Committees or Institutional Review Boards in other western countries, although they are different in that it is not compulsory for persons outside the health care professions to be members.

In recent years, the Spanish M.O.H. has been preparing a bill for the first Medicine Act. Since March 1989, this has been under debate for approval by the Spanish Parliament. In the bill, in the chapter on CT [3], the M.O.H. has included substantial changes from current legislation in order to incorporate elements that would bring Spain closer to the situation in other developed countries, for example, implementation of Ethics Committees, Good Clinical Practice Guidelines, insurance coverage for CT subjects, etc. An aspect that may require the most significant change is that referring to the procedure for obtaining informed consent (IC). Since 1982, Spanish clinical investigators, in accordance with the Declaration of Helsinki, have been required to obtain IC from the patient before his inclusion in any CT [1]. The investigator must verbally explain in “intelligible” language, and following his own criteria, the “purposes, methodology and possible risks” of the trial. When someone agrees to participate in a study, the investigator and a witness sign a standard consent form covering all types of clinical trials. This is the procedure which is currently legally in effect for all CT, except for Phase I CT and those specified by the M.O.H., where the subject must sign a standard IC form.

The purpose of the present study was to determine by means of an opinion survey on IC the views held by members of Clinical Trials Committees, persons who spend part of their time assessing protocols from the scientific and ethical standpoint, and who, in turn, in many cases perform CT. This subject has been extensively covered in the medical and bioethical literature, mainly in English-speaking countries [4], but has virtually been ignored in Spain.

Subjects and methods

The survey on IC was part of a large survey, which included various aspects of what is known as ‘Good Clinical Practice Guidelines’ for clinical investigators [5–8]. The questionnaire consisted of 11 sections (48 questions). The section concerning patient consent com-
The hospital departments to which the persons surveyed were conveyed was 41 (9) y. The ratio of men to women was 4:1. Of the 111 respondents, 81% of the total number of Clinical Trials Committees amounted to 128 (MA Serrano, M.O.H.; personal communication). All the hospitals were teaching hospitals. The total number of members of the 16 Clinical Trials Committees, 5 belonged to hospitals having < 500 beds, 5 to the 501 to 1000 bed category, and the remaining six to hospitals having more than 1000 beds. The hospital departments to which the persons surveyed belonged are shown in Table 1. The questions exactly as presented to the persons surveyed and their answers are listed in Table 2.

In special circumstances (Questions 5–7), 68% of the persons surveyed thought that the investigator could administer the drug without having obtained prior IC when the circumstances stated in Question 5 were applicable (Table 2). With reference to who should certify that those circumstances were present (investigator and/or coinvestigator, with or without the opinion of a physician not participating in the CT), it is difficult to obtain a clear picture, as a large number of the respondents marked as “essential” two or even three of the possible proposals. The majority (86%) thought that the Clinical Trials Committee should be urgently informed in writing of the event.

With respect to the minimum information sheet (Questions 8–12), there was virtually complete agreement (96%) in considering it as necessary, 91% felt that it should have previously been approved by the Clinical Trials Committee, and 76% responded that it should be read to the patient and that he/she should be provided with a copy. For most of those surveyed (89%), the period which should elapse from the time of handing the minimum information sheet to the patient and his/her agreement or refusal to participate in the trial should be at least “some” hours. As for the contents of the information to be provided to the patient, a response of “always” was obtained from at least 90% of respondents for the following questions (Table 2): invitation to participate in the CT (Q. 12.1), information about the CT purpose (Q. 12.2), informing the patient about the CT design (Q. 12.5), general (Q. 12.6) and specific (Q. 12.7) circumstances, the circumstances stated in Question 5 were applicable (Q. 12.11) and risks (Q. 12.12), declaring that the patient's participation was voluntary (Q. 12.19), and that refusal to participate in the CT did not imply loss of usual medical care (Q. 12.20). On the other hand, the replies “never” and “NA” (No Answer) exceed 10% in the case of information about the CT sponsor’s name (Q. 12.3), about the CT design (Q. 12.5), general (Q. 12.6) and specific experimental procedures (Q. 12.8), the number of patients to be included (Q. 12.14), about data confidentiality (Q. 12.15) and informing the patient about CT results (Q. 12.21).

### Results

Replies to the questionnaire were received from 104 persons, 81% of the total number of Clinical Trials Committee members surveyed, and by all members of the M. O. H. Evaluation Team. The mean age (SD) of the persons surveyed was 41 (9) y. The ratio of men to women was 4:1. Of the 16 Clinical Trials Committees, 5 belonged to hospitals having ≤ 500 beds, 5 to the 501 to 1000 bed category, and the remaining six to hospitals having more than 1000 beds. The hospital departments to which the persons surveyed belonged are shown in Table 1. The questions exactly as presented to the persons surveyed and their answers are listed in Table 2.

In the group of questions dealing with general aspects (Questions 1–4), almost all the respondents (97%) thought that IC must be obtained prior to including the patient in the CT. Sixty-eight % felt that IC must always be obtained in writing; 13% stated that IC should always be obtained verbally in the presence of a witness, and that in some cases written informed consent should be obtained; 10% believed that, depending on the type of CT, either verbal or written informed consent should be procured; while only 1% felt IC must always be verbal. While 87% of the respondents considered that the current legal document for IC should be approved by the Clinical Trials Committee, only 58% thought that a copy of it should be supplied to the patient.

### Discussion

Opinion surveys, questionnaires, and interviews, using various methodologies and for various purposes, have been used extensively to know how physicians and patients perceive the problems which IC raises from their different viewpoints [4, 10–16]. The survey on which this paper is based, apart from being the first to be carried out in Spain on this subject, is special in that it was carried out...