# Ethical Review and Informed Consent in Cardiovascular Research Reports in Argentina

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## Summary

**Background: Requirements for Institutional Review Board approval and informed consent for research involving human subjects have existed for more than 2 decades. However, evidence of fulfillment of these requirements is sometimes lacking in cardiovascular research reports in Argentina. Since ethical standards vary between committees, there may be some confusion among researchers regarding the need for an ethical review when conducting low risk research.**

**Objective: To examine the frequency of obtaining an ethical review and informed consent in cardiovascular research in Argentina.**

**Methods: Through a questionnaire, we contacted authors of 100 reports submitted to our annual scientific meeting during 2006.**

**Results: Thirty six per cent of questionnaires were resubmitted with confirmation of ethical review, 34% responded that ethical review was not obtained, 23% reported as being exempt and 7% were never resubmitted. Most articles obtaining ethical review were pharmacological trials or research involving assessment of new devices. On the other hand, most articles reporting lack of or exemption from ethical review come from epidemiological research or studies evaluating non-invasive methods. Sixty percent of phase IV pharmacological trials, research on cellular implantation or assessment of new devices met federal regulations requirements.**

**Conclusion: The rate of ethical review and use of informed consent in cardiovascular reports in Argentina vary among articles. Most research involving prospective observational studies and nearly 50% of protocols including intervention or invasive procedures do not report ethical review. This high proportion of articles lacking ethical review suggests the presence of legal and ethical flaws which should be discussed and overcome. (Arq Bras Cardiol 2008; 90(5): 290-293)**

**Key words: Ethical review; informed consent; publications for science diffusion; Argentina.**

## Introduction

In recent years there has been increased focus on human subject protection and documentation of ethical review in clinical studies, especially since media reports of ethical transgressions have been denounced[1-3]. Consequently ethical appraisals have gone from almost no rules to very strictly regulations including not only clinical pharmacological trials but also epidemiological research.

The requirements for Institutional Review Board (IRB) review and informed consent for research involving human subjects have existed for more than two decades, and in many countries federal regulations on clinical investigation demand approval by an ethics committee[4-8].

We questioned the fact that evidence of fulfillment of these requirements is sometimes lacking in cardiovascular research in Argentina. We hypothesize that, since ethical standards vary widely between different committees, researchers might be confused regarding the need for an IRB approval when conducting low risk clinical investigation, such as epidemiological research. In the same way, legal requirements for secure safeguards of personal data confidentiality could pass unnoticed, especially in observational studies involving follow-up.

The aim of this study was to examine the frequency of obtaining IRB approval and informed consent in cardiovascular reports in Argentina.

## Methods

We reviewed all reports of cardiovascular research involving human subjects submitted to our annual scientific meeting (Argentine Congress of Cardiology) during 2006. Articles were divided into pharmacological clinical trials, research involving interventional cardiology, electrophysiology or surgery, trials evaluating new devices, prospective studies assessing new diagnostic methods or new applications of known technology and prospective observational or epidemiological studies that did or did not

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involve biochemical determinations or non-invasive methods for diagnosis. Retrospective observational or epidemiological studies, meta-analyses and case reports were excluded from the analysis since consensus exists on no need for ethical review. The remaining articles were examined and authors contacted to determine if they could document IRB evaluation, informed consent mechanisms and fulfillment of requirements of the Department of Drugs & Clinical Trial Evaluation of the Argentine Federal Agency (A.N.M.A.T.). If either of these features could not be corroborated, authors were asked to explain reasons for the lack thereof.

This research project has been approved by our local Institutional Review Board, according to the Declaration of Helsinki.

## Results

Of 341 abstracts involving research with human subjects, 100 (29.3%) were prospective studies which met inclusion criteria to be evaluated. Classification of articles revealed that 34 (9.9%) were prospective studies assessing new diagnostic methods such as coronary angiography with multislice computed tomography (CT), or new applications of well-known methods like magnetic resonance for atrial septal defect evaluation. Thirty-two papers (9.4%) were prospective epidemiological articles; these comprise observational research based on prospective records, including or not non-invasive or low-risk procedures such as biochemical determinations, X-rays, etc. Research involving invasive procedures such as surgery or interventional cardiology comprised 24 abstracts (7.0%). This group also included controlled trials assessing new medical devices such as stents, heart valves, etc. Finally, 10 articles (2.9%) were typical clinical trials of pharmacology or cellular therapy. Table 1 resumes recommendations for IRB evaluation, informed consent and local federal regulations requirements for each type of article[9-14].

Authors of these 100 papers were contacted by means of a questionnaire asking for ethics information. Thirty-six per cent of questionnaires were resubmitted with confirmation of ethics review, 34% responded that ethical review was not obtained, 23% reported as being exempt from review and 7% were never resubmitted. Most articles obtaining ethical review were pharmacological clinical trials or research involving assessment of new medical devices (Table 2). On the other hand, most articles reporting lack of or exemption from ethics review come from epidemiological research or studies evaluating new non-invasive diagnostic methods.

Seventy per cent of phase IV pharmacological clinical trials, research on cellular implantation or assessment of new devices met federal regulation requirements.

## Discussion

This study suggests that the rate of IRB review and use of informed consent vary among types of articles. Most research involving prospective observational studies and 53% of protocols including intervention or invasive procedures do not report ethical appraisals. The high proportion of articles lacking ethical review suggests the presence of legal and ethical flaws which should be discussed and overcome.

There is no doubt that clinical investigation must be

**Table 1 - Classification of 341 abstracts involving research with human subjects**

| Type of study | n | % | IRB and informed consent[9-14] | Federal Regulations |
|---|---|---|---|---|
| Retrospective obsevational, meta-analyses or case reports | 241 | 70.7% | unnecessary | unnecessary |
| Prospective studies assessing new diagnostic methods or new applications | 34 | 9.9% | recommended | unnecessary |
| Prospective epidemiological involving or not biochemical determinations or non-invasive diagnostic methods | 32 | 9.4% | recommended | unnecessary |
| Research involving interventional cardiology, electrophysiology, surgery or new devices | 24 | 7.0% | usually necessary | usually necessary |
| Pharmacological clinical trials | 10 | 2.9% | necessary | usually necessary |

**Table 2 - Fulfillment and documentation of Institutional Review Board (IRB) approval, informed consent and federal regulations requirements (100 abstracts)**

| Type of study | IRB Yes(%) | Informed consent Yes(%) | Federal regulations Yes(%) |
|---|---|---|---|
| Prospective studies assessing new diagnostic methods or new applications | 35% (12/34) | 32% (11/34) | unnecessary |
| Prospective epidemiological involving or not biochemical determinations or non-invasive diagnostic methods | 25% (8/32) | 16% (5/32) | unnecessary |
| Research involving interventional cardiology, electrophysiology, surgery or new devices | 42% (10/24) | 29% (7/24) | 67% (4/6) |
| Pharmacological clinical trials | 80% (8/10) | 80% (8/10) | 70% (7/10) |

supervised by institutional boards in order to judge the ethical viability of research during elaboration, implementation and development stages. Some kinds of protocols evaluating new drugs or devices do require official authorizations from the national Federal Agency whose requirements always include IRB review and approval. On the other hand, need for an ethics committee approval in epidemiological studies remains controversial.

Most observational epidemiological research is based upon already existing data, usually obtained by retrospective chart review. In these cases, consensus exists that there is no need for ethical review as long as investigators provide secure safeguards of confidentiality. Nearby 70% of articles evaluated in this paper were of this type. Similarly, 72% of authors perceived that prospective epidemiological research involving low-risk procedures were also exempt from ethics review and informed consent, though this opinion is not usually shared by many IRB. Researchers' attitudes could be justified taking into account that several international ethical guidelines for epidemiological research suggest that when the research design involves no more than minimal risk and requirement of individual informed consent would be impracticable (for example, where research involves only excerpting data from subjects' records), the IRB may waive some or all of the elements of informed consent[13-14]. It is noteworthy that waiver of the need for informed consent does not exempt the research from review by an ethics committee, which will decide whether or not to waive this requirement. In this way, IRBs would evaluate every protocol in order to commit researchers in securing safeguards of personal data confidentiality. Likewise, in prospective epidemiological studies involving low-risk procedures such as extra biochemical determinations or non-invasive methods for diagnosis, ethical appraisals are necessary to decide the requirements for informed consent.

Another special case is regarding investigations assessing new non-invasive diagnostic methods or new applications of known technologies. In our study 9.9% were of this type, and one-third of these were considered by researchers as exempt from ethical appraisal because of being low-risk clinical investigations. In this situation, researchers tend to underestimate the risk of procedures, such as was the case of a protocol assessing an exercise test using a bicycle ergometer in patients with critical valvular aortic stenosis.

A high proportion of articles lacking ethical review were found in research involving invasive methods such as interventional cardiology, electrophysiology or surgery. Although these invasive procedures are frequently employed in cardiology, associated risk cannot be considered low. In these cases, lack of IRB approval and informed consent cannot be accepted; much work must be done for investigators to fulfill current ethical standards in this type of protocols.

Scientific societies and local journals usually alert the researcher to the need for IRB review, but subsequent monitoring of fulfillment of said requirements is often neglected, especially when abstracts are communicated in a scientific meeting. Editors and scientific organizations must rectify this problem by enforcement of national and international ethical standards in the research studies that authors send for evaluation and publication[3].

Some studies have explored the attitudes of researchers from developing countries regarding the role of local IRB in ensuring the adequacy of ethical standards in multinational research conducted in those countries. Although researchers have reported that the local review process generally takes place, they admitted that gaps in the review procedure can result in a number of research projects not being reviewed by an ethics committee[15].

United States' federal regulation identifies three levels of review for human subjects research. These are expedited review, full review, and exemption from review. A study suitable for expedited review is one involving minimal risk to the research subject. As defined by federal regulation, "minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests"[9]. In this case, ethics committees could provide a simplified application for an expedited review of research involving a review of patient data, records, or specimens. However, considerable variability in IRB processes for minimal risk studies has been reported[10,12]. Expedited studies that include chart and radiograph reviews, observational or epidemiological studies, and research that involve routine physical exercise, blood drawing, and other minimal risk procedures[9], may be reviewed by a subcommittee or administratively within the office, instead of full IRB approval[12]. Studies requiring full evaluation are those that pose greater than minimal risk to research subjects; these include most clinical trials involving drugs, devices or invasive procedures, as well as research including vulnerable populations. Finally, studies exempted from IRB include retrospective reviews of de-identified data or collection of de-identified tissue samples; however these exemptions must be made by an ethics committee, since research intended for publication generally warrants review by an IRB.

Research must rest upon accepted ethical standards, but these standards must be applied taking into consideration the balance between the risk involved in the investigation and the benefits provided by research. Within this scope, IRB approval and informed consent must be mandatory when assessing new drugs, devices or invasive methods, but requirements for informed consent could be waived for prospective observational studies involving low-risk procedures, or trials evaluating new non-invasive diagnostic methods. In short, since ethical appraisals are often time consuming and costly, it is reasonable to address all protocols taking risk and benefits into consideration[16].

Improving research ethical standards for clinical investigation will require additional education for investigators and clearer guidelines for IRB members. Research adherence and full documentation of ethical review in clinical studies will improve protection for research subjects as well as the public trust in the process.

In conclusion, this study demonstrated that the rate of IRB

review and the use of informed consent in cardiovascular research reports in Argentina vary according to the type of article. Most research involving prospective observational studies and nearly 50% of protocols including intervention or invasive procedures do not report ethical appraisals. The high proportion of articles lacking ethical review suggests the presence of legal and ethical flaws which should be discussed and overcome.

The study was reviewed and approved by the Institutional Review Board (Bioethics Committee) of the Argentine Society of Cardiology on November 22, 2006. The discussion of the study was registered in Book 1 (one), page 16 of this Board. If necessary a hard copy of the text can be obtained by contacting the IRB of Argentine Society of Cardiology (www.sac.org.ar), Azcuénaga 980, 1115 Buenos Aires, Argentina (bioetica@sac.org.ar)".

**Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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**Study Association**

This study is not associated with any graduation program.

## References

1. Perkins AC, Choi JM, Kimball AB. Reporting of ethical review of clinical research submitted to the Journal of the American Academy of Dermatology. J Am Acad Dermatol. 2007; 56: 279-84.
2. Adams BB, Gloster HM. Institutional review board use among dermatology researchers. J Am Acad Dermatol. 2007; 56: 346.
3. Block MI, Khitin LM, Sade RM. Ethical process in human research published in thoracic surgery journals. Ann Thorac Surg. 2006; 82: 6-11.
4. Matot I, Pizov R, Sprung CL. Evaluation of Institutional Review Board review and informed consent in publications of human research in critical care medicine. Crit Care Med. 1998; 26: 1596-602.
5. Weil E, Nelson RM, Ross LF. Are research ethics standards satisfied in pediatric journal publications? Pediatrics. 2002; 110: 364-70.
6. Lopez-de-la-Pena XA. Informed consent and the approval of evaluation committees in Mexican medical research. Rev Invest Clin. 1995; 47: 399-404.
7. Myles PS, Tan N. Reporting of ethical approval and informed consent in clinical research published in leading anesthesia journals. Anesthesiology. 2003; 99: 1209-13.
8. Roggin KK, Chwals WJ, Tracy TF. Institutional Review Board approval for prospective experimental studies on infants and children. J Pediatr Surg. 2001; 36: 205-8.
9. Protection of human subjects. [texto internet]. Department of Health and Human Services. [acesso em 2005 Jun 23]. Disponível em: http://www.nihtraining.com.
10. Valji K. IRB approval – who needs it? J Vasc Interv Radiol. 2002; 13: 225-6.
11. Hirshon JM, Krugman SD, Witting MD, Furuno JP, Limcangco MR, Perisse AR, et al. Variability in institutional review board assessment of minimal-risk research. Acad Emerg Med. 2002; 9: 1417-20.
12. Parvizi J, Tarity TD, Conner K, Smith JB. Institutional Review Board approval: why it matters. J Bone Joint Surg A. 2007; 89: 418-26.
13. Good Epidemiological Practice (GEP). Proper conduct in Epidemiologic Research. IEA Brazil Council meeting. January 9, 2007. [acesso em 2007 Jan 9]. Disponível em: http://www.dundee.ac.uk/iea/GEP07.htm.
14. The Council for International Organizations of Medical Sciences (CIOMS). International ethical guidelines for biomedical research involving human subjects. Geneva, Switzerland: The Council for International Organizations of Medical Sciences (CIOMS), 2002.
15. Hyder AA, Wali SA, Kjan AN, Teoh NB, Kass NE, Dawson L. Ethical review of health research: a perspective from developing country researchers. J Med Ethics. 2004;30:68-72.
16. Dickler HB, Korn D, Bhat S, Hedge TT, Sugarman J, Emanuel EJ, and the Consortium to examine Clinical Research Ethics. The costs of institutional review boards. N Engl J Med. 2005;353:315-7.