Intensive Care Med (2009) 35:613–615
DOI 10.1007/s00134-008-1343-x

SPECIAL ARTICLE

Michael Wolzt
Christiane Druml
Daniela Leitner
Ernst A. Singer

Protocols in expedited review: tackling the workload of ethics committees

Received: 1 September 2008
Accepted: 19 October 2008
Published online: 1 November 2008

M. Wolzt · C. Druml · D. Leitner · E. A. Singer
Ethics Committee of the Medical University of Vienna, Vienna, Austria

M. Wolzt (✉)
Department of Clinical Pharmacology, Allgemeines Krankenhaus Wien, Währinger Gürtel 18-20, 1090 Vienna, Austria
e-mail: michael.wolzt@meduniwien.ac.at
Tel.: +43-1-404002981
Fax: +43-1-404002998

Abstract *Purpose:* This paper describes the experience of the Ethics Committee of the Medical University of Vienna, Austria, while managing the workload of clinical study applications. *Methods:* An expedited review process was introduced for initial review of study protocols regarded as minimal risk interventions in March 2004. *Results:* A total of 504 study protocols were submitted for review in 2003 and this number has increased to 743 in 2007. Two hundred sixty eight studies were classified as minimal risk in 2007 and allocated to a subgroup of the Committee for review. The time to full approval was shorter for these studies as compared to other protocols. *Conclusions:* Implementation of initial expedited review can improve the performance of an Ethics Committee. A framework to achieve a single opinion for multisite research of minimal risk interventions should be considered to facilitate these low risk studies.

Keywords Ethics Committee · Minimal risk · Expedited review · European legislation

Introduction

In 1998, the Department of Health and Human Services (DHHS 45 CFR 46.110) and Food and Drug Administration (FDA 21 CFR 56.110) regulations were revised and enabled US Ethics Committees fast track approval of biomedical studies where only minimal risk is involved. Under this section, the review and approval may be carried out by the chairperson or assigned members of the Institutional Review Board (IRB). Potentially eligible protocols for this expedited review procedure may be identified from a list, which is held and updated by the FDA in the Federal Register. This procedure may be applied also to clinical studies of drugs and medical devices, and to initial applications as well as to minor changes in previously approved research.

Despite this standard, a wide range of processes to review and approval of IRB applications persists in the US, even when protocols are designed to meet expedited review criteria [1, 2]. Variability in the timelines and consistency of IRB review is in particular evident in the review of studies outside the typical pattern of industry-sponsored trials [3]. Surprisingly, expedited review may not even guarantee swifter processes than full review and may actually take longer for approval [4].

This expedited review procedure of study protocols is not generally employed by European Independent Ethics Committees (IEC) or at least the terminology unused. In fact, most Ethics Committee chairs have already taken the opportunity to assign one or more of the experienced Committee members to allocate additional time outside IEC regular meetings' hours to conduct the review of amendments, notifications, adverse events, periodic reports and other paperwork, which are part of the continued tasks that IEC perform during clinical trials. This procedure is also in agreement with operational guidelines

for Ethics Committees by the World Health Organization [5]. Other IEC review and approve amendments during their plenary sessions.

This literature summarizes the efforts taken by the IEC of the Medical University of Vienna to streamline initial review of clinical study applications. In 2003, a total of 504 study protocols were submitted for review and this number has increased to 743 in 2007. An expedited review process was introduced for initial review in March 2004. Full meetings of the IEC are held at monthly intervals.

Selection of minimal risk studies

One of the difficulties of the expedited review system is clearly the definition of "minimal risk" interventions that subjects may be exposed to. Obviously, harm or discomfort anticipated in the research or by standard tests should not be greater than that encountered in daily life or during the performance of non-invasive routine examinations. Expedited review should also be available for medical research projects involving drugs or medical devices when they are used in accordance with their marketing authorization, i.e. non-investigational. This is consistent with European guidance documents, which define investigational medicinal products (IMP) and non-investigational medicinal products [6] and imply important differences regarding the administrative burden of clinical studies by provisions laid down in Directive 2001/20/EC of the European Parliament and of the Council [7]. This Directive has to be followed when drug treatment and comparator are assigned by protocol, even when these therapies are used within their labeling. Such clinical studies are, therefore, excluded from expedited review in our IEC. A simplified procedure in this case would benefit both industry and non-commercial sponsors.

Unlike the US system, no generally accepted listing of potential minimal risk studies exists in Europe. In an effort to identify minimal risk protocols in our IEC, all proposals are briefly reviewed by the chair once received. Studies involving IMP or medical devices, which are used outside their labeling are exempted from expedited review. Likewise, studies including vulnerable patients, prospective sampling of genetic material or introducing more than minimal risk such as extensive sample collection or invasive procedures will also be selected for full review, which is done by experts in the field on the basis of a structured questionnaire. The remainder of the applications is presented by the chair to a selected group of IEC members who meet monthly for discussions and act as expedited review board. Classification of studies or interventions as "minimal risk" cannot be proposed by applicants. A lawyer, a biostatistician and a clinician are permanent members of this board and other specialists are invited as required by the spectrum of trial applications. This composition is not defined by law but has been included into the operational procedures of the IEC.

The classification of a protocol as "minimal risk" research is mainly based upon hazard to subjects in clinical trials. It would be plausible to develop a risk strategy related to data protection, public health or other parameters also.

Opinion finding in expedited review

Similar to the US system, the appointed reviewers of this expedited review board may not reject research applications. If the reviewer would have disapproved the project, it is automatically referred to the standard IEC full review process. The requirements for informed consent (or its waiver or alteration) apply regardless of the type of review and full access to files for IEC members remains as for others applications.

If unanimously agreed by the expedited review board members, their appraisal and requested changes will be proposed to the full Committee, which thereby retains the power to approve or reject protocols and to demand alterations. This formal requirement of a two-step procedure strengthens the position of the opinion set forth by the IEC, the importance of the convened meeting, and prevents hasty decisions of the expedited review board. It seems possible to reduce this procedure to a single step within the regular IEC meeting; on the other hand, this would leave review of minimal risk studies to IEC members present and potentially delay opinion finding of studies, where issues might have been sorted out by preceding review and early protocol revision.

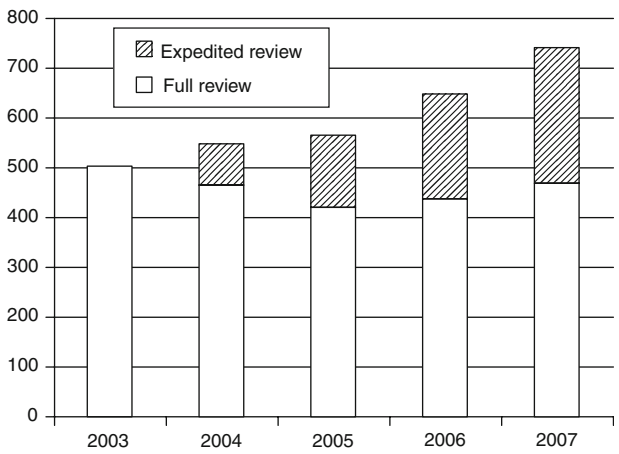

Fig. 1 Study protocols submitted for initial review at the Medical University of Vienna between 2003 and 2007. Protocols selected for expedited review are indicated

Experience and performance

Allocation of minimal risk studies by the chair of the IEC to a subgroup of Committee members should not be perceived by others as the Roman principle of "divide et impera". This is achieved by means of opening the process to all Ethics Committee members to review files and to provide comments, which is also possible via an electronic intranet platform. The representation of specialists in the respective fields of research on the board ensures quality of the scientific review. Further, preferential treatment of applications is avoided by the selection algorithm and the principle of unanimity of this IEC substructure.

Our experience has shown that the number of protocols eligible for expedited review increased over time and yielded 37% of all study proposals in 2007 (Fig. 1). In particular student diploma theses, which are part of the medical curriculum since 2002, often qualify as minimal risk studies. The initial expedited review has shortened the duration of full IEC meetings without jeopardizing the quality of science, review process or protection of subjects. Importantly, time to approval by the IEC was also shorter for studies in expedited review in 2007: the median duration from submission was 43 days as compared to studies in full review that took a median 65 days until unconditional approval. This shortened time to approval is probably more because minimal risk studies lead to less queries and comments, and questions may be readily answered and protocols more rapidly corrected.

Limitations of minimal risk study review

General biomedical research such as minimal risk studies is not facilitated by most legal systems but require review and approval at a local level to meet standards of the scientific community and to prevent ethical concerns. These multisite review processes sometimes unnecessarily impede realization of multicentre research projects without improving participant safety [4] or enhancing the scientific quality of the research. In some cases, minor risk procedures fall outside the remit of Ethics Committees, which are primarily established by the government to review studies with new drugs and medical devices. These difficulties faced by researchers are not counteracted and illuminate the necessity of means to receive approval without major delay and inconsistencies, e.g. a centralized review or the possibility to achieve a single opinion from selected Ethics Committees valid for a project in a country. This improvement has been introduced by the Clinical Trials Directive [7] for drug trials in Europe, and national authorities should extrapolate this experience to biomedical research.

A risk-based strategy for expedited ethical review may be used to develop risk-based requirements for clinical research in general. Relevant ethical and legal issues such as the need for a sponsor, the assessment by the competent authority, the reporting of adverse events other than suspected unexpected serious adverse reactions, the need for insurance coverage, and monitoring and archiving requirements could also be simplified. The legislators should consider a European regulatory framework to facilitate rather than impede low-risk studies, which is particularly relevant for academic clinical research.

Acknowledgments We gratefully acknowledge the administrative assistance of Ursula Angerer, Medical University of Vienna.

References

1. Vick CC, Finan KR, Kiefe C, Neumayer L, Hawn MT (2005) Variation in institutional review processes for a multisite observational study. Am J Surg 190:805–809
2. Green LA, Lowery JC, Kowalski CP, Wyszewianski L (2006) Impact of institutional review board practice variation on observational health services research. Health Serv Res 41:214–230
3. Dyrbye LN, Thomas MR, Mechaber AJ et al (2007) Medical education research and IRB review: an analysis and comparison of the IRB review process at six institutions. Acad Med 82:654–660
4. Larson E, Bratts T, Zwanziger J, Stone P (2004) A survey of IRB process in 68 US hospitals. J Nurs Scholarsh 36:260–264
5. World Health Organization (2000) Operational guidelines for Ethics Committees that review biomedical research. Available at http://www.who.int/tdr/publications/publications/pdf/ethics.pdf. Accessed 01 Sept 2008
6. European Commission (2006) Definition of investigational medicinal products (IMPs), definition of non investigational medicinal products (NIMPs). Available at http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2006/07_2006/def_imp_2006_07_27.pdf. Accessed 01 Sept 2008
7. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (2001) J Eur Commun L 121:34–44