

Ethics-committee authorization in Germany

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Abstract

On 9 August 1994 the German legislature revised the German Drug Law (AMG). Included in the revision is a passage requiring, for the first time, that the sponsors and investigators of clinical studies involving human subjects first obtain the approval of an ethics committee before carrying out such studies. According to the legislation, which takes effect on 17 August 1995, approval is to come from 'an independent ethics committee, set up and administered according to state law [emphasis added]' (1).

Although it is clear according to the text that the 16 federal states have been empowered to establish ethics committees within their jurisdictions, this does not mean that the state governments are free to transfer exclusive authority in the matter to their respective medical associations, a step that would effectively abolish Germany's private ethics committees. First, the legislation does not rule out the authorization of private ethics committees. Second, as legal scholars attest, the exclusive control of ethics committees by the medical associations would constitute an illegal monopoly. Third, it is arguable that medical-association ethics committees fail to meet the one prior federal requirement, that of independence.

There is a great deal of confusion in Germany today about which kinds of ethics committees (public and/or private) the states will sanction before 17 August 1995. In an attempt to sort things out we present a brief explanation of how there came to be two kinds of ethics committees in Germany, review the legal battle between the two over the issue of authorization, point out how the German legislature, in passing the recent bill, has missed an opportunity to clarify the issue and, finally, suggest why the administration of ethics committees by the medical associations may be incompatible with the requirement that ethics committees be independent.

I: Origin of the controversy

For a period of about ten years beginning in the

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mid-seventies Germany's medical associations responded with foot-dragging to the idea of ethics committees (2). This should not be thought incriminating, as it may simply reflect both a deeper commitment to personal responsibility and an understandable interest in avoiding anything suggestive of unwieldy bureaucracy. Nonetheless, these ten years proved pivotal to the development of ethics committees in Germany. For at that time the idea of ethics committees had long since won broad acceptance elsewhere, but also within the clinical research community in Germany, many of whose members were well aware that getting their study results published in certain international medical journals was contingent on having had their studies reviewed by an ethics committee. The lack of a prompt response on the part of the medical associations meant that private ethics committees entered the field to fill the demand for the ethical and legal review of clinical research (3).

On the face of it, establishing private ethics committees was easy, since a blueprint was there to follow in the form of long published American Institutional Review Board (IRB) operating procedures. One needed only to assemble a relevantly qualified, interdisciplinary committee with female representation, and answer to misgivings about financial dependence by organizing the committee on a non-profit basis and pegging fees exactly to those applicable to experts appointed by the courts. But the ease of setting up shop, whether public or private, tends to belie the importance of experience in achieving a high level of competence. Added to the difficulty is the fact that, unlike an American IRB, ethics committees in Germany have had no counterpart to the supervening authority of the Food and Drug Administration.

When, in 1986, the medical associations and faculties of medicine had at last jump-started a plausible minimum of ethics committees, they discovered that many investigators and sponsors were reluctant to make the switch away from the more experienced and reliable private ethics committees, thus giving rise to a legal battle over authorization.

II: Court proceedings prior to the enactment of the new law

The legal battle centres on a decision made by the federal medical association in May 1988 to revise a passage of its professional order so as to require that its member-physicians conducting research involving human subjects call upon an ethics committee set up and administered by a state medical association or by a faculty of medicine for ethical review. Prior to 1988 the passage in question, section 1, paragraph 4, read:

‘Prior to conducting clinical trials involving human subjects ... the physician *ought to* call upon an ethics committee administered by a medical association or faculty of medicine to obtain advice on professional, legal and ethical issues associated with his/her project [emphasis added]’ (4).

The revised text reads:

‘Prior to conducting clinical trials ... the physician *must* call upon ... [emphasis added]’ (5).

While the federal medical association is not competent to draw up statutes, it does issue recommendations which may be taken up by the various state medical associations which do enjoy the right to draw up statutes for the purpose of standardizing the professional obligations of their members. To date the medical associations in fifteen of the sixteen federal states have revised their professional orders in conformity with the revised section 1, paragraph 4 of the federal professional order (the lone exception being the state of Baden-Wuerttemberg). Seeing as how all physicians in Germany are bound by their professional order, being compulsory members of the medical association of their respective states, this re-wording effectively established a monopoly over ethics committees in Germany.

When the state of Hessen, a state with a high concentration of clinical research facilities, followed suit in December 1988, two members of the Freiburg Ethics Commission (a private ethics committee) and two physicians from the state of Hessen brought legal charges against the state medical association before Hessen’s administrative court, to have this particular requirement of the professional order struck down as unconstitutional. They saw it as a case of a by-law intruding upon the rights of third parties, non-physicians such as the representatives of pharmaceutical companies, test-subjects and the members of private ethics committees.

The court’s verdict, issued in July 1993, did strike down the passage in question, but on a technicality not related to the issue of its constitutionality, which the court addressed only obliquely (6). The verdict thus left it open to Hessen’s medical association to re-draft its professional order according to the letter of the law and to re-submit it to the Ministry for

Youth, Family and Health for approval. This the medical association did, and approval was granted. The Freiburg Ethics Commission, *et al*, appealed the decision immediately.

While the latest revision of the AMG obviates further legal proceedings in this particular venue, the issue of whether the exclusive control over ethics committees by the medical associations is unconstitutional has not gone away. Should the federal states attempt to transfer such control to their medical associations, further litigation will be necessary to determine whether the result constitutes an illegal monopoly.

III: Legislative inattention

While the lack of responsiveness on the part of the medical associations may have invited rival ethics committees into the field in the first place, and thus muddled the issue of authorization, some blame for the abiding lack of clarity in the matter of ethics-committee authorization in Germany can be assigned to the German legislature. Having the authority to amend the AMG at any time, it has been conspicuously slow in making provisions for ethics committees, despite clear recommendations from prominent international organizations.

The World Medical Association (WMA), for instance, first recommended ethics committees as a way to protect test-subjects in its Revised Declaration of Helsinki from 1975. According to section 1, Basic Principles, Point 2 of the declaration:

‘The design and performance of any experimental procedure involving human subjects should be clearly formulated in an experimental protocol, which should be transmitted to a specially appointed independent committee for consideration, comment and guidance’ (7).

Nonetheless, it wasn’t until eleven years later (1986) that the German legislature answered to one half of this recommendation, adding Nr 7a to section 40, paragraph 1 of the AMG (sections 40 and 41 pertain to clinical studies) so as to require that a study protocol reflecting the current state of scientific knowledge be drawn up to accompany each study. While most European countries had long since incorporated this particular recommendation in its entirety into federal law, requiring also that the study protocols be reviewed by an ethics committee, the German legislature surprisingly omitted to incorporate the part about ethics committees. Nor was it prompted to do so in light of the European Community’s *Note for Guidance: Good Clinical Practice for Trials on Medicinal Products* which also states: ‘the sponsor or investigator of a clinical trial must obtain the opinion of an ethics committee’ that is *independent* of the ‘investigator, sponsor, and relevant authorities’ (8).

Standing in the way of timely legislation have been the competing interests of the government and the federal states, and of the governing coalition and the opposition. This conflict was also strongly in evidence during negotiations leading up to the latest revision of the AMG (the German Drug Law), which does at last make good on the WMA's recommendation from 1975, but which, because it does not address the unresolved legal proceedings involving a constitutional issue, leaves unclear which kind of ethics committees will be permitted to take up the work of reviewing clinical trials after 17 August 1995.

The legislative process began when the German Lower House (Bundestag), representing the Federal Republic and controlled by the governing coalition, submitted for approval a package proposal for amending the AMG to the Upper House (Bundesrat), representing the federal states and controlled by the opposition. According to the proposal, section 40 of the AMG was to be amended through the addition of line 1a to paragraph 1, line 1, as follows.

Section 40

(1) ... 'The clinical investigation of a drug involving human subjects may be carried out if and only if:

1a) those intending to carry out the study first obtain the written opinion of an independent and interdisciplinary ethics committee, which is registered at the Federal Health Agency and whose members are suitably qualified for the task of reviewing the study protocol and other required documents from ethical and legal points of view. Registration shall entail the drafting and publication of procedural rules wherein an appropriate honorarium and the names, addresses and qualifications of the members are expressly stated. In the case of multi-centre studies a single vote shall be regarded as sufficient. Liability for the clinical study shall remain with those who sponsor and carry out the study' (9).

The adoption of this proposal would have placed regulatory authority over matters concerning ethics committees in the hands of a single federal agency, would have promoted a high degree of standardization through the application of specific criteria concerning ethics-committee composition and operating procedures, would presumably have allowed for the authorization of private ethics committees, and may, depending upon the agency's construal of 'independent', also have allowed for the authorization of ethics committees affiliated with the medical associations.

While not rejecting the entire legislative package, the Bundesrat made use of its right to call forward a special inter-house committee to negotiate its various details, including the Bundestag's plans for revising section 40. In the time-constrained and trade-off context of attempting to push through the whole legislative package, the Bundestag's proposal for the regulation of ethics committees did not

survive. Enacted in its place was the following addition to section 40 (as mentioned above).

'The clinical investigation of a drug involving human subjects ... may only be carried out if it has received the prior approval of an independent ethics committee established according to state law ...' (1).

The new law, which unambiguously cedes regulatory authority to the states, was initially interpreted as a straightforward victory for the German medical association and a certain ouster for private ethics committees. Indeed, in the weeks following its announcement some federal states signalled their intention to make ethics committees the exclusive domain of their medical associations and faculties of medicine. But this interpretation may have arisen from a narrow focus on the legislative process, during which the representatives of private ethics committees and of the German medical association were allowed to testify: the representatives of private ethics committees to voice their support of the Bundestag's proposal, the representatives of the medical association to voice their opposition. In the meantime the initial interpretation has given way to confusion as more and more in the field of clinical research in Germany realize that although regulatory authority belongs to the states, it is another question whether it is open to them simply to transfer authority to their medical associations and faculties of medicine.

IV: The problem of the monopoly

The explanation of why the issue of authorization is not simply and straightforwardly a matter of state discretion is as follows. First, the law empowers the state legislatures, and not the medical associations, to specify the formal requirements that are to apply to ethics committees. The taking up of this task by the medical associations through the instrument of their own by-laws would be an unconstitutional elaboration of the AMG. Only the legislature has the authority to elaborate the AMG (10).

Second, if the state legislatures, in drafting the formal requirements that are to apply to ethics committees, specify that the medical associations and faculties of medicine alone are permitted to assume the task of reviewing clinical studies from legal and ethical points of view, the result will be a public-law monopoly, at odds with the German constitution and with European Community regulations, both of which protect the rights of third parties against such monopolies.

Taking the representatives of pharmaceutical companies as an example of a third party illustrates the issue. Pharmaceutical companies assume the responsibility and financial risks of developing drugs. They are bound by law to conduct clinical trials, and to see to it that these trials are carried out according to the law. In case of non-compliance they (their

representatives) face the threat of prison sentences of up to one year and financial penalties of up to DM 50,000 (11). In light of this responsibility they ought to have the freedom to call upon the ethics committee in which they have the most confidence, and not be bound to a certain ethics committee on account of an existing monopoly.

Furthermore, assuming that the state legislatures issue precise and comprehensive formal requirements in establishing which ethics committees are eligible for authorization (the Bundestag's proposal recommends itself), it would be difficult to defend the view that there is no credible alternative to medical-association ethics committees, a situation that *would* justify a monopoly (12).

V: Independence

In our view the legislative decision to grant regulatory authority in the matter of ethics committees to the states is out of step with the international nature of medical science, and, more importantly, with a common commitment in Europe and elsewhere to notions of procedural justice that relate to the composition and *modus operandi* of ethics committees. For instance, requiring that ethics committees make provision for female and lay-person representation, and requiring that committee members appear in person for oral discussion may be ways of adjusting the *form* and *procedure* of review so as to improve, other things being equal, the likelihood of just decisions. At a time when some would see the validity of these principles affirmed through their adoption into binding international (European-wide) regulations, the German legislature has left them, and to some extent the whole issue of a European-wide unification of regulations, to the authority of the various federal states.

But one principle of procedural justice having to do with the regulation of ethics committees and the ability of these ethics committees adequately to represent the public was not left to the discretion of state authority. In keeping with the laws of almost every European country the new German Drug Law also stipulates that ethics committees must be *independent*. Indeed, whereas much of the importance widely attached to the WMA's Declaration of Helsinki relates to the repugnance felt about too many cases of mistreatment and abuse found in the history of medicine, and the determination to prevent any more such cases, the very idea of setting up ethics committees to assume a guardian role in preventing abuse in the medical world – a world increasingly perceived as alien by the general public, even as its events have a profounder societal impact – suggests scrutiny from an independent perspective.

With this in mind we would suggest that there is a presumption in favour of not allowing medical associations to administrate ethics committees. To be sure, medical expertise is indispensable to the

assessment of the facts of medical research. But this requires only that appropriately qualified physicians be appointed to ethics committees as members who share the task of reviewing research from *legal* and *ethical* points of view, not that ethics committees be operated by medical associations.

The two main concerns are a lack of professional independence and a lack of organizational independence. The importance of professional independence is reflected in the attention paid to multidisciplinary representation in committee membership. Failing this, the process of review may suffer from insularity, a case of physicians and medical researchers left accountable to physicians and medical researchers, that is, accountable to people whose intuitions and sympathies one could reasonably expect to be apologetic towards the medical community. While it is open to the medical associations to make their ethics committees broadly multidisciplinary at any time, they have as yet paid only minimal attention to multidisciplinary membership (13).

This leaves the issue of organizational independence. Members of a professional society or association co-operate in ways that unassociated individuals do not. For instance, they have a collective interest in upholding high standards and safeguarding the reputation of their society or association. Overall, the result of such co-operation is highly beneficial. But there are times, perhaps especially when mistakes have been made, as in the case of HIV-tainted blood supplies in Germany, that the same interest in upholding reputation can create a pressure to cover up mistakes, after which, in the conspiracy of silence, further damage can occur. Requiring that ethics committees be organized in accordance with a more robust sense of independence is one way to factor out such conflicts of interest right at the beginning.

To conclude, let us clarify that we are not suggesting that medical-association ethics committees cannot operate with a sufficient level of impartiality. Furthermore, there may be an answer to concerns about organizational independence, for example, through measures that improve the transparency of review. However, we do want to suggest that deference to the notion of independence should bar the medical associations from having a monopoly over ethics committees in Germany.

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References and notes

- (1) *Bundesgesetzblatt*. Fünftes Gesetz zur Änderung des Arzneimittelgesetzes, issued on 16 Aug 1994: 2078.

There is no official English translation. All translations are by the author.

- (2) The World Medical Association first recommended that study protocols be submitted to ethics committees as a means of reviewing experimentation involving human subjects in 1975. In 1979 Germany's federal medical association issued a recommendation to its member state medical associations to begin establishing ethics committees. The recommendation was not carried out in full until 1986.
- (3) The private ethics committees referred to in this article, of which there are currently five in Germany, are those established by private individuals, and do not include those *in-house* ethics committees established by pharmaceutical companies. The only record-keepers, and thus the only reliable source of information for determining the percentage of all clinical studies handled by private ethics committees in Germany, are the pharmaceutical companies. All of those we contacted refused to release relevant figures. The Freiburg Ethics Commission International reviews more than 300 studies per year. Of these about half are slated for a second review by an ethics committee affiliated with a medical association or faculty of medicine. Rather than face sometimes considerable delays many investigators get their studies underway after receiving a completed review from the Freiburg Ethics Commission International, and await the second review, although not exactly to-the-letter-of-the-law, as fulfilment of regulations.
- (4) See *Musterberufsordnung*, the physicians' professional order, as amended at the 88th Assembly of German Physicians.
- (5) See *Musterberufsordnung*, the physicians' professional order, as amended at the 91st Assembly of German Physicians.
- (6) Hessischer Verwaltungsgerichtshof, 11 Senat, 11 N 2442/90. Issued 1993 Jun 29.
- (7) World Medical Association. *Declaration of Helsinki*, as amended by the 29th World Medical Assembly, Tokyo, Japan, Oct 1975: section 1: Basic principles, point 2.
- (8) Committee for Proprietary Medicinal Products. Good clinical practice for trials on medicinal products in the European Community. *Dietharmazeutische Industrie* 1990; 52, 12: 1474–1504.
- (9) Adopted by the Bundestag with minor alteration from, Pfeiffer G. Rechtliche Aspekte der klinischen Prüfung von Arzneimitteln am Menschen im EG-Binnenmarkt. In: *Klinische Pharmakologie Aktuell* 1991; Oct: 51–52.
- (10) Pfeiffer G. Fünftes Gesetz zur Änderung des Arzneimittelgesetzes. *Versicherungsrecht* 1994; 34: 1381.
- (11) See Article 1, sections 96 and 97 of the German Drug Law (Gesetz über den Verkehr mit Arzneimitteln (AMG)), as amended on 11 April 1990.
- (12) For an exhaustive assessment of the issue of ethics-committee monopolies, see Pfeiffer G, Tiedemann I K. Ethikkommissionen. In: *Medizinische Klinik* 1989; 84: 557–561; see reference (1): and Schenke W R, in *Neue Juristische Woche* 1991; 37: 2313–2315.
- (13) Most medical-association ethics committees include one non-physician, in almost all cases, a lawyer. Given a choice the subsidiaries of USA pharmaceutical companies have their studies reviewed by private ethics committees, many of which are not only multidisciplinary but include female and lay-person representation, so as to better comply with FDA regulations.