CLINICAL STUDIES IN THE INTENSIVE CARE UNIT

ETHICAL AND LEGAL ASPECTS

*Erwin Deutsch**

This article draws on international experience to explore the ethical and legal aspects of performing clinical studies on patients in intensive care units. It discusses aspects of consent relevant to clinical studies in this medical environment, it considers the involvement of ethical committees, and the role and appropriate level of insurance cover.

I FACTUAL STARTING POINT

Clinical studies that are performed in the intensive care unit (ICU) take place on patients, not probands. Two rules of the Revised Declaration of Helsinki by the World Medical Assembly, as amended in Hong Kong in 1989, limit experimentation on patients. The rules are:[1]

> I. 10
>
> When obtaining informed consent for the research project the doctor should be particularly cautious if the subject is in a dependant relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a doctor who is not engaged in the investigation, and who is completely independent of this official relationship.

* Professor of Law, University of Gottingen, Visiting Professor, Law Faculty, Victoria University of Wellington.

1 The World Medical Association: Declaration of Helsinki: Recommendations guiding medical doctors in biomedical research involving human subjects adopted by the 185th World Medical Assembly as revised by the 29th World Medical Assembly (1975). Recent changes of the Revised Declaration of Helsinki did not concern these two rules.

II. 6

The doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

A patient in hospital, especially one in the ICU, is dependent on the personnel employed by the hospital and especially on the doctors. Therefore using a patient in a clinical study necessitates employing another doctor to obtain the informed consent that has to be given by the patient. Rule I. 10 of the Revised Declaration of Helsinki assumes that there is a bond between the doctor who provides professional care and the patient. That bond should not be used as a means of obtaining the informed consent.

Rule II. 6 of the Revised Declaration of Helsinki allows medical research to be combined with professional care. This does not go without saying because using one's patient as an experimental subject is not self-evident in research. There are limitations as well. The medical research has to be justified by its potential diagnostic or therapeutic value for the patient. This seems to disallow purely scientific research on a patient done by the doctor who also provides professional care.

The abovestated rules apply to all patients under professional care but especially to patients in the ICU. Here the bond between the doctor and the patient is a strong one and the doctor's influence is even greater than in the normal ward or in the office of the practitioner.

II RESEARCH ON PATIENTS UNABLE TO CONSENT

The Revised Declaration of Helsinki allows research in I. 11 on subjects unable to consent.

In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation.

The Revised Declaration of Helsinki does not mention research based on presumed consent. On the other hand, in II. 5 it is stated that if the doctor considers it essential not to obtain informed consent the specific reasons for this proposal should be stated in the experimental protocol, for transmission to the independent committee. It looks as if under certain circumstances research without consent is allowed, maybe even in the case of an unconscious patient, if the ethics committee approves it and the doctor has specific reasons not to tell the patient.

The final version of the European Convention on Human Rights and Biomedicine addresses the protection of persons not able to consent to research with the following words:[2]

A 17.1. Research on a person without the capacity to consent as stipulated in Article 6 may be undertaken only if all the following conditions are met:

i. The conditions laid down in Article 16, sub-paragraphs (i) to (iv), are fulfilled;

ii. The results of the research have the potential to produce direct benefit to his or her health;

iii. Research of comparable effectiveness can not be carried out on individuals capable of giving consent;

iv. The necessary authorisation provided for under Article 6 has been given specifically and in writing; and

v. The person concerned does not object.

2. Exceptionally, under protective conditions prescribed by law, where the research has not the potential to produce results of direct benefit to the health of the person concerned, such research may be authorised subject to the conditions laid down in paragraph 1, sub-paragraphs (i), (iii), (iv) and (v) above, and to the following additional conditions:

i. The research has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition.

ii. The research entails only minimal risk and minimal burden for the individual concerned.

The European Convention on Human Rights and Biomedicine allows in another way medical experimentation on persons not able to consent. The approach of the Convention is an abstract and a general one: there is no distinction between the three main groups of persons not able to consent to research, ie children, incompetent (especially old) adults, and the unconscious. On the other hand, Arts 6 and following of the Convention on Human Rights and Biomedicine distinguishes, under the heading "Consent", between children, incompetent adults and persons who have a mental disorder and gives rules concerning

2 Convention for the protection of the human rights and dignity of the human being with regard to the applications of biology and medicine: Convention on Human Rights and Biomedicine by the Council of Europe, 6 June 1996.

emergency situations and previously expressed wishes. But that chapter is devoted to medical treatment and not medical research. Art 16 on the other hand refers generally to Art 6, but does not make use of the distinction. As least as far as purely scientific research is concerned that does not have the potential to produce results of direct benefit to the health of the experimental subject, the distinction should be made again. There is a great difference between research on children on the one hand and research on the unconscious, for instance as far as the formation and use of a control group is concerned.

III GENERAL PREREQUISITES FOR CLINICAL STUDIES

Clinical studies in general have to meet the following conditions. Even if the distinction is made between therapeutic and non-therapeutic research on the one hand, and the formation of a test and a control group or different arms of test groups of a study on the other, there have to be some basic requirements:

An acceptable medical risk;

Informed consent;

A research protocol that shows the scientific merit of the study;

Inclusion and exclusion criteria;

The number of experimental subjects used;

The duration of the study;

Specific reasons for termination of the study;

The protection of privacy;

Means and restriction of publication;

The positive vote of an IRB or an ethics committee.

Naturally there are specific rules, for instance prohibiting experimentation on prisoners or other people who are deprived of freedom against their will, experimentation with the mentally handicapped persons, or children etc. These rules are to be found in different expressions in all the national and international guidelines, declarations, judgments, laws and conventions. The following may be mentioned by way of example: the Prussian directive of 1900[3]; the case of *United States v Rose*;[4] trials of war criminals before the

3 Anweisung an die Vorsteher der Kliniken usw v 29.12.1900, Zentralblatt der gesamten Unterrichtsverwaltung in PreuBen 1901, 188 f.

4 *United States v Rose* as part pro toto of the so-called Medical case.

Nuremburg Military Tribunals;[5] the Declaration of the World Medical Association;[6] Recommendations guiding doctors in clinical research, the Convention on Human Rights and Biomedicine by the Council of Europe;[7] the French statute of 1988;[8] the German drug law of 1976;[9] and the Good Clinical Practice guidelines of the European Commission.[10]

All these requirements have to be fulfilled in a clinical study that takes place in the ICU. Special problems are posed by the informed consent requirement.

IV CONSENT TO CLINICAL STUDIES IN THE ICU

In the intensive care unit there are "normal patients" ie patients with all their faculties intact. However, they are not willing probands from the outside, rather patients dependent on the doctor, the nurses and the other personnel in the ICU. From a strict legal point of view these patients are able to be informed and to give their free consent. The local ethics committee will naturally ask whether a doctor, who is not taking part in the treatment, is going to inform the patient and ask for the consent and whether there is any pressure or friendly persuasion factors that should be absent. Generally speaking experimentation on these patients is not very different from clinical studies on patients in the hospital generally.

Another typical patient in the ICU is the disabled one. This patient is not able to give free and timely informed consent. Sometimes these patients are unconscious; others are handicapped in receiving the information and weighing the pros and cons of giving the consent because they are, for example, heavily sedated. Here the problem of substituted consent arises. The following types of substituted consent should be discussed.

Anticipated Consent

The patient is able to give consent before becoming disabled, for instance by anaesthesia. Two cases show the extent of anticipated consent. In *Halushka v University of Saskatchewan*[11] a student had agreed for $50 to participate in a research project. He had been told that a new drug would be tried out on him and that a catheter would be used. The drug turned out to be the general anaesthetic Fluoromar, and the catheter even reached the

---

5 Trials of War Criminals before the Nuremburg Military Tribunals, Vol 2 (1947).

6 Above n1.

7 Above n2. Convention on Human Rights and Biomedicine, by the Council of Europe, 6 June 1996.

8 Loi No 88 - 1138, 20.12.1988, Gaz Pal, Legislation 1988, 605.

9 Gesetz zur Neuregelung des Arzneimittelrechts, 24.8.1976 BGBI. 1976 I 2445.

10 Good Clinical Practice for Trials on Medical Products in the European Community 1991.

11 *Halushka v University of Saskatchewan* (1965) WWR 608 (Court of Appeals, Saskatchewan).

heart. During this stage, for a short time, the heart stopped beating, but it was restored to its function again. The court allowed the anticipated consent, in scientific experimentation, but the student won the case. The information had been incomplete and his consent was therefore invalid.

In the case of *Karp v Cooly*[12] the patient had agreed to receive an artificial heart that was still in the experimental stage. During an operation it became necessary to install the experimental device. The patient died two days later having received a heart transplant in between. In this case the court held that the patient was able, after full information, to agree to the therapeutic experimentation that could have saved his life.

Consent by Proxy

In treatment it has become accepted practice that another person, especially the spouse or a near relative, is given the power of attorney in health care. In a German case of 1990[13] the patient had stipulated that according to the findings of the neurosurgeons, his wife should make the decision whether to perform a certain extirpation or not. The operating team forgot to ask the wife of the patient and went on. Because of the mixed result of the surgery the patient sued and won the case. The same measure of informed consent by an empowered relative could be used in medical experimentation, at least if it is of therapeutic value.

Consent by Guardian

The legal representative of a child or a mentally handicapped adult is able to consent to experimental medical measures. Some statutes give the parents this right in a limited way, eg the German drug statute § 40 Abs. 4 AMG and the French statute of 1988. In the California case of *Nielsen v Regents of the University of California*,[14] a former member of the IRB sued the university to abstain from a purely scientific experimentation on children. Healthy children were to be compared with children whose parents had already developed allergic reactions. All kinds of tests were envisaged, especially the taking of blood and injections under the skin like a puncture. The parents were to be paid $300 for the participation of their children in the clinical trial. The court allowed the trial because it did not seem cruel for the children to participate.

---

12 *Karp v Cooly* 493 F2s 408 (1974) (Court of Appeals).

13 LG Göttingen VersR 1990, 1401.

14 *Nielsen v Regents of the University of California*, Superior Court of California, 8 December 1975.

Presumed Consent

Consent should be given in writing, orally, or at least, for example by participation, implied. Intensive care, especially on unconscious victims of traffic accidents, works on the principle of presumed consent. The presumption being that the patient would allow all medical interventions in the patient's favour, unless otherwise stipulated. Presumed consent is sometimes invoked in clinical studies as well. The Hanover Ethics Committee has agreed to a clinically controlled study on patients with severe burning concerning Beta-Interferon. While the control group received the normal treatment for severe burning, the patients in the test group were given Beta-Interferon additionally. Since all patients were unable to give a valid consent this was done under the presumption of consenting to promising medical measures. Participation in the trial did not cause any danger to the control group, however those patients did not receive the new treatment.

Deferred Consent

The ratification of a measure in a clinical study, that has been performed on the patient already, could be termed deferred consent. It is probably based on the assumption of presumed consent also. In the late eighties in Berlin there was a study of elderly patients who had suffered nearly fatal tachycardiac symptoms. The clinically controlled study concerned about 300 patients, half of whom got a calcium antagonist and the other half who were infunded with a placebo. The patients, having become conscious later on, were told that they had been included in the clinical study and were asked for their belated permission. If the permission was given, the study at least retrospectively had been performed with consent. If the permission had been withheld or the patient had died, all the doctors could do was to fall back on the idea of presumed consent.

Summary

The above discussed examples show that in the cases that reach courts or ethics committees there was a difference between the single measure intervention as in the *Karp v Cooly* and the *Halushka* cases and the clinically controlled trials as in the Hanover and Berlin cases. The clinically controlled studies leave the doctor less room to adapt the medical measures for the purposes of the patient. On the other hand the outcome is statistically more relevant. The more the discretion of the doctor is removed, and objective criteria of the research protocol take over, the less there is reason for presumed consent because patients will rarely contemplate taking part in a clinical study. But on the other hand they might think of an accident with grave consequences where an unproved method was indicated. Therefore it is easier to assume they would have consented as far as the single measure is concerned. To ascertain the opinion of the patient the doctor should ask near relatives or other people who know the patient well. In questions of clinical studies for the benefit of the patients in the test group usually the idea of necessity comes into play.

If the patient were not enrolled in the study, the chance of becoming better would be missed. The presumed consent might be based on this ground.

The other difference is that of the purely scientific experimentation as against the study that might directly be of benefit to the health of the patient. A purely scientific enterprise was the basis of the case of *Halushka v University of Saskatchewan*. The trying out of a totally new general anaesthetic on a proband was of purely scientific nature. But the proband gave his anticipated consent. A case of medical experimentation for the direct benefit of the patient can be found in *Karp v Cooly*. Here the use of an artificial heart was the last step in a desperate fight to save a person. The patient had already consented and under these circumstances what the doctors did was unusual but justified.

If one may draw a conclusion from the international and national rules, the researcher has to exclude purely scientific research with no possible direct benefit to the patient in cases where presumed consent or deferred consent are indicated. Even in a controlled clinical study where the control group just gets the standard treatment, one could still argue, although with less justification, that participating in the study somehow enhanced the chances of the patient for recovery.

V RESEARCH ON BRAIN DEAD PERSONS

The discussion whether brain dead persons are dead or dying does not concern this article. If experimentation on brain dead persons happens in the ICU it will rarely be done as a clinical study. The Göttingen Ethics Committee a few years ago had such a proposal. The research protocol was drafted with the idea of testing all kinds of reflexes of brain-dead persons awaiting explantations of at least one of their organs. Since the patients' relatives had not been informed or asked for their permission and because of other reasons the Ethics Committee did not grant approval.

The recent Milhaud case in the Conseil d'État in France[15] concerned a single experiment on a brain-dead person. Here a forensic physician was called upon to testify in a murder trial. His expert testimony was to answer the question whether someone could have been killed with a certain mixture of different gases. To prove his point the doctor administered that mixture to a person declared brain dead. The relatives of the patient had not been asked. The ethics committee had not been consulted. The case went up to the highest French administrative court where the principle that brain-dead persons are really dead was approved. Nevertheless, the court required the doctor to get the permission of the ethics committee and to ask the near relatives whether that experimentation could be performed.

---

15 Lebreton "Le droit, le medicine et la mort" Recueil Dalloz-Sirey 1994 Chronique 352.

VI ICU STUDIES AND ETHICAL COMMITTEES

ICU studies are not the normal fare of ethical committees, in fact some members of ethics committees are a bit apprehensive about going over a protocol from the ICU. They know that all kinds of problems will arise: the doctor/patient relationship, less competent or totally incompetent patients, the question whether a control group is necessary, the difference between therapeutical and purely scientific studies.

Normally on an effective ethics committee there are sitting members who are familiar with the routine in ICU's or running ICUs themselves. It is absolutely necessary for an ethics committee to have a clear picture of what is going on in an ICU, and whether a clinical study can be performed there under the circumstances. In this respect the number of available patients/probands is important; sometimes it is doubtful whether there will be enough participating patients to give a meaningful statistical answer. The ethics committee should be local. This committee alone should judge whether the facilities of the hospital are sufficient for such a study. Permission or positive advice by so-called "international", "European" or "independent free" ethics committees are not helpful in this respect. They will not be able to judge the local conditions. This applies even to multi-centre studies where different ICUs are part of the deliberation of the ethics committee. That the ethics committee is involved in such studies reveals the Revised Declaration of Helsinki II.5. There it is stated that the doctor may consider it essential not to obtain informed consent. In this case a specific reason should be stated in the protocol for transmission to the independent committee. The independent committee is the local ethics committee and the circumstances under which the doctor thinks it necessary not to obtain the informed consent can be therapeutical privilege or a presumed, maybe even deferred, consent.

Rule II.5 of the Revised Declaration of Helsinki lets the ethics committee act as a kind of substitute for the person. The ethics committee in doing this should insist that the a doctor involves the next of kin of the patient in the process of decision-making. The relatives or persons with whom the patient has been living are used to find out what the response would have been if the patient had been faced with the question. The presumed consent has to be tailored to the individual patient. The relatives cannot give the consent themselves unless appointed guardian. At least under continental European law, they are simply persons who can tell the doctor about the positions, beliefs and statements the patient has made or held earlier. The ethics committee has to make certain that best endeavours are made to find out and follow the patient's wishes.

VII LIABILITY AND COMPENSATION

In nearly all countries in the world there is liability for medical negligence if it has not been especially abolished by law, as in New Zealand.[16] But even there punitive damages can be asked for.[17] Court cases because of negligent experimentation go back to 1767.[18] Liability for clinical trials that were not consented to has been upheld in recent times again and again in the United States,[19] as well as in the Federal Republic of Germany.[20] Negligence not only provides for material damages, but includes payment because of pain and suffering. Negligence implies that the standard of care has not been adhered to, but this is hard to prove. Because medical experimentation (especially clinical studies) ask the participant to make a personal sacrifice for the good of humankind, there are many instances where compensation or some kind of third party insurance, or even an objective liability, is provided.

The French law of 1988 gives an example of an objective liability:[21]

---

16 Palmer *Compensation for Incapacity* (Oxford, 1979); Giesen *International Medical Malpractice Law* (1988) No. 1098 ff; Deutsch *Kunstfehler und medizinischer Behandlungsunfall in Neuseeland* VersR 1980,201.

17 *Green v Matheson* [1989] 3 NZLR 564 (Court of Appeal).

18 *Slater v Baker and Stapelton* (1767) 95 ER 1860.

19 *United States v Stanley* 107 S Ct 3054 (1987); *Fiorentino v Wenger* 227 NE 2d 296 (New York Court of Appeals, 1967); *Valenti v Prudden* 397 NYS 2d 181 (1977).

20 BGHZ 20, 61 (1956); OLG Stuttgart VersR 1981, 342.

21 Loi No. 88-1138 20.12.88 i.d F des Loi No 90-86 23.1.90

Art. L. 209-7. - Pour les recherches biomédicales sans bénéfice individuel direct, le promoteur assume, même sans faute, l'indemnisation des conséquences dommageables de la recherche pour la personne qui s'y prête, sans que puisse être opposé le fait d'un tiers ou le retrait volontaire de la personne qui avait initialement consenti à se prêter à la recherce.

Pour les recherches biomédicales avec bénéfice individuel direct, le promoteur assume l'indemnisation des conséquences dommageables de la recherche pour la personne qui s'y prête, sauf preuve à sa charge que le dommage n'est pas imputable à sa faute ou à celle de tout intervenant, sans que puissent être opposé le fait d'un tiers ou le retrait volontaire de la personne qui avait initialement consenti à se prêter à la recherche.

Pour toute recherche biomédicale, le promoteur souscrit une assurance garantissant sa responsabilité civile telle qu'elle résulte du présent article et celle de tout intervenant indépendamment de la nature des liens existant entre les intervenants et le promoteur. Les dispositions du présent article sont d'ordre public. (Gaz Pal, Legislation 198, 605; J.O. 25.1.90).

Art. L. 209-7

In the case of biomedical research which has no direct individual benefit, the promoter undertakes, even in the absence of fault, to provide compensation for all the consequences of the research which cause loss for the person who participates in it, and that liability is not affected by the act of a third party or the voluntary withdrawal from the research of a person who had initially agreed to it.

In respect of biomedical research which has direct individual benefit, the promoter of the research assumes liability to compensate the person who participates in the research for any loss suffered as a consequence of that research, unless the promoter proves that the loss is not a result of its fault or of any other person involved, but the liability is not excluded by the act of a third person or the voluntary withdrawal from the research programme of a person who initially consented to participate.

In the case of all biomedical research, the promoter must take out insurance which guarantees compensation for any civil liability which may result under the present article or which may result from any other participant regardless of the nature of the relationship which might exist between those other persons and the promoter. The provisions of this article are a matter of public policy.

The French law has regulated all biomedical research, but the German Pharmaceutical Act of 1976 deals only with testing pharmaceuticals. In Germany the experimental subject will be granted relief by a third party accident insurance even if nobody is liable for the experimental accident:[22]

---

22 40 Abs. 1

Allgemeine Voraussetzungen

(1) Die klinische Prüfung eines Arzneimittels darf bei Menschen nur durchgeführt werden, wenn und solange

1. die Risiken, die mit ihr für die Person verbunden sind, bei der sie durchgeführt werden soll, gemessen an der voraussichtlichen Bedeutung des Arzneimittels für die Heilkunde ärztlich vertretbar sind;

2. die Person, bei der sie durchgeführt werden soll, ihre Einwilligung hierzu erteilt hat, nachdem sie durch einen Arzt über Wesen, Bedeutung und Tragweite der klinischen Prüfung aufgeklärt worden ist, und mit dieser Einwilligung zugleich erklärt, dass sie mit der im Rahmen der klinischen Prüfung erfolgenden Aufzeichnung von Krankheitsdaten und ihrer Weitergabe zur Überprüfung an den Auftraggeber, an die zuständige Überwachungsbehörde oder die zustundige Bundesoberbehorde einverstanden ist;

3. die Person, bei der sie durchgeführt werden soll, nicht auf gerichtliche oder behödliche Anordnung in einer Anstalt untergebracht ist;

4. sie von einem Arzt geleitet wird, der mindestens eine zweijährige Erfahrung in der klinischen Prüfung von Arzneimitteln nachweisen kann;

7th Section - Protection of the Human Being during the Clinical Trial

S40- General preconditions

(1) The clinical trial of a drug shall only be performed on human beings if and as long as

1. the risks, which are involved, for the person with whom the trial is to be carried out, are medically justifiable, when compared with the anticipated significance of the drug for medical science;

2. the person, with whom the clinical trial is to be carried out, has given his consent, having been informed by a physician of the nature, significance and scope of the clinical trial;

3. the person with whom the trial is to be carried out, is not confined by order of neither judicial nor administrative authorities;

4. it is run under the supervision of a physician, who can prove to have gained at least two years experience in the field of the clinical trial of drugs;

5. an appropriate pharmacological-toxicological test has been carried out complying with the respective prevailing level of scientific findings;

---

5. eine dem jeweiligen Stand der wissenschaftlichen Erkenntnisse entsprechende pharmakologisch-toxikologische Prüfung durchgeführt worden ist;

6. die Unterlagen über die pharmakologisch-toxikologische Prüfung, der dem jeweiligen Stand der wissenschaftlichen Erkenntnisse entsprechende Prüfplan mit Angabe von Prüfern und Prüforten und die Voten der Ethik-Kommissionen bei der zuständigen Bundesoberbehörde vorgelegt worden sind;

7. der Leiter der klinischen Prüfung durch einen für die pharmakologisch-toxikologische Prüfun verantwortlichen Wissenschaftler über die Ergebnisse der pharmakologisch-toxikologischen Prüfung und die voraussichtlich mit der klinischen Prüfung verbundenen Risiken informiert worden ist und;

8. für den Fall, dass bei der Durchführung der klinischen Prüfung ein Mensch getötet oder der Körper oder die Gesundheit eines Menschen verletzt wird, eine Versicherung nach Massgabe des Absatzes 3 besteht, die auch Leistungen gewährt, wenn kein anderer für den Schaden haftet.

(2) ...

(3) Die Versicherung nach Absatz 1 Nr. 8 muss zugunsten der von der klinischen Prüfung betroffenen Person bei einem im Geltungsbereich dieses Gestezes zum Geschäftsbetrieb zugelassenen Versicherer genommen werden. Ihr Umfang muss in einem angemessenen Verhältnis zu den mit der klinischen Prüfung verbundenen Risiken stehen und für den Fall des Todes oder der dauernden Erwerbsunfähigkeit mindestens eine Million Deutsche Mark betragen. Soweit aus der Versicherung geleistet wird, erlischt ein Anspruch auf Schadensersatz.

(4) ...

6. the documents on the pharmacological-toxicological test are deposited with the competent federal higher authority;

7. the person directing the clinical trial has been informed by a scientist responsible for the pharmacological-toxicological test about the findings of said test and the risks to be anticipated with the clinical trial.;

7a. a test plan according to the present level of scientific findings is available and

8. should a person be killed or the body or the health of a person be hurt in the course of the clinical trial, an insurance as specified in para 3 exists which guarantees benefits even if no other party is liable.

(2) A consent as specified in para 1 sub-para 2 shall only be effective if the person giving it

1. has legal capacity and is in the position to comprehend the nature, significance and scope of the clinical trial and to determine his decision accordingly'

2. has given the consent in person and has given it in writing.

The consent may be revoked at any time.

(3) The insurance specified in para 1 sub-para 8 must be taken out in favour of the person undergoing the clinical trial with an insurer authorised to carry out business within the purview of this law. The scope of the insurance must be in an adequate proportion to the risks involved in the clinical trial and in the case of death or permanent disability must total at least five hundred thousand Deutschmarks. As far as benefits are paid by the insurance, any claim for damages shall be extinguished.

(4) In respect of a clinical trial carried out with minors, paras 1 to 3 shall apply with the following conditions:

1. The drugs must be intended to diagnose or prevent diseases in minors.

2. The administration of the drug must be considered necessary pursuant to the findings of medical science to diagnose or prevent diseases in the minor.

3. Adequate test results pursuant to the findings of medical science are not to be anticipated from the clinical trial carried out with adults.

4. The consent shall be given by the legal representative or guardian. It shall only be effective if this person has been informed by a physician of the nature, significance and scope of the clinical trial. If the minor is in the position to comprehend the nature, significance and scope of the clinical trial and to determine his decision accordingly, then his written consent shall also be required.

In other countries guidelines issued by associations of the pharmaceutical industry are helpful. In Great Britain the Association of the British Pharmaceutical Industry obliges its

members to provide compensation on an objective basis for patients taking part in a clinical trial. As in Germany the British self-rule applies just to drug testing, not to other biomedical research as in France. There have been some problems in Great Britain with pharmaceutical companies that sponsor drug trials shouldering their responsibility. Some ethics committees have now put specific questions to the companies and only after a satisfactory statement is obtained ethical approval will be given.[23]

VIII CONCLUSION

Up to now it looks like the French and the German statutory provisions are most satisfactory, if one disregards the limitation on drug trials in Germany. Whether the liability for presumed fault in cases of therapeutic experimentation or the strict liability for purely scientific experimentation is better than a third party accident insurance should only be answered after some time and the opportunity to compare the outcome of both systems.

Because of the special circumstances of clinical research in ICUs there should be an insurance coverage that does not apply just in cases of negligence, but that applies on an objective basis either as liability insurance for strict liability or as accident insurance directly granted to the experimental subject.

---

23 Barton, McMillan and Sawyer "The Compensation for Patients Injured in Clinical Trials" Journal of Medical Ethics 1995 (21) 166 et seq. Cf. Milne "Compensation for Adverse Consequences of Medical Intervention" in Goldberg ed *Pharmaceutical Medicine and the Law* (1991) 111.