

Clinical Trial Compensation Guidelines



Preface

These guidelines contain two distinct sections:

- Phase I Clinical Trials Compensation Guidelines
- Phases II, III and IV Clinical Trials Compensation Guidelines

The purpose of these guidelines is to remove the distinction between the compensation arrangements benefiting healthy volunteers in Phase I trials that do not have the target disease and those patient volunteers in Phase I trials that do have the target disease, but where there is no reasonable prospect of direct benefit.

These guidelines will apply to all clinical trials commenced from 1st January 2015 onwards.

Background

The ABPI has long encouraged member companies to make special arrangements to compensate participants in clinical research that they have sponsored and who suffer injury as a result of such participation. The first guidelines relating to Phase I “healthy (non-patient) volunteer” studies were issued in 1970 and guidelines relating to clinical trials at Phases II-IV were first issued in 1983. The distinction between the compensation arrangements for “healthy volunteers” and for “patient volunteers” was based on the fact that “healthy volunteers” in Phase I studies would normally have no real prospect of personal benefit from participation in a Phase I study, whereas patients suffering from the target disease, participating in clinical trials at Phases II-IV, did have a prospect of benefit. It was viewed as ethically reasonable that patient volunteers should accept some of the risks inherent in testing new treatments for their disease, particularly where side-effects were foreseeable and the subject of warnings in trial information.

Since the two sets of guidelines were originally published, the ABPI has conducted periodic reviews of them and amendments have been adopted.

Recently, in relation to Phase I studies, it was noted that an increasing number of studies at Phase I with a new chemical or biological entity involve patients as well as (or instead of) healthy subjects. Many such studies explore disease-specific biomarkers; they do not investigate efficacy. Therefore, patients with the target disease participating in single dose administration and / or limited repeat dose administration studies at Phase I are not expected to gain therapeutic benefit and would not ordinarily be offered access to the medicinal product under investigation beyond the end of the study. In the circumstances, it is no longer thought ethically appropriate to distinguish between the compensation arrangements benefiting healthy volunteers that do not have the target disease and those patient volunteers that do have the target disease, but where there is no reasonable prospect of direct benefit from participation.

The ABPI and our members believe that the same compensation arrangements should apply to all patients enrolled in Phase I studies who have no prospect of direct benefit, including those with the target disease; and henceforth no distinction will be made between the status of subjects participating in Phase I research who have no prospect of direct benefit. Oncology or other studies at Phase I where material side-effects are foreseeable because of the nature of the product under research, but where patient volunteers may reasonably expect to receive therapeutic benefit, are not affected by this change of policy.

The new guidelines

Previous guidelines in this area have been replaced in order to reflect the agreed ABPI position:

- the 1988 Non-Patient Guidelines are now replaced by the compensation provisions set out in the Phase I Clinical Trials Compensation Guidelines; and
- the 1991 Clinical Trial Guidelines are now replaced by the compensation provisions set out in the Phases II, III and IV Clinical Trials Compensation Guidelines

Consequential changes to the relevant section on compensation in the ABPI's Guidelines For Phase I Clinical Trials (2012 Edition) have also been made.

Phase I Clinical Trial Compensation Guidelines

Background

The Association of the British Pharmaceutical Industry requires member companies that sponsor Phase I studies that offer no prospect of direct therapeutic benefit to research subjects to ensure that the arrangements they put in place for the conduct of such studies create a legally binding obligation, through the terms of the consent form and subject information, to pay compensation to the volunteer in the event of injury due to participation in the study.

1. The following principles should be reflected in these arrangements:
 - 1.1 The volunteer should be given a clear commitment that if he/she suffers bodily injury through participation in the trial, appropriate compensation will be paid without the volunteer having to prove either that such injury arose through negligence or that the product was defective in the sense that it did not fulfil a reasonable expectation of safety. The company should not seek to remove the right of the volunteer, as an alternative, to pursue a claim on the basis of either negligence or strict liability, if the volunteer wishes to do so.
 - 1.2 Where pharmaceutical companies sponsor studies to be performed by an outside research establishment, the responsibility for paying compensation should be clarified and reflected in the contractual documentation with the volunteer. Where the sponsoring company directly provides the undertaking regarding compensation, it is recommended that the text of the undertaking reflects an unqualified obligation to pay compensation to the volunteer on proof of causation. The company can protect its rights of recourse against the research establishment in its agreement with that establishment so as to cover the position where the negligence of its contractor may have caused or contributed to the injury by the volunteer. A volunteer can reasonably expect that compensation will be paid quickly and that any dispute regarding who will finally bear the cost of the compensation paid to him will be resolved separately by the other parties to the research.
2. It is also recommended that a simple arbitration clause is included as part of the provisions concerning compensation for injury, whereby any difference or dispute in relation to the implementation of the compensation provisions may be resolved with a minimum of formality.
3. The prospect of receiving no therapeutic benefit from the trial is critical to the application of these Guidelines. Patient volunteers in oncology or other studies at Phase I who may reasonably expect to receive therapeutic benefit would not be covered by these Guidelines.

Whether such a reasonable expectation exists should be readily apparent from the study information sheet and consent form. Such studies would be governed by the principles of the revised Phase II-IV Clinical Trial Guidelines.

4. The following standard provisions reflect the type of commitment that is generally viewed as acceptable:

“The company sponsoring the study confirms that:

- i. If the volunteer suffers any significant deterioration in health or well-being caused directly by participation in the study, compensation will be paid to the volunteer by the sponsoring company.
- ii. The amount of such compensation shall be calculated by reference to the amount of damages commonly awarded for similar injuries by an English court if liability is admitted, provided that such compensation may be reduced to the extent that the volunteer, by reason of contributory fault, is partly responsible for the injury (or where the volunteer has received equivalent payment for such injury under any policy of insurance effected by the company for the volunteer’s benefit.)
- iii. Any dispute or disagreement as to the application of paragraph (i) and (ii) above shall be referred to an arbitrator to be agreed between the volunteer and the company, or in the absence of agreement, to be appointed by the President of the Royal College of Physicians of London, with power in the arbitrator to consult a barrister of 10 years’ standing in respect of any issue of law including the amount of damages to be awarded as payment of compensation.
- iv. This agreement to pay compensation shall be construed in accordance with English law and, subject to paragraph (iii) above, the English courts shall have sole jurisdiction over any dispute which may arise out of it.”

Phase II, III And IV Clinical Trial Compensation Guidelines

Background

The Association of the British Pharmaceutical Industry favours a simple and expeditious procedure in relation to the provision of compensation for injury caused by participation in clinical trials. The Association therefore recommends that a member company sponsoring a clinical trial at Phase II, III and IV should provide without legal commitment a written assurance to the investigator – and through him to the relevant research ethics committee – that the following Guidelines will be adhered to in the event of injury caused to a patient attributable to participation in the trial in question.

1. Basic Principles

- 1.1 Notwithstanding the absence of legal commitment, the company should pay compensation to patient-volunteers suffering bodily injury (including death) in accordance with these Guidelines.
- 1.2 Compensation should be paid when, on the balance of probabilities, the injury was attributable to the administration of a medicinal product under trial or any clinical intervention or procedure provided for by the protocol that would not have occurred but for the inclusion of the patient in the trial.
- 1.3 Compensation should be paid to a child injured in utero through the participation of the subject's mother in a clinical trial as if the child were a patient-volunteer with the full benefit of these Guidelines.
- 1.4 Compensation should only be paid for the more serious injury of an enduring and disabling character (including exacerbation of an existing condition) and not for temporary pain or discomfort or less serious or curable complaints.
- 1.5 Where there is an adverse reaction to a medicinal product under trial and injury is caused by a procedure adopted to deal with that adverse reaction, compensation should be paid for such injury as if it were caused directly by the medicinal product under trial.
- 1.6 Neither the fact that the adverse reaction causing the injury was foreseeable or predictable, nor the fact that the patient has freely consented (whether in writing or otherwise) to participate in the trial should exclude a patient from consideration for compensation under these Guidelines, although compensation may be abated or excluded in the light of the factors described in paragraph 4.2 below.
- 1.7 For the avoidance of doubt, compensation should be paid regardless of whether the patient is able to prove that the company has been negligent in relation to research or development of the medicinal product under trial or that the product is defective and therefore, as the producer, the company is subject to strict liability in respect of injuries caused by it.

2. Type of Clinical Research Covered

- 2.1 These Guidelines apply to injury caused to patients involved in Phase II and Phase III trials, that is to say, patients under treatment and surveillance (usually in hospital) and suffering from the ailment which the medicinal product under trial is intended to treat but for which a product licence does not exist or does not authorise supply for administration under the conditions of the trial.

- 2.2 These Guidelines do not apply to injuries arising from Phase I studies where there is no prospect of personal benefit for the subject, whether or not they occur in hospital. Separate Guidelines for compensation exist for such studies.’
- 2.3 These Guidelines do not apply to injury arising from clinical trials on marketed products (Phase IV) where a product licence exists authorising supply for administration under the conditions of the trial, except to the extent that the injury is caused to a patient as a direct result of procedures undertaken in accordance with the protocol (but not any product administered) to which the patient would not have been exposed had treatment been other than in the course of the trial.
- 2.4 These Guidelines do not apply to clinical trials which have not been initiated or directly sponsored by the company providing the product for research. Where trials of products are initiated independently by doctors under the appropriate provisions of The 2004 Medicines for Human Use (Clinical trials) Regulations (SI 2004-1031), responsibility for the health and welfare of patients rests with the doctor alone (see also paragraph 5.2 below).

3 Limitations

- 3.1 No compensation should be paid for the failure of a medicinal product to have its intended effect or to provide any other benefit to the patient.
- 3.2 No compensation should be paid for injury caused by other licensed medicinal products administered to the patient for the purpose of comparison with the product under trial.
- 3.3 No compensation should be paid to patients receiving placebo in consideration of its failure to provide a therapeutic benefit.
- 3.4 No compensation should be paid (or it should be abated as the case may be) to the extent that the injury has arisen:
- 3.4.1 through a significant departure from the agreed protocol;
 - 3.4.2 through the wrongful act or default of a third party, including a doctor’s failure to deal adequately with an adverse reaction;
 - 3.4.3 through contributory negligence by the patient.

4 Assessment of Compensation

- 4.1 The amount of compensation paid should be appropriate to the nature, severity and persistence of the injury and should in general terms be consistent with the quantum of damages commonly awarded for similar injuries by an English Court in cases where legal liability is admitted.
- 4.2 Compensation may be abated, or in certain circumstances excluded, in the light of the following factors (on which will depend the level of risk the patient can reasonably be expected to accept):
- 4.2.1 the seriousness of the disease being treated, the degree of probability that adverse reactions will occur and any warnings given;
 - 4.2.2 the risks and benefits of established treatments relative to those known or suspected of the trial medicine.

This reflects the fact that flexibility is required given the particular patient's circumstances. As an extreme example, there may be a patient suffering from a serious or life-threatening disease who is warned of a certain defined risk of adverse reaction. Participation in the trial is then based on an expectation that the benefit/risk ratio associated with participation may be better than that associated with alternative treatment. It is, therefore, reasonable that the patient accepts the high risk and should not expect compensation for the occurrence of the adverse reaction of which he or she was told.

- 4.3 In any case where the company concedes that a payment should be made to a patient but there exists a difference of opinion between company and patient as to the appropriate level of compensation, it is recommended that the company agrees to seek at its own cost (and make available to the patient) the opinion of a mutually acceptable independent expert, and that his opinion should be given substantial weight by the company in reaching its decision on the appropriate payment to be made.

5 Miscellaneous

- 5.1 Claims pursuant to the Guidelines should be made by the patient to the company, preferably via the investigator, setting out details of the nature and background of the claim and, subject to the patient providing on request an authority for the company to review any medical records relevant to the claim, the company should consider the claim expeditiously.
- 5.2 The undertaking given by a company extends to injury arising (at whatever time) from all administrations, clinical interventions or procedures occurring during the course of the trial but not to treatment extended beyond the end of the trial at the instigation of the investigator. The use of unlicensed products beyond the trial period is wholly the responsibility of the treating doctor.
- 5.3 The fact that a company has agreed to abide by these Guidelines in respect of a trial does not affect the right of a patient to pursue a legal remedy in respect of injury alleged to have been suffered as a result of participation. Nevertheless, patients will normally be asked to accept that any payment made under the Guidelines will be in full settlement of their claims.
- 5.4 A company sponsoring a trial should encourage the investigator to make clear to participating patients that the trial is being conducted subject to the ABPI Guidelines relating to compensation for injury arising in the course of clinical trials and have available copies of the Guidelines should they be requested.
- 5.5 If a legal remedy is pursued and the case is the subject of adjudication or settlement, the patient may not bring a further claim, based on the same facts, under these Guidelines.

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