Insurance in clinical research

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Abstract

Aims and Objectives: Sponsors need to pay for management of all serious adverse events suffered by subjects in a clinical trial and to compensate for injuries or deaths related to the trial. This study examines if insurance policies of trials, cover all contingencies that require reimbursement or compensation. **Materials and Methods:** Insurance policies of trials submitted to Sahyadri Hospitals between January 2013 and December 2013 were studied, with respect to the policy period, the limit of liability, deductibles, and preconditions if any. **Results:** All the policies studied had some deficiencies, in one respect or the other and none had a provision to pay full compensation if required. Some insurers have put in preconditions that could jeopardize the payment of compensation to subjects. **Conclusions:** Insurances are complicated documents, and need to be critically examined by the ethics committee before approval of the study documents.

Key words: Compensation, insurance, preconditions, trial injuries

INTRODUCTION

Review of clinical trial insurance has received little attention during trial approval process by ethics committees (ECs). The need for insurance was not mentioned in the Nuremberg Code[1] or the Declaration of Helsinki.[2] The Belmont report, which laid the foundation for ethical research in the US too did not look into the provision of insurance.[3] The requirement for trial insurance initially featured in the ethical guidelines for biomedical research on human subjects published by the Indian Council of Medical Research in 2000. These guidelines prepared under the Chairmanship of Justice M.N. Venkatachaliah, former Chief Justice of India were reviewed in 2006 under the chairmanship of Dr. M.S. Valiathan.[4] The new version made little change in the requirement of insurance for reimbursement, management and compensation to subjects injured during trials.

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These guidelines in the "principles of nonexploitation" state that "Each research shall include an in-built mechanism for compensation for the human participants either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive aftercare, including treatment during and after the research or experiment, in respect of any effect that the conduct of research or experimentation may have on the human participant and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary."

In the section "compensation for accidental injury," the guidelines state the obligation of the sponsor as mentioned below.

"The sponsor whether a pharmaceutical company, a government, or an institution, should agree, before the

research begins, in the a priori agreement to provide compensation for any physical or psychological injury for which participants are entitled or agree to provide insurance coverage for an unforeseen injury whenever possible".

The guidelines issued by the Council for International Organizations of Medical Sciences in collaboration with the World Health Organization[5] mention that the protocol should contain details of insurance coverage for treatment and compensation of trial related injuries.

The issue of compensation has become crucial, with the first amendment (of 2013) to drugs and cosmetics rules, which has made the payment of compensation an important responsibility of the sponsor. Prior to this amendment, some sponsors were paying compensation; however, the payment or the amount were not uniform across the board and this contributed significantly to the enactment of the amendment.

The rule 122 DAB has made the EC responsible for recommending the amount of compensation for both fatal and nonfatal injuries during clinical trials. The rule spells out clearly, that the EC should review each serious adverse event (SAE), decide the causality and the need for compensation, and recommend the same to the regulators. The amendment also provided a formula for calculating the compensation (and revised the same), in case of death due to an SAE, however, no formula has been provided to calculate the compensation in case of nonfatal injury.

The good clinical practice guideline of the Central Drugs Standards and Control Organization requires that the protocol should contain a section on 'Finance and Insurance' in which there is evidence that the subjects are satisfactorily insured against any injury caused during the study (2.3.1.12 d).

It is acknowledged that, following the recommendation of the EC, if the regulator asks the sponsor to compensate the subject or nominee, the compensation must be paid within a specified period. Failure to do so can result in the regulator stopping the trial and preventing the sponsor from undertaking any further trials in the country. Thus, there are adequate provisions to ensure that the sponsor does not default in payment of compensation. This does not preclude the intervention of EC in assuring that all provisions exist to pay compensation to subjects.

The EC during the approval of the research proposal is required to review all the documents related to the trial, including the insurance policy. In case the insurance policy does not make adequate provisions for paying compensation, the sponsor will have to bear the costs, but during this period, the subject or nominee may suffer due to delay in payment. In an internationally publicized case, the sponsor did refuse to pay for the trial injuries, citing lack of adequate insurance coverage.[6]

In case of injuries or death of subjects, there are many ways to calculate the amount of compensation to be offered.[7] It can be argued that money can never really compensate for a life, and it is true. However, there is no other way of compensating for a subjects death, hence monetary compensation is the best option available. It could also be argued that the sponsor is responsible for payment of compensation, whether this comes from the sponsor's profits or insurance should not duly concern the EC. It will be accepted by all that the main role of the EC is to protect the rights and well-being of the subjects, therefore EC has the right (as well as the duty) to examine the insurance policy critically before approving the trial.

MATERIALS AND METHODS

Insurance policies submitted for EC review between January 2013 and January 2014 at Sahyadri Clinical Research and Development Center, Pune were selected for detailed study. All policies were for phase III studies. The following aspects were critically examined.

Policy period

Every policy has a period of coverage, thus coverage of a policy may begin on 1.1.2013 (at 0.00 am) and end on 12.31.2013 (at 2400 h). The insurer will consider only those claims that refer to any event occurring between these two limits:

- Limit of liability
  Most policies specify the amount that may be paid to the claimant. Unlike indemnity, insurance does not compensate proportional to the loss, but the compensation is fixed.
  a. Per claim
     The compensation for every claim is fixed.
  b. Total
     This is the total amount that the insurer may have to pay in case of multiple claims.
- Deductible
  The insurer deducts a fixed amount from every claim, supposedly for expenses related to processing the claim.
- Preconditions if any.

Policies of public sector companies were separated from those of private sector companies, these two groups were compared with check if any differences exist in the policies of these two types of insurers.

There are certain preconditions for every policy. Insurers specify clauses or conditions under which insurance will not be paid, these are preconditions of the policy.

RESULTS

Of the 13 policies critically reviewed, the breakup of insurers was as shown in Table 1.

Policy period

Most policies are for a period of 1 year, but in case of a particular policy the duration stated was from April 1, 2013 to May 31, 2014, that is 14 months. This policy issued by Bajaj Allianz could be typographic error. There were two policies for 3 years each.

Limit of liability

There is a wide variability with which the policies show the limits of liability.

- Some policies show per claim liability and a total liability.
- Some policies show only the aggregate liability.
- Some policies show the same value for per claim and aggregate liability.

The per claim liability ranged between Rs. 1,500,000 and Rs. 5,000,000.

While the total or aggregate liability ranged between Rs. 2 Cr and Rs. 14 Cr.

Two policies issued by ICICI Lombard show the same figure for individual and aggregate claims.

Deductibles

On every claim pressed, the insurer deducts a certain amount for legal and other expenses these are calculated and put under the head of deductibles.

The lowest deductible was of Rs. 100,000 and the maximum was Rs. 168,630. Surprisingly, there seems to be no relation between the aggregate liability and deductible. In three policies, the amount of deductible was not clear, whereas one policy clearly mentioned that the deductible was 5% of every claim.

Table 1: Break up of insurance policies

Insurer	Type of the insurer	Number of policies
National Insurance Co. Ltd	Public sector	3
New India Assurance Co. Ltd.	Public sector	1
Bajaj Allianz General Insurance Co. Ltd.	Private sector	5
ICICI Lombard General Insurance	Private sector	2
HDFC Ergo General Insurance	Private sector	1
Pioneer Insurance and Reinsurance Brokers Pvt. Ltd	Private sector	1

Preconditions

There is a very wide variation of preconditions mentioned in different policies; some had an exhaustive list, whereas some had none. The most exhaustive list appeared in the HDFC Ergo general insurance policy and the policy issued by National Insurance Company. These are dealt with in detail in the discussion.

Type of insurer

Four of the policies were issued by public sector companies, while nine were issued by the private sector companies. There was no significant difference between the policies by the type of insurers. One Public Sector Company and one private sector company had very exhaustive preconditions, while others did not have.

DISCUSSION

The role of sponsors in providing medical/surgical treatment of trial related injuries and death has long been a topic of intense debate. While some sponsors have followed rules that exist, often the compliance is in the letter and not in the spirit.[8] Compensation for injuries in clinical trials is required in many countries where clinical trials are conducted; however, the mechanisms and rules differ significantly. In the United States, which leads the world in the number of ongoing trials, there are no compensation rules.[9] The Affordable Care Act of 2010 requires that insurance providers cover individuals taking part in clinical trials; however, the act has not been uniformly applied.[10] In the UK, there are no regulations, but the association of British pharmaceutical industry has guidelines[11] that dictate the payment of compensation for trial related injuries. While European countries require the provision of "no fault" compensation, the guidelines show a wide variety across the continent.[12] In Japan, the rate of compensation is higher, raising the doubt of overestimating trial related injuries.[13]

Under the US law, sponsors are not required to provide compensation for trial related injuries, and subjects may press claim under the law of "Torts." The law of torts may be strong in the US, and trials swift, but there are worries when US companies sponsor studies overseas, especially where the law of Torts is not as strong.[14] Alternate compensation mechanisms have been proposed, so as to make US sponsored research acceptable in countries where resistance is setting in.[15] There are significant differences among universities sponsoring research toward treatment of research related injuries and compensation, and a total lack of uniformity.[16] Current federal policy, which applies to federally funded research with "more than minimal risk"

to participants, requires that institutions that maintain a compensation system must inform participants of its existence as part of the informed consent process (45 C. F. R. 46.116 (a (6)).

For long there has been a demand for compensation for trial injuries in the US. Expert after expert has damned the US policy of not having a uniform compensation policy, especially since the country has the largest number of clinical trials running at any time. Elliot in a critique of the US system says that "Not a single academic medical center in the United States makes it a policy to compensate injured subjects or their families for lost wages or suffering."[17] He argues for compulsory insurance or indemnity of injured patients to make the US system more patients friendly. Now 'Nature' has added its weight behind the demand for a compensation policy, so eloquently put forward by a number of ethicists.[18]

The importance of conducting medical research on a global or international platform cannot be overemphasized in current times. Sponsors are encouraging international clinical trials for reasons of efficiency, speed and access to larger affected populations. Therefore, it is all the more necessary to understand the requirements for compensation and insurance in different countries, at least those which are the large sources of drugs. Widely varying rules on insurance, around the developed world have become a stumbling block in going international with clinical trials.[19] At the trial level, the fear of denial of reimbursement by insurers can be a significant barrier to clinical trial participation too.[20]

Thankfully the Indian government has not followed the US policy, leaving the compensation in the hands of the courts. The extremely slow legal system in India has found critics among lay people, government officials, lawyers and often judges themselves. Delays in the Indian legal system are so well-known that readers will acknowledge their existence without citing any reference.

Understanding insurance policies and making sense out of them, takes time, effort and a lot of patience. It is often beyond the scope and capacity of lay people, and most people who have taken insurance have not carefully read the policies. None the less the ECs need to critically examine all policies submitted for approval. The different formats, language, and terminology used by different companies in different policies, makes it difficult to compare policies and understand exactly what they offer. Probably, that is the secret of the success of insurance companies. In the last decade, insurance business has shown a compound annual growth rate of 15.5%, and insurance business, which was estimated to be worth 72 billion USD is expected to grow to 280 billion USD in 2020.[21]

The government requires sponsors to have trial insurance, so the sponsors insure their trials. Yet how effective and how subject friendly these are, remains to be seen. Compensation rules have just about completed 1 year, as yet there are no reports of disagreements on compensation amounts and hence it is not clear how smooth the process of paying compensation is going to be. It would be wise to examine this aspect so that we are at least familiar with the mechanism before the problems hit us. While critically evaluating insurance policies, we were struck by the fact that compared to insurance, how simple science is. This is not the position in India alone, elsewhere too insurance mechanisms are extremely complex.[22]

Most policies examined by us are for the period of 1 year, while the trials are for a longer period. It is expected that the insurance will be renewed; however, there is no guarantee that it will be. In case, there are a large number of trial related SAEs, and compensation mounts, the insurer may refuse to extend the period of insurance. Another insurer may not be too keen to take up the responsibility, if it is known that large amounts of compensation have already been paid. What happens to the trial and the subjects then? The HDFC Ergo policy makes this a precondition for the issue of a policy requiring data on claims, stating.

'If a clinical trial has already started, all necessary information and a statement that no claim has occurred so far or all information about reported or known claims and circumstances."

In general, policies specify the liability per claim and the aggregate liability, which seems to be the norm, but not all policies follow this. In policies where per claim liability is not mentioned, it is not clarified how many subjects are totally covered by the policy. A policy with an aggregate liability of Rs. 2 Cr may be great if only four patients are involved, but Rs. 10 Cr policy may not amount to much if it covers 500 patients.

Under the Indian rules, the compensation may vary from Rs. 4 lakhs to Rs. 73.6 lakhs. None of the policies reviewed by us, had a provision for payment of the maximum compensation, if it were to be required. It is acknowledged that the highest compensation is only awarded in the death of a healthy individual aged 16, which is not a very likely possibility. Yet insurance should be able to take care of all possible, probable, and improbable cases too.

Every claim processed by the company comes with a deductible. This is the amount which will be deducted

from every claim processed. Thus, the value of the policy shown boldly on the document is not what is going to be ever paid out. The maximum amount that will ever be paid is the aggregate liability, less the deductibles multiplied by the number of claims. The larger number of claims, the lesser is the payment. If there are a dozen small claims the insurer makes more money than if there are one or two large claims.

By far the most disturbing features of these policies are the preconditions for payment of a liability claim. The largest list of preconditions appears in the HDFC Ergo policy, and we acknowledge that a number of them are logical, but a few some run contrary to the rules in the country, and negate a large part of the good that insurance does.

The precondition of HDFC Ergo "no products guarantee" or the one in the policy of National Insurance Company "compensation will not be paid for the failure of a drug or product under trial to perform its intended purpose" implies that in case an investigational product fails to produce its intended therapeutic effect, no compensation will be paid. This runs contrary to the Rule 122 DAB 5(c). It is appreciated that this clause is hotly contested by most stakeholders of clinical research. The drug technical advisory board has recommended that this clause be deleted,[23] so has the Dr. Ranjit Roy Chowdhury committee,[24] but the official response to these recommendations is still awaited. As of today, the failure of an investigational product to produce an intended therapeutic effect, qualifies as a trial related factor, and makes the subject eligible for compensation.

The precondition of HDFC Ergo, "no compensation for pain and suffering" defies logic. All ethics guidelines urge that pain and suffering to subjects be reduced to absolute minimal. The whole system is working to rid patients of pain and suffering, yet the insurer says that pain and suffering are not grounds to compensate. The same insurer also states that malpractice shall not be compensated for, while the Rule 122 DAB 5(b) states that injury or death due to "violation of the approved protocol, scientific misconduct or negligence by the sponsor or his representative or the investigator;" is to be compensated for.

The HDFC Ergo insurance states that "children below 1 year of age are not covered under this policy" It is not clear whether sponsors, investigators and EC members are aware of such conditions, especially if the policy is for pediatric trials. This caution is necessary because these preconditions seem to be standard ones in the policy and if one is not careful these words could be incorporated in the policy for a pediatric trial.

The insurer Bajaj Allianz also has a set of preconditions in its policy, some of these are among those spelt out by HDFC Ergo. Its policy quotes various sections of Rule 122 DAB and they have derived conditions from the rule. An EC is required to recommend the quantum of compensation to the Drug Controller General of India, within 21 days of receiving the final SAE report from the sponsor. If the EC fails to meet this deadline, the insurer states that the claim will not be honored. While the responsibility of the EC is acknowledged, punishing the subject for the negligence of the EC is not right and we do not think is approved by the government of India.

In clinical research, the subjects depend upon the EC to protect them. Helping subjects get their due, in addition to protecting their rights and well-being is the main cause for the existence of the EC. Members should spend time and effort in understanding the insurance policies placed before them, to make sure that faulty policies will not jeopardize the interest of the subjects.

Insurance as a business is a very profitable one and that is why so many industrial houses and banks have entered this sector in the last two decades. The whole purpose of insurance was to help the insured in times of unexpected tragedies, but somewhere down the years, the interests of the insured have been forgotten. Insurance policies and procedures have become more and more complicated and the terminology used has become less people friendly. Somewhere hidden in the fine print are clauses, which help the insurer profit at the expense of the insured. Insurance is a tricky business and people familiar with the writings of John Grisham in general and "The Rainmaker" in particular, will surely agree.

CONCLUSION

Ethics committee members have the right and duty to critically examine insurance policies submitted along with other documents for approval of proposals. These policies may not cover the entire period of the trial and contain clauses or conditions which would make payment of compensation to subjects difficult. It is finally the responsibility of sponsors to pay compensation, irrespective of whether their insurance covers it or not, yet due diligence on the part of ECs will go a long way in ensuring that the subjects' rights and well-being are protected.

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