Review Article

Compensation for research related injury

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INTRODUCTION

In March 2006, eight healthy volunteers in a phase I trial received a T cell agonist at Parexel's clinical pharmacology research unit at Northwick Park Hospital, London.[1] This was the first human trial of TeGenero's TGN1412, a new humanised monoclonal superagonist of the CD28 T cell surface receptor,[2] designed to mitigate autoimmune and immunodeficiency disease. The six men who received the active component rapidly developed catastrophic multisystem failure; the remaining two, who received a placebo, were unharmed. The participants who had developed serious complications received very little compensation for their injuries because Parexel, the CRO that conducted the trial for TeGenero, maintained that it had carried out all procedures correctly and hence was not responsible for the unforeseen reactions caused by the drug and the insurance cover (£ 2 million) that TeGenero (the sponsor) had, was not enough to cover the long-term health consequences of this disaster, as the volunteers are at risk of developing life-threatening conditions such as autoimmune diseases or cancer later in life.[3,4]

More recently and closer home, in early 2010, of the 25 deaths described as "trial related" in clinical trials carried out in India, only five families had received "compensation for trial related death" with an amount ranging from Rs 1.5 to 3 lakhs initially.[5] Following instructions from the DCGI, families of 22 clinical trial victims were paid around Rs 50 lakh by 10 Pharmaceutical companies, with the compensation ranging from Rs 1.08 lakh to Rs 10 lakh, with most families receiving between Rs 1.5-2.5 lakh as a one-time package.[6]

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Both these incidents highlight the different ethical dilemmas surrounding the issue of compensation for research related injuries, which will be discussed in this article along with a review of the relevant local and international guidelines and laws.

Definitions

When an injury occurs as a result of participation in a research study it is called a "research related injury" and these are sometimes inevitable. Such injuries may range from relatively minor harms (such as bruises due to a study procedure or vomiting due to a new drug) to major injuries (such as organ damage or temporary physical disability) to catastrophic injuries (such as permanent disability or death). Injuries can be physical, psychological/emotional, social or economic and may require only acute or emergency care, or long term medical care.

Harm is defined as economic, physical, psychological and social damage. Economic Harm is financial loss resulting from participation in a research project, which may include direct losses such as amounts the claimant had to spend to try to mitigate problems and consequential economic losses resulting from lost income. Physical Harm is death, bodily injury to, illness or disease in any person. Psychological Harm is negative self-perception,

emotional suffering (e.g., anxiety or shame), aberrations in thought or behaviour, or long-lasting intense psychological distress and fear, which in extreme cases might result into suicide. Disability is physical or mental impairment that substantially limits one or more of the major life activities of such individual-including communication, walking, and self-care (such as feeding and dressing oneself) -and which is likely to continue indefinitely, resulting in the need for supportive services[7,8].

Compensation is defined as 'the act or process of making amends for something' or 'something, typically money, awarded to someone in recognition of loss, suffering or injury'.[9]

Indian guidelines and regulations

The Indian law for clinical trials i.e. amended Schedule Y of 2005, Indian GCP Guidelines for Clinical Trials (in Clause 2.4.7) [http://cdsco.nic.in/html/schedule-y%20%28amended%20version-2005%29%20original.htm; last accessed 10th Sept., 2012],[10] the Indian GCP Guidelines [http://cdsco.nic.in/html/GCP.htm; last accessed 10th Sept., 2012] and the ICMR Ethical Guidelines for Biomedical Research on Human participants, 2000 (Section V in General ethical Issues) and 2006 (in Chapters III and IV) [http://icmr.nic.in/ethical_guidelines.pdf; last accessed 10th Sept., 2012][11] have mentioned the need for provision of compensation to participants for research related injuries. Both Schedule Y and the ICMR guidelines specify that this be an essential element of the Informed consent document (ICD). Research participants who suffer physical injury as a result of their participation are entitled to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability, according to the guidelines. In case of death, their dependents are entitled to material compensation. Furthermore, applications submitted to Ethics Committees for prospective studies should provide the proposed financial plan (including, if necessary, insurance) to manage adverse events and compensation for trial related injuries. These principles enunciated in the ICMR guidelines are in consonance with Guideline 19 of CIOMS[12] and the Declaration of Helsinki.[13]

In spite of these provisions, no major efforts were seen in compensating research participants for injuries in clinical trials and neither regulators nor Ethics Committees had raised any issues regarding compensation, even though several clinical trials [453 in 2009, 505 in 2010 and 271 in 2011] have been approved by the Drugs Controller General of India (DCGI) office, over the last 3 years.[14]

Current scenario

A study was undertaken by us in 2008[15] to assess the extent of awareness regarding the compensation issue among various clinical research stakeholders. The study was carried out in three parts: A questionnaire-based survey regarding awareness of the present guidelines and/or policies related to compensation for trial related injuries, implementation of the same in case of research related injuries and management of compensation claims arising out such injuries, in-depth interviews with select stakeholders to identify reasons/solutions to this issue and a review of Informed Consent and Insurance documents of projects submitted to 3 Ethics Committees to assess the implementation of the various Indian Guidelines and the types of packages planned for managing research related injuries.

We found that although 53% investigators said they were aware of the requirements in the Indian laws and guidelines regarding provision of clinical-trials insurance and/or compensation for injuries during a clinical trial, only two actually mentioned that the ICMR guidelines formed their referral document. Comparatively more EC members (74%) were aware of the guidelines/laws applicable. Of these, four said that they complied with the ICMR guidelines, two with Schedule Y while two followed ABPI guidelines for compensation. Among sponsors, 24 (89%) indicated their awareness of the guidelines regarding compensation of which five said that they were compliant with the Indian GCP guidelines, two with Schedule Y while three complied with the ICMR guidelines.

Only 12 of the 30 (40%) investigators and 7 of 23 (30%) EC members said that their Institutions had policies for the management of compensation issues in case of research related injuries while all the sponsors replied in the affirmative. However the policy was mainly to provide immediate free medical care or reimbursement of expenses incurred for the acute management of the adverse event. Compensation for loss of time/wages, death, physical disability or long term incapacitation was not included. All the stakeholders agreed that the financial responsibility of the trial related injury was that of the Sponsor, as documented in the CTA with a provision of an insurance cover. However, 20 (67%) investigators and 11 (48%) EC members said that the research participants or relatives had to first pay to manage the trial related injury and they were reimbursed after providing proof of such a payment.

The major point that was emphasised by all interviewees during the in-depth interviews was the lack of awareness among investigators and EC members regarding compensation for trial related injuries. Investigators (and through them EC members) relied entirely on sponsors to make arrangements for payment and never went into the details. Interestingly, Sponsors suggested that ECs should play a more active role in ensuring that AEs are

managed efficiently by Investigators both medically and financially i.e., confirmation of payment or reimbursement of medical expenses and that there should be quality audits of investigators and study sites for compliance with such policies. A common refrain from the interviewees was the need for nationally relevant guidelines on compensation issues, especially on the extent.

A review of ICDs and insurance documents showed that compensation issues were inadequately discussed with only insurance certificates being submitted to ECs for review and 83% of EC members being unaware of the details of insurance contracts. It was in ICDs from 2003 that we found a mention of this issue as a separate point in the document. Interestingly, ICDs of intramural research projects and trials related to herbal medicines tended not to have any compensation mentioned. In 2003, 50% of the ICDs mentioned the issue of compensation, and this increased to 62, 71, 91 and 83% over the years from 2004 to 2007 respectively. In the ICDs that mentioned compensation for trial related injury, it was noted that most ICDs mentioned that "medical care" would be provided for management of trial related AEs and that the financial burden would be borne by the sponsors. Only in two cases (in 2005) was it actually mentioned that the sponsor would provide monetary compensation of medical expenses for management of research related injury. We also found that 4% ICDs in 2004, none in 2003 and 2005, 16% ICDs in 2006 and 33% ICDs in 2007 stated that compensation would be given only after it was confirmed that the injury was due to the trial drug or procedure and if the medical care of the adverse event was not covered by the subject's own or hospital's insurance policy. None of the ICDs referred to compensation for lost wages/disability/discomfort/or death or did not provide for the same.

Revised indian compensation guidelines

The ICMR in collaboration with the Indian Society for Clinical Research (ISCR) and Forum for Ethics Committees in India (FERCI) had issued Draft Guidelines for Compensation to Participants for Research Related Injury in India in 2008[7,8,16] which would apply to all clinical research, whether sponsored by the pharmaceutical or medical device industry, government or academia or individual investigators.

Recently, in November 2011, the Drug Controller General of India (DCGI) published the new draft rules under the Drugs and Cosmetic Rules, 1945 (3rd Amendment, 2011) Rule 122 DAB for '*Compensation in case injury or death during the clinical trial*'.[17] These draft rules mainly reiterate the ICMR guidelines on Compensation for research injuries with some important differences. The rule mandates that participants or family (as the case may be) be compensated for permanent injury or death occurring due to participation in clinical studies and that this should be responsibility of the Sponsor. It also states that all ICDs should incorporate this clause. A further step taken by the DCGI's office in August 2012 has been to circulate draft guidelines to determine the quantum of financial compensation to be paid in case of clinical trial related injury or death.[18] These guidelines describe the methods to be followed by the Ethics Committees for calculating the quantum of financial compensation to be paid in case of clinical trial related injury or death.

In the meantime, the ICMR has withdrawn its guidelines, in order to have a common standard in the country although it is likely that these will be re-issued later to apply to clinical research other than regulatory clinical trials covered by Schedule Y.

A number of ethical issues underlie these draft rules.

Principle of 'No-fault compensation'

The main principle behind both the ICMR guidelines (point 3.4)[7,8] and the 3rd Amendment of the Schedule Y draft rules for compensation[17] is the '*no-fault approach*' wherein trial participants are to be provided compensation for research related injuries without having to prove that the injury was caused due to medical negligence or error on the part of the study Investigators and/or sponsor. The responsibility of providing medical care to the injured participant lies with the Investigator and Sponsor. This principle is unlike that of '*tort liability*' wherein the trial participant has to prove that the injury was caused as a result of participation in the clinical trial.[19] It is believed that in our country a no fault approach is a more sustainable method as it aims at providing compensation without ascribing blame. Secondly, it enables participants to receive compensation in situations where negligence cannot be proved. This is of critical importance especially in clinical trials where the injuries sustained are often independent of any negligent act. A no fault approach is also favorable for the sponsor/investigator as the amount payable can be calculated on the basis of certain parameters such as age, salary, previous medical history etc. Thus, compensation under such an approach appears more predictable which will help in effective cost management for investigators/sponsors in cases of clinical trials.

Informed consent

The issue of compensating for research related injuries when trial participants have voluntarily consented to take part in the trial usually leads to a debate. One school of thought says that all trial participants sign the informed consent document after being explained and having understood the risks and benefits of participating in the

study, taking an informed decision to go ahead in the study. In such a scenario, when the participant has accepted that there may be risks and harms that can occur as a part of the study, why then should he/she be compensated in case of an injury?[20]

The other school states, however, that this goes against the ethical principles of justice and respect for persons. The informed consent document respects the individual's decision making process of being a part of a trial. However, it cannot be extrapolated to argue that he/she also consents to be harmed during the trial. Risk and harm are often unknown and unexpected. Hence the concept of "no fault" compensation for the injury lies at the root of the rules.

Additionally, in India, often the question is raised "how informed is the informed consent"? It is well established that the patient-physician relationship is generally one of dependence; this is all the more true in India, where economic and other inequalities exacerbate this dependence.[21,22] It is also true to state that awareness about clinical research is lacking in our country as also the awareness of the rights that the patient reserves while participating in a trial.[23] Thus, although valid informed consent requires that the consenting person should have the capacity to understand and make decisions voluntarily and without coercion, in practice, this is not always the case as the level of understanding, the multitude of languages and the issue of therapeutic misconception makes informed consent challenging. Studies have shown that trial subjects may not fully understand the investigative nature of clinical trials and their degree of comprehension of the various components of the informed consent process may not always be satisfactory.[24-26] In fact, a meta-analysis of 7 studies (describing 904 Indians) showed that personal health benefits, source of extra income, and trust in physicians were among the factors motivating people to participate in a trial while mistrust of trial organizations, concerns about efficacy and safety of trials, loss of confidentiality, and language barriers featured among those factors which acted as barriers to participate in the trial.[27]

Role of Ethics Committees

It falls on the Ethics Committee to thoroughly review the Informed consent document and also the consent process to ensure that adequate compensation for research related injuries has been provided for and this fact is informed to the trial participant. However, as seen in our study,[15] although the ECs insisted on submission of a compensation plan for research participants, due to paucity of time and lack of competence or expertise, very few members actually went through the documents for appropriateness and felt that it was the responsibility of the legal person in the EC to oversee all legal issues related to clinical trials. In view of the increasing burden on the ECs to ensure that compensation is paid to the participant, the EC members must be trained to review this process carefully.

Insurance

Clinical Trial Insurance (CTI) is another important issue in clinical research. Health insurance in India is still in its nascent stages with only 2% of the country's 1.2 billion population covered by the same, indicating that awareness about the advantages of having an insurance cover to protect against medical emergencies is yet to penetrate the minds of the lay public.[28] An irony is that unlike general health insurance schemes wherein an individual insures him/herself and/or his family members against unforeseen medical risks and so decides the amount of insurance cover and thus premium to be paid, in case of clinical trials, it is the Sponsor who takes this decision. The insurance amount and annual premium to be paid depends upon a number of things, including the size of the trial being conducted, trial phase, degree of risk and potential untoward adverse events envisaged, financial strength of the company conducting the trial, type of drug or device to be tested, and demographic profile of the group on which the trial will be conducted. The patient who is one of the benefactors of the scheme may be unaware of the fact that he/she has been insured against adverse events occurring in the trial and the details of what is covered in the insurance in order to claim the same if required, although the informed consent document is expected to cover this aspect clearly.[29]

What to compensate for?

The CDSCO draft rules[17] on compensation now state that compensation should be provided in case of research injury or death due to:

- Adverse effects of the investigational product/s.
- Departure from approved protocol, scientific misconduct or negligence by the Investigator/Sponsor/CRO.
- Failure of an investigational product to provide intended therapeutic effect.
- Administration of placebo providing no therapeutic benefits.
- Adverse effects due to concomitant medications.
- Compensation be paid to a child injured *in utero* through the participation of the parent in a clinical trial.

Some of these points need further clarification as discussed later.

How much to compensate?

The moot question is how to quantify harm and leading from that how much to compensate? The DCGI draft rules on compensation for research related injuries mention that

the quantum of compensation to be paid is to be decided by the EC within 30 days of the matter being referred to it. In case no formal claims are made by the trial subject, then the EC should review the SAE and recommend the amount of compensation. In case of any dispute or differences between the parties then the decision of the EC is final. Thus, the final responsibility lies with the EC. The recent draft guidance document released by the DCGI office[18] describing calculation of the quantum of financial compensation to be paid in case of clinical trial related injury or death by Ethics Committees has listed certain parameters that need to be considered. These parameters are:

a. Age of the deceased
b. Income of the deceased
c. Seriousness and severity of the disease, the subject was suffering at the time of his/her participation into the trial and
d. Percentage of permanent disability.

A formula has been given to determine the amount of compensation in case of trial related death i.e., $C^1 = A \times B\ (1 - F/100)$ wherein 'A' reflects the income of the deceased/injured per month from which a deduction (50 % in case of death and 40% in case of injury) should be made in regard to the amount which the deceased would have spent on himself by way of personal and living expenses. The balance, which is considered to be the contribution to the dependent family, constitutes 'A'. Multiplier 'B' depends on the age of the deceased and period of his/her active career. A table of multipliers (Annexure 1) has been provided from which an appropriate multiplier should be selected with reference to the age of the deceased.

In case of healthy participants, the actual calculation of the compensation amount would be $C = (A \times B)$. In case of diseased subjects/patients, C1 would be the compensation amount which would be a fraction of the amount arrived as 'C' depending on seriousness and severity of the disease. The disease seriousness and severity will be determined on a scale of 0 to 100 with 0 representing no risk (i.e., healthy volunteers) and 100 representing fatality. 'F' is the risk factor of the trial participant which should be assessed by the Study Investigator study from the above mentioned scale of 0 to 100. For the purpose of calculation of the compensation, 'F' should not be more than 50. Thus, the amount of compensation to be paid in such cases shall be arrived by using the formula: $C^1 = A \times B\ (1 - F/100)$

In case of trial related injuries, the amount of compensation to be paid shall be determined by the formula $C^2 = A \times B\ (1 - F/100) \times D/100$ wherein 'D' is the percentage disability caused to the participant due to the clinical trial.

However there are some aspects that may need discussion and clarification, e.g. there is no definition of the term 'percentage disability' and how is the EC to calculate the same? Additionally, the document mentions that research injury can be physical or psychological/emotional, but does not describe how to quantify psychological/emotional injuries? Also, the 'multiplicand method' may work for those with permanent salaried jobs. However what about those without a fixed source of income for example; students, housemaids, daily wage workers etc.; how is the EC expected to calculate their monthly incomes?

Challenges

Several challenges have been identified and are being discussed in the Government regarding these draft rules, for example:

Determining causality/relatedness of adverse events

At the root of the compensation issue is determining "relatedness" to the clinical trial. This is a technical process where factors such as temporal association of the adverse event, time-course relationship, co-morbid diseases/disorders; concomitant medications, de-challenge and re-challenge, expected or known adverse events (as per the Investigator Brochure) need to be considered. Causality is relatively simpler to determine in case of Phase I studies wherein young healthy volunteers are the participants as they are not generally on any other medications. However in case of Phase II/III studies, where the participants are patients, other factors like co-morbid disease conditions and/or concomitant medications can make causality determination extremely difficult. Most patients are frequently prescribed multiple drugs, most of which are standard or routine treatment which they would take regardless of whether they are research participants or not. Adverse events occurring due to the other concomitant medications are thus common and are in no way related to the research itself. Having to compensate for injuries resulting from these concomitant medications is illogical.[8,30-32]

Also the guidelines clearly mention trial related injury thus not limiting the causality to the study drug. Proving relatedness to the study can be even more challenging.

In general it is understood that the Investigator determines causality and if related to the study drug, this is verified by the sponsor. Are ECs also expected to verify causality or accept what is written by the investigator? This is a matter deserving some clarification and will also bring into focus the increased need for training of ECs.

Undue inducement

One of the requirements in the rule is that the compensation clause should be clearly described and explained in the ICD.

Will the promise of mandatory compensation impair the rational decision-making process taken by the patient or his/her surrogate to participate in a research study? Patients (or their surrogates), especially those with severe life threatening illness (e.g., advanced cancer, myocardial infarction, stroke, septic shock), may consent to participate in a trial with high risk of complications knowing that compensation will always be available.

Further, it has been cogently argued that insisting on the compensation clause may act as a deterrent to undertaking non-industry sponsored academic research as making such provisions may be beyond the means of individual investigators, academic groups of investigators and many academic institutes. Several authors have stated that "this can kill the research spirit especially for interventional research studies as such studies will be very expensive making it virtually impossible to conduct in academic settings".[8,30-32]

Training of ethics committee members

The revised compensation guidelines has put a huge responsibility on Ethics Committees by giving them the duty of determining the degree of risk and then calculating the compensation amount to be paid for research related injuries including death, with the decision of the EC being considered as final. Thus, the final responsibility has been left to the wisdom of the individual ECs, who are expected to take appropriate decisions depending upon local conditions. However, given the composition of Ethics Committees, it is unlikely that the EC members presently have the necessary expertise or experience to determine the exact quantum of compensation or whether fair compensation was paid and intensive training of EC members will be needed to ensure consistency in the process.

Other clauses in the CDSCO draft rules on compensation that need urgent discussion and clarification are the points that trial subjects should be compensated for (1) Failure of an investigational product to provide its intended therapeutic effect and (2) Administration of placebo providing no therapeutic benefits. With all drugs, whether used in a clinical trial or for therapy, there will be some patients who do not benefit. So it is entirely possible that, in a trial, many people in the investigational arm may not show therapeutic benefit and this is to be expected. If however compensation were to be paid in such cases, by extension, any patient who failed therapy with a licensed drug could also be considered entitled to compensation. Similarly, placebos are frequently used in clinical research where no effective alternative treatment exists primarily to avoid bias in interpreting the effects of the investigational drug. The placebo is not expected to provide therapeutic benefit though on occasion it has shown to do so. Compensation being provided to patients because the placebo does not have a therapeutic effect also raised challenges.[8,30-32]

Another issue that the CDSCO draft rules raises is the delivery of compensation. One of the clauses states that 'in case of death, the legal heir/s are entitled to financial or material compensation and it is the Investigator's responsibility to inform the trial subject and his/her heirs regarding their right to claim compensation'. In the absence of a will or clear legal-heir documentation, how should the Investigator/Sponsor/Ethics Committee decide on the beneficiary? Does that mean that every potential trial participant should specify his/her beneficiary for compensation prior to participating in the study and that every Investigator should ensure that this is done in order to avoid legal hassles later on?

International scenario

United States of America

In the USA, it is not mandatory by law for sponsors and Institutions to provide either free medical care or compensation for research related injuries to trial participants, apart from general tort law principles that apply to everyone.[33-35] Thus, if a research subject is seriously injured; neither the Investigator nor the sponsor has any legal obligation to pay for that subject's medical care. In fact, only 16% of academic medical centers in the United States make it a policy to pay for the care of injured subjects. If a subject is permanently disabled and unable to work, sponsors have no obligation to pay compensation for his or her lost income. Even in case of death of a trial subject, sponsors have no financial obligations. Additionally, various legal doctrines exclude some types of trial subjects from the tort system entirely; *viz.*, international subjects and subjects in federally sponsored studies. Thus, in the context of clinical trials, tort litigation is an unworthy candidate as compensation is contingent upon the proof of fault. In fact, recent legal developments and a transformation in the global research landscape have made continuation with the tort system for compensating research injury victims morally indefensible and practically unsustainable. Although several attempts have been made over the last 40 years by the various National Advisory Commissions to change the system to the no-fault compensation scheme, including the latest effort in late 2011, wherein the Presidential Commission for the Study of Bioethical Issues released a report titled *Moral Science: Protecting Participants in Human Subjects Research,* their recommendations for change however have largely been ignored.[19]

European Union (EU)

Many European countries mandate the provision of clinical trials insurance, through which subjects are

often covered regardless of fault. The European Union Clinical Trials Directive, now transposed into National law through the Medicines for Human Use (Clinical Trials) Regulations 2004 has legally defined responsibilities on those commissioning and carrying out drugs trials as well as the responsibilities of the Ethics Committees and the Medicines and Healthcare Products Regulatory Agency (MHRA). These include the need for those commissioning and conducting drug trials to have adequate insurance should the trial go wrong. Countries, such as France, Germany and Spain, have compulsory insurance laws with variations in the specifics and minimum coverage required. In fact, aware of the need for a legal framework to protect those involved in biomedical research led the French Parliament to pass a law for the "Protection of Persons Undergoing Biomedical" Research commonly known as the Huriet Law. This law makes the sponsor financially responsible to research participants for adverse events occurring during clinical trials through mandatory insurance coverage. Scandinavian countries like Sweden, Finland, Denmark and Norway favor a no-fault principle in dealing with medical injuries, relying on insurance rather than litigation.[15]

United Kingdom (UK)

The Association of the British Pharmaceutical Industry (ABPI) guidelines on compensation for trial related injuries also recommend that subjects suffering from research related injuries be compensated on a 'no fault' basis although clinical trials insurance was not mandatory in the United Kingdom.[36] Recently however, the ABPI, BioIndustry Association (BIA) and the Clinical Contract Research Association (CCRA) in conjunction with the UK Department of Health (DoH) and the National Research Ethics Services (NRES) have jointly published guidance on insurance and compensation for Phase I clinical trials in the UK. The document sets the standard of insurance cover required to protect volunteers which will cover them both for injury compensation as well as legal expenses. Currently, these guidelines apply only for Phase I studies however the Government has indicated that further advice would be issued soon.[37,38]

These ABPI guidelines have been modified and adopted by many other countries such as South Africa, Australia and New Zealand. Unfortunately, these guidelines clearly state that there is "no legal commitment" to pay compensation for research related injuries thus not adequately protecting research participants.[15] These Guidelines however do not apply to clinical trials that have not been initiated or directly sponsored by or on behalf of the Pharmaceutical companies providing the product/s for research, so that academic studies have been kept out of their oversight.

South East Asian countries

In China, drug and device-related injuries are perceived to be caused by counterfeit or inferior drug or device products, or by adverse drug or device reactions. Article 93 of the Drug Administration Law specifically provides for compensation for any injury to a drug user caused by a violation of this Law by a drug manufacturer, distributor or healthcare institution while Article 22 of the General Principles of the Civil Law and Chapter 4 of the Product Quality Law provide for compensation caused by defective products. Chinese law does not employ a strict "no-fault" approach to determination of the liability of the manufacturer or distributor in drug and device-related injuries. In practice, the manufacturer or distributor is only liable for injuries caused by "defective" products. If a national or industry standard for a specific product exists, compliance with the standard will render the product not defective. The current legal regime provides certain protection only to those patients injured by counterfeit or inferior drug or device products. In case of approved drugs, if the drug causing the injury was approved by the State Food and Drug Administration of China (SFDA) and conformed to the national or industry standard (if any), by statutory definition it is not defective. Therefore, injured patients are normally not entitled to any compensation. In most cases where the Courts have ordered compensation for injury, the compensation amount is quite small. The patient is only entitled to recovery of the actual loss he suffered from the injury (*Article 44, Product Quality Law*), which is basically limited to the direct loss, and Chinese laws and judicial interpretations have established a fairly clear and rigid method for calculation of the direct loss.[39]

Other countries like Japan,[40] Malaysia,[41] Singapore, Phillipines, Indonesia and Thailand[42,43] do mention that they follow GCP guidelines for clinical research adapted from the ICH-GCP guidelines. These guidelines do recommend that the ICD mention the issue of compensation for research related injuries however whether this is implemented or not is not discernable.

CONCLUSION

While we need to applaud the good intentions behind the efforts of the Indian Government to introduce regulations to protect research participants and compensate them for involuntary harm, it is important to take into consideration the economic, cultural, social and political practices of the community in which these are to be implemented rather than just enforcing laws that may be detrimental to academic research and therapeutic progress. Further

all stakeholders *viz.* Investigators, Ethics Committee members and Sponsors need to understand their responsibilities towards patient protection against research related injuries while Regulators need to take into consideration the apprehensions of the other stakeholders and remove ambiguities in the current guidelines in order to ensure that these are effectively implemented. Patients too need to be educated about compensation to avoid it becoming an undue inducement.

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