EXPRESS Pharma

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Sharing accountability for SAEs

__Manisha Singh__, Senior Associate, and __Riku Sarma__, Partner, Corporate Law Group explain the responsible way to handle issues related to compensation in case of untoward medical occurrences during clinical trials

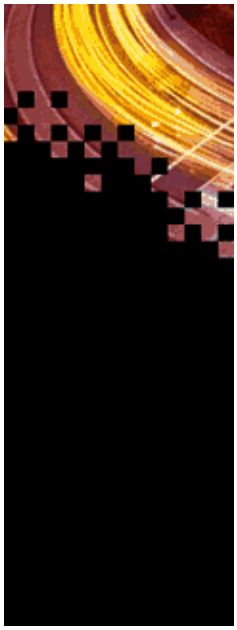
We all know that a clinical trial (CT) is a systematic study of any drug in order to generate data for discovering or verifying clinical, pharmacological or adverse effects of that drug with the objective of determining its safety and efficacy. In India, CTs are regulated by Schedule Y of the Drugs and Cosmetics Rules (DCR), 1945. The rules are enforced by the office of the Drug Controller General of India (DCGI) who is also responsible for monitoring all CTs submitted to his office for approval.

The CT sponsors are responsible for ensuring that the CTs are conducted in compliance with the Good Clinical Practices (GCP) Guidelines issues by the Central Drug Standard Control Organisation (CDSCO), Director General Health Services (DGHS) or other statutory requirements. The first Indian GCP was formulated around the same time with the amendment of DCR in 2005 and had considered WHO, ICH, US FDA, European GCP guidelines as well as the ICMR Ethical Guidelines for Biomedical Research on Human Participants (ICMR Ethical Guidelines) applicable at that time. Though the investigators are not regulated under the rules, they are, however, required to conduct the CTs as per the ethical guidelines laid down by the ICMR and this has been specifically prescribed in the MCI Code of Ethics, 2002.

Till January 2005, CTs of new drugs being developed outside India were permitted only with a "phase lag"—a phase II trial could be conducted in India only after phase III trials were completed elsewhere. Phase I trials of foreign drugs were not permitted, except for drugs of special relevance to India. As of January 2005, an amendment of Schedule Y of the DCR did away with the phase I in international CTs conducted by foreign sponsors.

Recent debate on CTs in India

Post 2005 amendment of the DCR, there has been a quantum leap in the number of CTs being conducted in India. Time and again concerns have been raised about lack of clear laws and guidelines to effectively monitor CTs and to fix clear liabilities on the sponsors. These concerns were further intensified recently with a number of Parliamentary questions being asked on CTs, particularly those related to causality and compensation issues in



case of trial related serious adverse events (SAE).

SAE in drug trials involving human participants is any untoward medical occurrence during treatment with a pharmaceutical product in a patient or a human volunteer that is associated with death, inpatient hospitalisation, prolongation of hospitalisation (in case the study was being conducted on in-patients), persistent or significant disability or incapacity, a congenital anomaly or birth defect, or is otherwise life threatening. SAE does not necessarily have a relationship with the treatment being given.

CDSCO draft guidance on reporting SAEs

On May 12, 2011, the CDSCO came up with a nine page draft guidance on reporting SAEs in case of CTs to achieve uniformity and completeness of data filed by different companies and Clinical Research Organisations (CROs) for SAE reporting in CTs. Annexure I to the draft guidance specifies the data elements for reporting SAE in CTs within 14 calendar days.

On causality, while the draft guidance requires the investigator and the medical monitor of sponsor /CRO to clearly mention whether the SAE occurred is related or not related and prohibits usage of situations like unlikely, possibly, suspected, doubtful etc., it is silent as to who would be the final arbiter in the event there is a difference of opinion between the investigator and the medical monitor of the sponsor/CRO.

With regard to compensation, the draft guidance requires furnishing of details about compensations provided for injury or death. In case no compensation has been paid, reason for the same is required to be submitted. The draft guidance specifically requires for complete medical care as well as compensation in case of study related deaths or injury. There are, however, a number of outstanding issues on compensation and the most obvious being as to who will determine the monetary compensation amount and on what principle will the adequate compensation be determined.

The recent controversies in CTs have made the Government realise that the current applicable guidelines may be inadequate to protect the interest of CT subjects in the event of SAEs. The Government, therefore, is taking a step in the right direction to streamline and harmonise SAE reporting in all CTs as it clarifies to some extent the sponsor/CRO responsibilities towards ensuring complete medical care as well as compensation for the trial related injury or death.

Outstanding issues

Going forward, it is imperative for the Government to delve on the above outstanding issues to ensure that there is clarity enabling the sponsors to immediately recompense and provide rehabilitative measures to subjects who suffer a trial related injury or to the dependents of the subjects who suffer trial related death. This becomes all the more important because any lack of uniformity and consistency in awarding compensation in CT related deaths or injury would be a matter of grave concern. Divergent and inconsistent determination of the quantum of compensation by various ethics committees across India under similar circumstances will lead to dissatisfaction and distrust in the system. It is therefore necessary that a method of working out 'just' compensation should be developed for CT related deaths and injuries which would introduce reasonable certainty and uniformity in the matter of determination of compensation

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In Sarla Verma vs DTC, (2009) 6 SCC 121, the Honourable Supreme Court has observed that "Assessment of compensation though involving certain hypothetical considerations, should nevertheless be objective. Justice and justness emanate from equality in treatment, consistency and thoroughness in adjudication, and fairness and uniformity in the decision-making process and the decisions. While it may not be possible to have mathematical precision or identical awards in assessing compensation, same or similar facts should lead to awards in the same range. When the factors/inputs are the same, and the formula/legal principles are the same, consistency and uniformity, and not divergence and freakiness, should be the result of adjudication to arrive at just compensation."

For the purpose of ensuring appropriate monetary compensation, a pre-determined formula may be applied across the country. The concept of predetermined formula for calculation compensation is not new under Indian jurisprudence. Existing laws on the issue of liability and personal injuries have laid down a comprehensive guide for computation of compensation in cases of accidents causing injuries to deaths of the victims such as the Motor Vehicles Act, 1988. One such principle is the multiplier method is the one provided under the motor accident cases and which is applied in other personal injury and liability cases where the law on compensation has not been codified. The Honourable Supreme Court has consistently held in various cases that multiplier method is logically sound and legally well-established method of ensuring a just compensation which will make for uniformity and certainty of awards.

While the Government is considering developing appropriate guidelines/rules/regulation to streamline and regulate CTs in India, it may consider development of a pre-determined formula for compensation in cases of CT related deaths and/or injuries on the lines of the Motor Vehicles Act and the Supreme Court judgments on compensation. Apart from determinants like the age of the deceased, age of claimants; life expectancy; marital status, education and employment of the claimants; loss of pecuniary benefits, some additional determinants for a formula in case of CTs could be the medical history; seriousness of the disease being treated, the degree of probability that adverse reactions will occur and any warnings given and the availability

and relative efficacy of alternative treatments that the patient could have had if he had not volunteered for the trial. Such a mechanism will help develop a fair, transparent and expeditious method for determination of compensation which is both predictable and easy to implement for all parties concerned particularly for the subjects which the guidelines seek to protect.

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