GOVERNMENT OF INDIA
HEALTH AND FAMILY WELFARE
LOK SABHA

UNSTARRED QUESTION NO:3291
ANSWERED ON:30.08.2013
NOTIFICATION ON CLINICAL TRIALS
Panda Shri Baijayant

Will the Minister of HEALTH AND FAMILY WELFARE be pleased to state:

(a) whether the Government had amended the Drugs and Cosmetics Rules, 1945 recently through a notification regarding grant of compensation in cases of injury or death during the clinical trials and the procedures for review of the serious adverse events in the country;

(b) if so, the details thereof;

(c) whether the Drugs Technical Advisory Board (DTAB) has also recently recommended certain changes in the said notification; and

(d) if so, the details thereof and the reasons therefor?

Answer

THE MINISTER OF HEATH AND FAMILY WELFARE (SHRI GHULAM NABI AZAD)

(a) & (b): Yes. Drugs and Cosmetics Rules, 1945 have been amended vide G.S.R. 53(E) dated 30-01-2013 specifying procedures to analyze the reports of Serious Adverse Events occurring during clinical trials and procedures for payment of compensation in case of trial related injury or death as per prescribed timelines as under: (i)Insertion of a new Rule 122 DAB relating to compensation in case of injury or death during clinical trials.

(a)As per the Rule in the event of injury of the trial subject, he /she shall be provided free medical management by the sponsor or his representative as long as required.

(b)In the event of injury or death due to following reasons which are considered as clinical trial related injury or death, the sponsor or his representative shall provide financial compensation for the injury or death.

1.Adverse effect of investigational product(s);

2.Violation of the approved protocol, scientific misconduct or negligence by the sponsor or his representative or the investigator;

3.Failure of investigational product to provide intended therapeutic effect;

4.Use of placebo in a placebo-controlled trial;

5.Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;

6.For injury to a child in−utero because of the participation of parent in clinical trial;

7.Any clinical trial procedures involved in the study.

(ii) Serious Adverse Events (SAEs) including deaths are reported, analyzed within the prescribed timelines and in case of clinical trial related injury or death compensation are paid as per the prescribed procedures.

(iii) Insertion of definition of Serious Adverse Events (SAEs) and detailed procedures for reporting and examination of such events, in Schedule 'Y'.

(iv) The check list for study subject's informed consent documents has been amended to include statements describing that in the event of injury of the trial subject, he /she shall be provided free medical management as long as required and in the event of clinical trial related injury or death, the sponsor or his representative shall provide financial compensation for the injury or death.

(v) The Format of Informed Consent Form for clinical trial subjects has been amended to capture the information relating to address, qualification, occupation, annual income of the subject and name & address of his nominee (for the purpose of compensation in case of trial related death). It has also been made mandatory for the Investigator to hand over a copy of the patient information sheet and duly filled Informed Consent Form to the subject or his/her attendant.

(vi) Insertion of a separate Appendix XII related to compensation in case of injury or death during clinical trials in Schedule 'Y'. The Appendix prescribes the detailed procedures for examination of Serious Adverse Event (SAE) reports including deaths and payment of financial compensation in case of trial related injury or death as per the prescribed timelines.

As per the procedures:

(a) Investigator shall report all Serious Adverse Events (SAEs) to the DCG (I), sponsor or his representative and the Ethics Committee within 24 hours of their occurrence.

(b) In case of death, an independent Expert Committee constituted by DCG (I) shall examine the case and give recommendations to DCG (I) to determine the cause of death and also to decide the quantum of compensation, in case of clinical trial related death. The Expert Committee, while examining the event may take into consideration, the reports of the Investigator, the sponsor or his representative and the Ethics Committee. DCG (I) after considering the recommendations of the Expert Committee, shall determine the cause of death and decide quantum of compensation to be paid by the sponsor or his representative in case of trial related deaths within three months of receiving the report of SAE of death.

c) In case of Serious Adverse Events (SAEs) other than death, the DCG (I), after considering the reports of the Investigator, the sponsor and the Ethics Committee, shall determine the cause of injury and also decide the quantum of compensation to be paid by the sponsor or his representative in case of clinical trial related injury within three months of receiving the report. However, DCG (I) has option to constitute independent Expert Committee to examine such Adverse Events.

(c) & (d): In view of the representations received from various stakeholders, the Drugs Technical Advisory Board (DTAB) recommended certain amendments in the said notification. The salient recommendations are as under:

(1) Free medical management

As per the clause (1) of rule 122 DAB, in the case of an injury occurring to the clinical trial subject, he or she shall be given free medical management as long as required.

The DTAB therefore recommended that the clause may be amended to read as under: 'In the case of clinical trial related injury to a subject occurring during the clinical trial, he or she shall be given free medical management as long as required'.

(2) Financial compensation in case of an injury

In the clause (2) of Rule 122 DAB, it has been provided that in case the injury occurring to the trial subject is related to the clinical trial, he or she shall also receive financial compensation as per order of the licensing authority defined under Rule 21(b). The financial compensation will be over and above any expense incurred on the medical management of the subject.

The DTAB recommended that a qualifying clause may be further added in the sub-rule that 'in case there is no permanent injury, the quantum of compensation shall commensurate with the inconvenience, loss of wages, transportation'.

(3) Entitlement for financial compensation

Sub-rule (5) of Rule 122 DAB provides the causes when injury and death would be considered as clinical trial related injury or death and entitlement for financial compensation.

(i) Clause (c) relating to providing financial compensation in the case of injury or death due to failure of investigational product to provide intended therapeutic effect may be deleted as there is always a possibility that the investigational product may fail to provide intended therapeutic effect and the trial is conducted with the objective of assessing the therapeutic effect of the drug along with safety.

(ii) In the clause (d) relating to the use of placebo in a placebo- controlled trial, DTAB recommended that the said clause may be modified to read as under: "Use of placebo in a placebo-controlled trial if the standard care is denied".

(4) The requirement of sponsor and investigator to report Serious Adverse Events of death to the Chairman of the Expert Committee constituted by the Licensing Authority under APPENDIX XII may be deleted wherever it occurs in the notification. The report will be forwarded to the expert committee, so constituted, by the office of DCG (I).

(5) DTAB, in respect of timelines to be followed by various agencies in reporting of the serious adverse events as well as recommendations by the Expert Committees and the decisions taken by the office of DCG (I) have recommended as under:

(i) The requirements of sponsor and investigator to report the Serious Adverse Events after due analysis in 10 days may be changed to 14 days, as per International practice.

(ii) The timelines to be followed by the Ethics Committees to forward the reports of Serious Adverse Events after due analysis along with their opinion on quantum of compensation (in case of related deaths), within 21 day may be changed to 30 days.

(iii) The time lines for Independent Expert Committee to examine the Serious Adverse Events of death and to recommend to the DCG(I) about the cause of the death and quantum of compensation (in case of clinical trial related death) within 30 days may be changed to 60 days.

(iv) The timelines for Licensing Authority i.e. Drugs Controller General (India) to determine the cause of the injury or death and decide the quantum of compensation to be paid may be amended to read as two months after receiving the report of the Expert Committee.

(6) The requirements of investigator to report all serious and unexpected adverse events whereas the sponsor is required to report all serious adverse events should be harmonized to make provision that both investigator and sponsor are required to report all serious adverse events.