Original Research Paper

Compensation Issue in Clinical Trials Recent Indian Scenario

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Abstract

Hon'ble Supreme Court has shown its concern for protection of human rights of those who were the research participants for clinical trials and suffered either death or serious adverse events. These research participants had not given adequate compensation or no compensation at all. A Public Interest Litigation (PIL) has been filed in the Supreme Court of India in the year 2012 by a NGO, consequently a committee has been constituted by the Ministry of Health and family Welfare, government of India to look into the matter of compensation.

Recently a formula to determine the quantum of compensation in the cases of clinical trial related Serious Adverse Events (SAEs) including deaths occurring during clinical trials have been evolved by a committee formed under the Drugs and Cosmetics Rules.

This research paper deals with critical issue of compensation in clinical trial related SEAs including deaths of the research participants and initiative taken by the concern authorities including the directions given by the Supreme Court of India from time to time and provisions in the Drugs and Cosmetics (Amendment) Bill, 2013.

Key Words: Serious Adverse Events, Clinical Trial, Compensation, Drug and Cosmetic Act

Introduction:

As per the information provided by the Union Government of India in the Supreme Court as many as 2644 research participants, died during the clinical trials. [1]

Out of which 80 deaths were found to be attributable to the clinical trials. Clinical trials of 475 new drugs were conducted and only 17 drugs were approved for marketing in India from January 1, 2005 to June 30, 2012.

Clinical trial of two drugs-Bayer's Rivaroxaban and Novartis's Aliskiren vs. Enalapril accounted for maximum number of deaths. Bayer's Rivaroxaban was first used for human trials in 2008 resulting in death of 21 of which it claimed that only five were related to clinical trial but it has till date paid compensation to kin of only two.

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Two years later, the same drug was again put on clinical trial and this time 125 deaths were reported, of which it was stated that five were related to clinical trial.

The Union Health Secretary stressed the importance of clinical trials of new drugs on humans. It was claimed that during the last 40 years, about 900 drug molecules of different therapeutic categories have been approved for marketing in India. Out of these 900, only seven drug molecules have been discovered and approved in India.

Rest of them are discovered and developed in other countries like US, EU, Japan after going through complex process of research and drug development including clinical trial in human beings.

Novartis used the investigational product listed as Aliskiren vs. Enalapril last year and it resulted in death of 47 of which only one has been attributed to clinical trial of the new drug.

Only another clinical trial of new drug on humans, Sun Pharma's Paclitaxel injection concentrate for nano-dispersion, registered a double-digit death figure (12) during the last seven years.

Majority of the pharmaceutical companies, whose drugs were permitted for clinical trial on human beings, were of foreign origin. Allegations have been made by NGO,

Swasthya Adhikar Manch, in its PIL that Indians were used as guinea pigs by foreign pharmaceutical majors for human trial of their new drugs, it claims that of the 57303 enrolled subjects, and 39022 completed the clinical trials. [1] SC in its order dated 6th March 2013 observed that it transpires from the record produced before the court that for these subjects neither any compensation has been provided nor paid. [2]

Historical Background:

The first International Statement on the ethics of medical research using human subjects namely, the Nuremberg Code was formulated in 1947. In 1948, Universal Declaration of Human Rights (adopted by the General Assembly of the United Nations on 10th December) expressed concern about rights of human beings being subjected to involuntary maltreatment.

In 1964 at Helsinki, the World Medical Association formulated general principles and specific guidelines on use of human subjects in medical research, known as the Helsinki Declaration which was recently amended in 2008 Sixth revision, 59th Meeting at Seoul.

In 1966, the International Covenant on Civil and Political Rights specifically stated, 'No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his consent to medical or scientific treatment.

In February 1980, the Indian Council of Medical Research released a 'Policy Statement on Ethical Considerations involved in Research on Human Subjects' for the benefit of all those involved in clinical research in India, which were amended in 2000 and recently in 2006. [3]

Recent Developments related to clinical trials:

The Union Secretary for Health & Family Welfare promised to the Supreme Court for stringent regime on clinical trials on the recommendations of the Parliamentary Standing Committee, which faulted the Drugs and Cosmetics (Amendment) Bill, 2007.

On the advice of the Ministry of Law, the Health Ministry had withdrawn the 2007 Bill and introduce a new the Drugs and Cosmetic (Amendment) Bill, 2013 in the Parliament on 29.8.2013.

The Bill has a separate chapter containing penal provisions for violation and non-compliance of the provisions relating to the conduct of the clinical trials and strict penal provisions relating to payment of compensation, Ethics Committee etc. [Para 5, 6; Order dated 26.07.2013] [2]

Provisions regarding Compensation for Clinical Trials in the New Bill, 2013: [4]

Chapter IIB has been inserted to cover the provisions related to mechanism for award of compensation in clinical trials if, serious adverse events happens. The important provisions related to following aspects:

- No clinical trial without permission
- Medical treatment and compensation for injury due to clinical trial
- Deferment of clinical data requirements by the Central Licensing Authority
- Registration of Ethics Committee
- Composition of Ethics Committee
- Functions and responsibilities of Ethics Committee
- Penalty for conducting clinical trial of cosmetics without permission
- Penalty for violation of conditions of permission
- Penalty for repeat offences
- Penalty for failure to provide compensation
- Penalty for contravention of any provision of this chapter
- Confiscation of stock, etc
- Cognizance of offences
- Powers of Central Government to make rules

Research Ethics and Professional Misconduct:

Clinical drug trials or other research involving patients or volunteers as per the guidelines of ICMR can be undertaken, provided ethical considerations are borne in mind.

Violation of existing ICMR guidelines in this regard shall constitute misconduct. Consent taken from the patient for trial of drug or therapy which is not as per the guidelines shall also be construed as misconduct. [5]

Role of MCI in Preventing Clinical Trial Related Professional Misconduct:

A complaint has been filed against Indore Clinical Trials conducted by doctors violating minimum ethical standards by Swasthya Adhikar Manch, Indore (M.P) and Smt.Brinda Karat, Member, Polit Bureau, CPI (M), Former Member, Rajya Sabha. [6]

Illustration 1: [6]

The Ethics Committee of MCI at its meeting held on 14.2.2012 noted and directed the Council to enquire from Drug Controller of India (DCG (I), Indian Council of Medical Research (ICMR), & Madhya Pradesh Medical

Council to know the action taken on the outcome of their enquiries.

In this regard, as per the report dated: 7.3.2012 received from Dr.V.M. Katoch, Director General, ICMR, New Delhi, he stated that the Role of ICMR is in capacity building, setting up various guidelines and standards for conducting Clinical Trials properly.

The DCG (I) and Medical Council of India may initiate action for proper enquiry. Accordingly, a letter was sent to DCG (I) with a request to inform the status of the enquiry, if any, initiated. The DCG (I) in its letter dt.15.5.2012 informed that CDSCO team constituted has carried out inquiry of various trials and the report is as under:

"I) 11 trials from January, 2008 to October, 2010 sponsored by:

1. M/s Cadila Healthcare Ltd., Ahmedabad;
2. M/s Emcure Pharmaceuticals, Pune &
3. M/s Intas Pharmaceuticals, Ahmedabad conducted by Psychiatrist of MGM Medical College at their private clinics with necessary permission DCG (I), involved 241 patients participation under following five Principal investigators:

Allegations:

1. The said department did not inform the concerned college authorities and did not submit ethical clearance from competent authorities attached to the college.
2. Dr.Raghulam Razdan & Dr.Pali Rastogi did not maintain any source data for trials conducted for Intas Pharmaceuticals and Cadila Healthcare which is contrary to **Drugs & Cosmetics Acts & Rules under Appendix VII of Schedule Y.**
3. Emcure Pharmaceutical did not monitor trial properly (for instance the Lab. finding value for the test on screening day & the last visit were exactly identical for 4 subjects of DAPOXITINE trial conducted by Dr.Abey Paliwal & transcription error of data from source by Dr.Ujjwal Sardesai.
4. The investigator site of Dr.Raghulam Razdan sponsored by Cadila Healthcare (subject code 011 male 39 years) shows 1st site visit on 7.3.2009 whereas the consent form of the subject patient is dt.9.3.2009. In another subject code No.34 female 42 years shows 1st site visit on 7.4.2009 and the **informed consent** is on 30.6.2009.
5. Dr.Raghulam Razdan in his study of efficacy/safety of fixed dose of PARAXETINE Hcl and CLONAZEPAM in comparison PARAXETINE reported adverse event as erectile dysfunction in subject No.27 female 45 which is not practical.
6. The report examined by CDSCO (HQ) observed that there were many discrepancies in respect of the clinical trials conducted by Dr.Raghulam Razdan for Cadila & Dr.Abhey Paliwal and Dr.Ujjwal Sardesai for Emcure.

Show Cause and Warning Notices Issued by the CDSCO:

Show cause notices were issued to the alleged doctors by CDSCO. CDSCO observed that there had been certain irregularities in conduct of clinical trials which were not in accordance with the Good Clinical Practices (GCP) guidelines for clinical research in India.

In view of the above, the said pharmaceutical firms and the investigating doctors have been issued warning by CDSCO vide letter dated: 2.5.2012 to be careful while conducting trials so as to ensure strict compliance of GCP guidelines and applicable regulations.

Illustration II: [6] Regulatory Authorities stopped clinical trial:

News report quoting use of drug TADALAFIL in Pulmonary Arterial Hypertension (PAH) trial conducted by Dr.Anil Bharani & Dr.Ashish Patel was investigated by the M.P. State Drug Controller Authority & CDSCO (WZ) on 10.8.2011. They found that the said trial was conducted without permission from DCG (I) and also the drug was not approved by DCG (I) for the said indication at the time of initiation of the trial (18.9.2005).

The said Regulatory Authorities directed the investigators to stop the trial and also restrict them to conduct any clinical trial for a period of six months. [Para II of Report] [6]

Illustration III: [6]

Report on Clinical Trial conducted by Dr.Hemant Jain at Chacha Nehru Hospital, Indore by the investigating team comprising DDC(I), West Zone, Drug Inspector & Experts constituted by CDSCO on 16-20 April revealed that out of the 26 clinical trials conducted after due permission of DCG(I), between 2006-2010, there were some irregularities in 23 trails.

The main findings in all the said 23 trials were **that the quorum of the Ethics Committee (MGM Medical College and M Y Hospital that reviewed & accorded approvals of the trials protocols) were not as per requirement of schedule 'Y' to Drugs & Cosmetic Rule as no lay person/legal expert were present in the meetings of the Ethics Committee. [Para III of Report] [6]**

MCI Observations:

The Ethics Committee observed that ethical irregularities have been **observed in the conduct of the clinical trials done by the concerned doctors** on the basis of the investigation report with supportive documents from the **Drug Controller of India** and action taken report from the **Madhya Pradesh State Medical Council** and **State Health Authorities** in the above cases. [6]

Therefore, the eight doctors were called for hearing with all supporting documents in the meeting scheduled subsequently. The committee also decided that the concerned doctors be sent all relevant papers so that they can attend the meeting with a written reply.

Media Highlighted the Issue of Clinical Trial: [7-12]

One of the media news highlighted the role played by politicians and different stakeholders in following words: "Brajesh Pathak, BSP's Rajya Sabha Member and Congress MP from Rajsthan, Jyoti Mirdha Gehlawat, daughter-in-law of former Haryana Minister Krishna Gehlawat are remembered for exposing corrupt and malpractices in medical profession."

It further reported that Jyoti Mirdha has taken up the issue of freebies to doctors by pharmacy companies for promoting their medicines. Her complaint to Prime Minister Dr. Manmohan Singh has forced the government to frame rules and regulations to prohibit Pharma companies from giving gifts to the doctors. She raised the issue concerning medical profession in Lok Sabha receiving appreciation from the Chair and Health Minister.

This unethical practice is costing patients dearly as doctors prescribes unwanted costly medicines just to promote sale of medicines of those particular companies that give them costly gifts and sponsor their foreign jaunts.

Brajesh Pathak has created history in his capacity as Chairman of Parliamentary Standing Committee for Ministry of Health and Family Welfare. He grilled officials of Drug Controller General of India, Indian Council of Medical Research and Health Ministry during review meetings.

Pathak has exposed as how the Central Drugs Standard Control Organisation, which is supposed to ensure that licences for manufacturing of medicines are given after proper clinical trial of its use, has given licences to a number of Pharma firms including one owned by the relatives of the then Union Railways Minister Pawan Kumar Bansal without clearing clinical trials.

Pathak was shocked to find that the mission of CDSCO has become to meet the aspirations, demands and requirements of the pharmaceutical industry rather than protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs.

He also exposed the nexus of officials of CDSCO, Indian Council of Medical Research and Health Ministry for giving permission for clinical trials to NGO PATH run by the former US President Bill Clinton in utter violation of rules which resulted into death of half a dozen tribals. Pathak has accused CDSCO of saving the interests of Pharma giants instead of people. [7]

Case before the Supreme Court of India in a PIL:

SC noted that this matter alleges **malpractices in clinical trials by Government and non-Government as well as by independent investigators.** SC was of the view that for proper consideration of the matter it shall be appropriate if the Secretary, Ministry of Health and Family Welfare, Government of India and/or Central Drugs Standard Control Organisation through Director General of Health Services, Government of India, give information on the following points:

i. The number of experimental **New Clinical Entities (NCEs)** approved for clinical trials by the **Drug Controller General of India (DCGI)** from **January 1, 2005 to June 30, 2012.**
ii. Whether deaths were suffered by subjects of clinical trials. If yes, the number of deaths.
iii. Whether serious side effects were suffered by the subjects of clinical trials. If yes, the number of such subjects and the nature of side effects, and
iv. The details of compensation paid to the subjects who suffered side effects or paid to the family of the subjects who suffered death. [Order dated: 08.10.2012, R.M. Lodha, J., Anil R. Dave, J.] [2]

SC Bench **directed the Chief Secretaries of the States other than State of Madhya Pradesh, Manipur, Union Territories of Dadar &** Nagar Haveli and Daman & Diu to file their written responses related to clinical trials in their respective States and UTs.

Meeting Convened by the Ministry of Health & Family Welfare:

On 26.7.2013, it was submitted that the Secretary, Ministry of Health would convene the meeting of the Chief Secretaries/Health Secretaries of the State Governments and the

Administrators of the Union Territories to discuss all the facets and aspects concerning the legal framework for strengthening the regulation of clinical trials and other incidental matters. [2]

It was stated that on 13.8.2013, the meeting of the Chief Secretaries/Health Secretaries of the State Governments and the Administrators of the Union Territories was convened. In that meeting, diverse issues were deliberated. [Para 4] [2]

Summary of Suggestions from States & UTs:

The views expressed by the States of Madhya Pradesh, Rajasthan, West Bengal, Punjab, Andhra Pradesh, Karnataka and Gujarat, have been particularly mentioned. Based on the deliberations, the Secretary, Ministry of Health and Family Welfare summed up and made the **following observations**:

1. Even though the concerns have been raised about the conduct of clinical trials in the country, clinical trials are necessary for the development of new drugs in the country.

India has the capacity and knowhow for drug discovery research. However, there should be a robust system for conducting clinical trials in the country to ensure that trials are conducted in a scientific and ethical manner and in compliance to the regulatory provisions.

2. Restricting clinical trials to Government Hospitals alone would not provide a solution.
3. The amount of money paid by the sponsor/companies to the investigator for conduct of clinical trial may act as an inducement to the investigator for conducting clinical trials. Sometimes such inducement may lead to bias in enrolment of subjects in the trials.
4. Regulatory provisions may be made so that information relating to the amount of money paid by the companies to investigators for conduct of clinical trials is in the knowledge of the regulatory authorities.
5. There are some concerns on certain clauses of the amendment of Drugs & Cosmetics Rules made on 30.1.2013 regarding compensation in clinical trials. Some amendments in these clauses may be required.
6. A Committee constituted under the chairmanship of Dr. Ranjit Roy Chaudhury for formulating guidelines on clinical trials and new drugs has submitted its report. The report will be helpful in further strengthening of the regulation of clinical trials in the country.
7. States' suggestions and views would be considered for further strengthening of the regulation of clinical trial.

Suggestions Received from Various Stakeholders:

The SC received suggestions by the Central Government and from various stakeholders namely;

(i) National Human Rights Commission;
(ii) Mr. Sanjay Parikh, advocate for the petitioners;
(iii) SAMA Resource Group for Women and Health & Locost Standard Therapeutics and
(iv) Indian Society for Clinical Research [2]

Constituting Apex Committee and Technical Committee:

In light of the order passed by the Supreme Court on 3.1.2013 that until further orders the clinical trials of new chemical entity shall be conducted strictly in accord with the procedure prescribed in Schedule 'Y' of Drugs & Cosmetics Act, 1940 under the direct supervision of the Secretary, Ministry of Health & Family Welfare, Government of India.

It was further stated that a system of supervision of clinical trials of new chemical entities by constituting Apex Committee and Technical Committee has been put in place. [Para 10] [2]

Appointment of Expert Committee:

The Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to prepare guidelines for approval of clinical trials and new drugs in the country was constituted which has submitted its report on 8.8.2013. It is stated that the said report is under consideration. [Para 7] [2]

Current Scenario on Status of Clinical Trials in India:

It was further stated that 577 clinical trial sites have been inspected and notices have been issued to the investigators/sponsors/ethics committees seeking clarifications in 235 cases. [Para 9] [2]

Giving factual details, it is stated that till 31.8.2013, [12] New Drugs Advisory Committees (NDACs) have met 78 times wherein a total number of 1122 applications for approval of clinical trials, new drugs and fixed dose combinations were evaluated.

Out of these 1122 applications, 331 were related to approval of Global Clinical Trial (GCT) including clinical trials of new chemical entities. Of these 331 GCT applications, NDACs

after deliberations have recommended for approval of 285 applications.

For 46 applications, no recommendation has been made. Out of above 285 applications so far, DCG (I) has given approval to conduct clinical trials in 162 cases. [Para 11] [2]

PIL raised the grievance that three parameters, namely,

- Assessment of risk versus benefit to the patients,
- Innovation vis-a-vis existing therapeutic option and
- Unmet medical need in the country, indicated by this **Court in the order dated 21.10.2013,** have not been followed in letter and spirit in granting approval to 157 NCEs. [2] [SC Order dated: 10.03.2013, Division Bench of R.M. Lodha, J., Kurian Joseph, J.]

Report submitted by Prof. Ranjit Roy Chaudhury & Existing Safety measures:

With regard to conduct of clinical trials in respect of 162 cases for which approval has been given by DCG (I), we keep the matter for consideration after two weeks to enable the Additional Solicitor General to place on record the report of Prof. Ranjit Roy Chaudhury and also the details of the existing regime which ensures the safety to the subjects of clinical trials and avoid any serious adverse event by such clinical trials. [Para 12] [2]

Procedures for Payment of Compensation Specified:

Pursuant to the order dated October 8, 2012, the Secretary, Ministry of Health and Family Welfare, Government of India has taken certain measures to strength regulation of clinical trials that included three amendments in G.S.R.s [13, 14, 15] as follows:

Procedures for Clinical Trials:

G.S.R. 53(E) [13] specifies:

- Procedure to analyse the reports of serious adverse events including deaths occurring during clinical trials and
- Procedures for payment of compensation in case of trial related injury or death. [Para 2]

Conditions for Conducting Clinical Trials Specified:

G.S.R. 63(E) [14] specifies:

- Various conditions for conduct of clinical trials,
- Authority for conducting clinical trial inspections and
- Actions in case of noncompliance.

Registration of Ethics Committee:

Similarly, G.S.R.72 (E) [15] provides for:

- **Requirements and guidelines for registration of Ethics Committee.**
- By amendment, it was proposed that no Ethics Committee can review and approve any clinical trial protocol unless it is registered with the Central Drugs Standard Control Organization and that in case of noncompliance, the registration can be suspended/ cancelled. [Para 4-6] [2] [Order dated: 26.7.2013], Bench of R.M. Lodha, J., Madan B. Lokur, J.]

Constitution of Three Independent Expert Committees:

Drugs Controller General (India) constituted three Independent Expert Committees [18] under the Chairmanship of **Dr. A K Agarwal, Maulana Azad Medical College.**

New Mechanism for Compensation:

- This **Independent Expert Committee** shall examine the report of serious adverse event of death and give its recommendation to the Licensing Authority within 30 days of receiving the report from the **concerned Ethics Committee.**
- The **DCG(I) shall, then decide the Quantum of Compensation** to be paid by the Sponsor or his representative and shall pass order as deemed necessary within three months of receiving the report on the Serious Adverse Event of death.
- **In case of clinical trial related injury or death, the Sponsor or his representative shall pay the** compensation as per the order of the DCG (I) within thirty days of the receipt of such order.

Formula for Calculation of Compensation in Clinical Trials:

The Committee after deliberation prepared formula to be followed for the determination of Quantum of Compensation in case of Clinical Trial related death. The following factors emerged for discussion:

- F1: Age of the Subject,
- F2: Risk of death,
- F3: Income of the Subject,
- F4: Co- morbidity of the subject at the time of SAE (Death),
- F5: Expected Survival,
- F6: Dependency on the deceased
- F7: Concomitant medication ,
- F8: Gender of the subject
  F9: Negligence during the conduct of Clinical Trial
- F10: Duration of the disease

- F11: Industry vs. Academia vs. Institute v/s Sponsor,
- F12: Expectedness of drug to cause death.

Basis for Selection of Criteria:

1. The criteria should not be discriminative in nature due to socio-economic conditions e.g. (a) income, (b) education
2. The criteria should not discriminate gender/sex
3. The criteria should not be such which may have minimal impact but may create large variability.
4. The formula should be such that the inter group variability of compensation value so arrived at, has little scope of discretion, thus avoid possible bias.

Factors Finalised for Calculation of Quantum of Compensation:

Thus, the **following criteria** were finally decided to be incorporated in the compensation formula.

- Age of the subject
- Risk factor depending on the seriousness and severity of the disease, presence of co-morbidity and duration of disease of the subject at the time of enrolment in the clinical trial.

Consideration of the Age of the Subjects:

The committee noted that **the Workmen Compensation Act (WCA)** [16] prescribes the factors (based on age) for calculation of the lump sum amount of compensation to be paid by the employer in case of permanent disablement and death depending upon age of the injured.

The factor ranges from 99.37 (for age of 65 or more) to 228.54 (of age not more than 16) depending upon the age of the injured. [Table 1]

After deliberating the above, it was suggested that the same factor may be applied for considering the age of the subject while calculating the amount of compensation in case of clinical trial related death.

The rationale for taking the age factor as per WCA [16] is that both are in general **"No Fault Compensation"** and the committee felt that both the situations are comparable so far as age factor is concerned.

Risk Factor:

After detailed discussion it was decided that the risk factor shall be divided in five grades of a scale. [Table 2]

Need and Criteria to have a Base Amount

The Committee deliberated and agreed that a constant base factor (amount) based on logic should be there, on which the variables (age & risk) should be applied upon to determine the quantum of compensation on case to case basis.

Several rounds of discussion were held to decide a base amount. A figure of 4 lacs was considered. [17] A figure of 6 lacs was also deliberated on the logic of making the nominee of the deceased a reasonable amount available.

However, the committee finally decided to a base amount that is more logical and which remains contemporary / dynamic.

After detailed discussion the committee decided that base amount should be such that if the nominee of the subject keeps that amount of compensation in bank by way of fixed deposit, he or she will get an monthly interest amount which is at least approximately equivalent to the minimum wages (reference: Minimum wages of Delhi) of the unskilled workers.

It was considered that the minimum wages as on date is Rs.7722.00 per month and accordingly a base amount (rounded) of Rs. 8.0 Lakhs would be appropriate.

This base amount should refer to the age of 65 yrs which corresponds to the factor of 99.37 of the table of WCA [16]. It is evident that the base amount will increase /change with the revision of minimum wage.

Final Formula for Compensation:

Following three factors will be used for calculation of the quantum of compensation in case of SAE (Death) related to clinical trials are:

1. Age
2. Risk and
3. Base amount

$$\text{Compensation} = \frac{B \times F \times R}{99.37}$$

Where,

- B = **Base amount** (i.e. 8 lacs)
- F = **Factor depending on the age** of the subject as per **Annexure 1** (based on Workmen Compensation Act)
- R = **Risk Factor** (Table 2)

Compensation for Healthy Volunteers or Subject of No Risk:

However, in case of patients whose **expected mortality** is 90% or more within 30 days, **a fixed amount of Rs. 2 lacs** should be given. Thus, it will be seen that the compensation amount will vary from **a minimum of Rs.4 lacs to a maximum of Rs.73.60 lacs depending on the age of the deceased** and **the risk factor.**

The committee will examine cases of SAEs of deaths and decide the final quantum of compensation after due diligence and application of mind on the risk factor and recommend the same to DCG (I) on case to case basis. The committee also considered the above formula as provisionally final.

Summary and Conclusions:

It is hoped that provisions related to compensation for SAE including deaths as a result of clinical trials in India will be enforced in true letter and spirit in the better interest of research participants.

Medical fraternity doing research and clinical trial will also take care of ethical aspect and not to indulge in professional misconduct by violating any of the relevant provisions of the law recently enacted and those already existed.

Research work and clinical trials are need of the hour but under strict supervision and vigilance by the newly constituted bodies. NGOs are expected to keep watch on these unethical practices by all stakeholders including MNCs.

Human rights issue of these research participants will be taken care by relevant agencies including NHRC/SHRC and various High Courts. The Supreme Court of India will come up with clear cut guidelines while disposing PIL pending before it so that Research Participants will get adequate compensation for their contribution and sacrifices for greater cause of humanity.

References:

1. Dhananjay Mahapatra.2644 died during clinical trials during 7 years. The Times of India, Oct, 2012
2. Hon'ble Mr. Justice R.M. Lodha, Hon'ble Mr. Justice Anil R. Dave. Swasthya Adhikar Manch, Indore & Anr. vs. Min. of Health & Family Welf. & Ors. WP (C) 33 of 2012, Order dated: 3rd January 2013, with W.P(C)No.79 of 2012, http://courtnic.nic.in/supremecourt/temp/wc%203312p.txt], 8.10.2012, 26.7.13
3. Ethical Guidelines for Biomedical Research on Human Participants Indian Council of Medical Research, New Delhi, 2006
4. The Drugs and Cosmetic (Amendment) Bill, 2013 (Bill No. LVIII of 2013)
5. The Indian Medical Council (Professional Conduct, Ethics & Etiquettes) Regulations, 2002, 7.22, CHAPTER 7: MISCONDUCT
6. Minutes of the meeting of the Ethics Committee held on 20th November, 2012 at 09:00 A.M. in the Council Office, Sector - 8, Pocket- 14, Dwarka, New Delhi – 77. Available at: http://www.mciindia.org/meetings/Ethics/2012/Minutes_20.11.2012.pdf
7. Pawan Kumar Bansal. Politicians who exposed malpractices in medical sector. Available at: http://www.merinews.com/article/politicians-who-exposed-malpractices-in-medical-sector/15894017.shtml#sthash.ctMh8LEV.fHC3L1ZZ.dpuf
8. MP Chief Secy cites laws to not submit drug trials report. The Times of India, Feb 1, 2012: 11.
9. Unfair practices: Pharma cos fined €13bn in 4 years. The Times of India, July 16, 2012.
10. Safdrajung hospital case. Dainik Jagran, June, 1, 2013.
11. Rema Nagarajan. 'Unethical' clinical trial leaves 254 women dead. The Times of India, April 21, 2014: 2, 8.
12. Dhananjay Mahapatra. 'Why no relief for those hit diversely by clinical trials?'. The Times of India, April 22, 2014: 8.
13. The Drugs and Cosmetics Rules have been amended vide GSR 53(E) dated 30-01-2013, Notification dated: 30.09.2013
14. The Drugs and Cosmetics Rules have been amended vide GSR 63(E) dated 30-01-2013, Notification dated: 30.09.2013
15. The Drugs and Cosmetics Rules have been amended vide GSR 572E) dated 30-01-2013, Notification dated: 30.09.2013
16. The Workmen's Compensation Act, 1929
17. The Railway Accident and Untoward Incidence (Compensation) Rules, 1990.
18. Appendix XII of the Schedule Y to the Drug & Cosmetics Rules 1945 on 14th March, 2013.

Table 1: Factor (F) for calculating the amount of compensation of Appendix 1 of WCA [R]

Age	Factors	Age	Factors
1	2	1	2
Not more than		Not more than	
16	228.54	41	181.37
17	227.49	42	178.49
18	226.38	43	175.54
19	225.22	44	172.52
20	224.00	45	169.44
21	222.71	46	166.29
22	221.37	47	163.07
23	219.95	48	159.80
24	218.47	49	156.47
25	216.91	50	153.09
26	215.28	51	149.67
27	213.57	52	146.20
28	211.79	53	142.68
29	209.92	54	139.13
30	207.98	55	135.56
31	205.95	56	131.95
32	203.85	57	128.33
33	201.66	58	124.70
34	199.40	59	121.05
35	197.06	60	117.41
36	194.64	61	113.77
37	192.14	62	110.14
38	189.56	63	106.52
39	186.90	64	102.93
40	184.17	> 65	99.37

Table 2: Risk Grade

S N	Grade	Description (Prognosis)	Survival
1	0.50	Terminally ill patient	Expected survival not more than (NMT) 6 months
2	1.0	Patient with high risk	Expected survival between 6 to 24 months
3	2.0	Patient with moderate risk	More than 2 years
4	3.0	Patient with mild risk	
5	4.0	Healthy Volunteers or subject of no risk	