

30-08-13

No.DCGI/MISC/2013(107)
Directorate of General of Health Services
Central Drugs Standard Control Organization
FDA Bhawan, Kotla Road, New Delhi
(O/o DCG (I))

OFFICE ORDER

Subject:- Furnishing of information in respect of financial support, fees, honorarium, payments in kind etc to be paid to the investigator as per contract entered into by the sponsor with the investigator / institution in clinical trials - regarding.

The Drugs and Cosmetics Rules provides that no clinical trial for a new drug, whether for clinical investigation or any clinical experiment by any institution, shall be conducted except under and in accordance with the permission in writing of the licensing authority defined in clause (b) of rule 21 i.e. Drugs Controller General (India). The detailed requirements and guidelines for undertaking clinical trials are provided under Schedule Y to the said rules. It is also specified under the rules that the clinical trial is conducted as per Good Clinical Practice (GCP) guidelines specified for the purpose.

The GCP guidelines provide that the sponsor should enter into a formal and legal agreement / contract with the investigator(s) / Institution(s) before the start of the trial on various terms of the trial. The agreement should also define the relationship between the investigator and the sponsor in matters such as financial support, fees, honorarium, payments in kind etc.

It has been decided that the information in respect of the payments made by the sponsor to the investigator for the conduct clinical trial should be made available.

In view of the above it is requested that the sponsor or his representatives while making an application to the office of DCG(I) for undertaking clinical trial shall also furnish the details of the contract entered by the sponsor with the investigator / institutions with regard to financial support, fees, honorarium, payments in kind etc to be paid to the investigator.

(Dr. G. N. Singh)

Drugs Controller General (India)

30.08.2013

To,

Applicants for clinical trials

FORMULA TO DETERMINE THE QUANTUM OF COMPENSATION IN THE CASES OF SERIOUS ADVERSE EVENTS (SAEs) OF DEATHS OCCURRING DURING CLINICAL TRIALS

The Drugs and Cosmetics Rules have been amended vide GSR 53(E) dated 30-01-2013 inserting a Rule 122DAB and a new Appendix-XII in Schedule 'Y'. The amendment specifies the procedure for processing of reports of Serious Adverse Events (SAEs) including deaths occurring during clinical trial to arrive at the cause of death/injury to the subject, and to determine the quantum of compensation, if any, to be paid by the Sponsor or his representative, whosoever have obtained permission from the Drugs Controller General(India) {DCG(I)} in a time bound manner.

As per the provisions of the amendment, an 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.

Drugs Controller General (India) constituted three Independent Expert Committees in pursuance of sub-clause (6) of appendix XII of the Schedule Y to the Drug & Cosmetics Rules 1945 on 14th March,2013 under the Chairmanship of DR. A K Agarwal, , Maulana Azad Medical College to examine the Serious Adverse Events of deaths occurring during clinical trial and to recommend the cause of death, and to determine the quantum of compensation, if any, to be paid by the Sponsor or his representative, whosoever had obtained permission from the DCG(I) .

The Committee after deliberation prepared formula to be followed for the determination of Quantum of Compensation in case of Clinical Trial related death. The details of deliberations held and the formula are as under:

1. Criteria and formula for determining the quantum of compensation in case of clinical trial related deaths

The members of Independent Expert Committee discussed the various possible factors that could be considered while deciding the quantum of compensation. The following factors emerged. (Listed below are not on the basis of priority)

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 V/s Academia V/s Institute v/s Sponsor,

F12: Expectedness of drug to cause death.

After deliberation in detail the committee agreed that although in ideal situation factors from F1 to F12 should be considered in deciding the quantum of compensation, however the committee felt that ,in order to have a formula which is simple yet meeting all important points be considered and the less important factors which will largely increase the complexity, be excluded. Thus a best fit formula need to be adopted.

The following criteria were finally adopted.

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.

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

- i) Age of the subject
- ii) 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.

a) Consideration of the age of the subjects

The committee noted that The Workmen Compensation Act 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. The table of the Workmen Compensation Act is at **Annexure 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 the Workmen Compensation Act 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.

b) Risk Factor:

After detailed discussion it was decided that the risk factor shall be divided in a scale of 0.50, 1.0, 2.0, 3.0 and 4.0. However in case of patients whose expected mortality is 90 % or more within 30 days, a fixed amount of Rs. 2 lac may be given. The five grade of the scale is divided as follows:-

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
4. 3.0 Patient with mild risk
5. 4.0 Healthy Volunteers or subject of no risk

c) 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 based on Railway Accident and Untoward Incidence (Compensation) Rules, 1990. 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 deliberation 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 deliberated 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.

It was also decided that this base amount should refer to the age of 65 yrs which corresponds to the factor of 99.37 of the table of Workmen Compensation Act. It is evident that the base amount will increase /change with the revision of minimum wage.

Computing the 3 factors viz. a) Age b) Risk and c) base amount, following formula emerged for deciding the quantum of compensation in case of SAE (Death) related to clinical trial:

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

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 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 between a scale of 0.5 to 4 as under:

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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
4. 3.0 Patient with mild risk
5. 4.0 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. However, in case of patients whose expected mortality is 90 % or more within 30 days, a fixed amount of Rs. 2 lac should be given

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.

Annexure-1

Factor (F) for calculating the amount of compensation

Age											Factors
1											2
Not more than	16	.	.	.	.	.	.	.	.	.	228.54
	17	.	.	.	.	.	.	.	.	.	227.49
	18	.	.	.	.	.	.	.	.	.	226.38
	19	.	.	.	.	.	.	.	.	.	225.22
	20	.	.	.	.	.	.	.	.	.	224.00
	21	.	.	.	.	.	.	.	.	.	222.71
	22	.	.	.	.	.	.	.	.	.	221.37
	23	.	.	.	.	.	.	.	.	.	219.95
	24	.	.	.	.	.	.	.	.	.	218.47
	25	.	.	.	.	.	.	.	.	.	216.91
	26	.	.	.	.	.	.	.	.	.	215.28
	27	.	.	.	.	.	.	.	.	.	213.57
	28	.	.	.	.	.	.	.	.	.	211.79
	29	.	.	.	.	.	.	.	.	.	209.92
	30	.	.	.	.	.	.	.	.	.	207.98
	31	.	.	.	.	.	.	.	.	.	205.95
	32	.	.	.	.	.	.	.	.	.	203.85
	33	.	.	.	.	.	.	.	.	.	201.66
	34	.	.	.	.	.	.	.	.	.	199.40
	35	.	.	.	.	.	.	.	.	.	197.06
	36	.	.	.	.	.	.	.	.	.	194.64
	37	.	.	.	.	.	.	.	.	.	192.14
	38	.	.	.	.	.	.	.	.	.	189.56
	39	.	.	.	.	.	.	.	.	.	186.90

40	.	.	.	.	.	.	.	.	.	184.17
41	.	.	.	.	.	.	.	.	.	181.37
42	.	.	.	.	.	.	.	.	.	178.49
43	.	.	.	.	.	.	.	.	.	175.54
44	.	.	.	.	.	.	.	.	.	172.52
45	.	.	.	.	.	.	.	.	.	169.44
46	.	.	.	.	.	.	.	.	.	166.29
47	.	.	.	.	.	.	.	.	.	163.07
48	.	.	.	.	.	.	.	.	.	159.80
49	.	.	.	.	.	.	.	.	.	156.47
50	.	.	.	.	.	.	.	.	.	153.09
51	.	.	.	.	.	.	.	.	.	149.67
52	.	.	.	.	.	.	.	.	.	146.20
53	.	.	.	.	.	.	.	.	.	142.68
54	.	.	.	.	.	.	.	.	.	139.13
55	.	.	.	.	.	.	.	.	.	135.56
56	.	.	.	.	.	.	.	.	.	131.95
57	.	.	.	.	.	.	.	.	.	128.33
58	.	.	.	.	.	.	.	.	.	124.70
59	.	.	.	.	.	.	.	.	.	121.05
60	.	.	.	.	.	.	.	.	.	117.41
61	.	.	.	.	.	.	.	.	.	113.77
62	.	.	.	.	.	.	.	.	.	110.14
63	.	.	.	.	.	.	.	.	.	106.52
64	.	.	.	.	.	.	.	.	.	102.93
65 or more	.	.	.	.	.	.	.	.	.	99.37

