Insurance, Compensation and Indemnification of Trial Subjects

Module 8 Topic 4

Indemnify	Insure
Compensation for damage, loss, or injury suffered	To make sure, certain, or secure
Insure someone against legal responsibility for their actions	Pay money in order to receive financial compensation if something is lost or damaged or someone is hurt or killed

Insurance & Indemnity

Indemnity is giving an undertaking that compensation will be paid

- Indemnity is the provision of a written assurance or contract confirming that liabilities will be provided
- Purpose is to ensure that in the event of injury there is a facility that compensation (financial) can be paid to reinstate the claimant to the same financial position that they were in prior to the incident

Insurance & Indemnity (contd)

Whereas

Insurance is paying a premium for an insurance policy, so that the insurer will pay compensation in the event of a claim for injury or bodily harm being made

- Insurance is a contract or policy which requires premium to be paid into a fund from which compensation payments can be made in the event of a claim

Liability

The state of being legally obliged & responsible to pay money to another – as insurer

Definition

- SI 190 of 2004

"Insurance or indemnity" includes a contract of insurance, a contract of indemnity, a guarantee, a surety, a warrant and a bond and which in any case shall be available to cover the liability of the sponsor and the investigator to provide for compensation in the event of any injury, loss or damage to, or the death, of any subject arising out of the arrangement for, or conduct of, the clinical trial and which the sponsor, or investigator, shall become liable to pay to such subject, or in respect of such subject, by way of damages or costs."

Compensation arrangements in practice

- Under prevailing guidelines of the ABPI, before the start of a Phase I study the Sponsor must have agreed with the research subject to provide compensation for injury whenever a causal relationship with participation is demonstrated.

Compensation arrangements in practice (contd)

- The essence of the undertaking is as follows:
  - If the health or wellbeing of the volunteer deteriorates significantly as a result of taking part in the study, the Sponsor will compensate the volunteer, irrespective of the ability of the volunteer to prove fault on the part of the Sponsor or anyone else connected with the study;
  - The amount of compensation should be calculated by reference to the amount of damages that would commonly have been awarded for similar injuries by an English court had liability been proven. The amount of compensation may be reduced if the volunteer is partly responsible for the injury or if the volunteer is separately compensated under any other insurance policy;

Compensation arrangements in practice (contd)

- The Sponsor and volunteer agree to refer any dispute about whether compensation is payable or the amount of such compensation to an arbitrator with power to consult a barrister of ten years' standing on any issue of law, including the amount of damages to be paid. If the Sponsor and volunteer cannot agree on the identity of an appropriate arbitrator, the President of the Royal College of Physicians of London will be invited to appoint an arbitrator;

Compensation arrangements in practice (contd)

- The undertaking to compensate the volunteer will be construed in accordance with English law and, subject to the provisions above, the English courts have sole jurisdiction over any dispute that may arise out of it. The nature of the Sponsor's compensation policy should be made clear to the volunteer as part of the consent process. Volunteers should be given a copy of the relevant ABPI guidelines and should be invited to seek clarification of any aspect of the undertaking that is not clear to them

Insurance

- The Medicines for Human Use (Clinical Trials) Regulations 2004 state that a clinical trial may be undertaken only if provision has been made for "insurance or indemnity" to cover the liability of the Investigator and Sponsor in relation to the trial
- The current advice from the Department of Health is that this requirement is not met by the Sponsor providing evidence of his financial ability to meet a claim made in response to the contractual undertaking given under the ABPI compensation guidelines
- The Department argues that insurance or an indemnity by a third party is required and "self-insurance" does not suffice

Insurance or indemnity of the Investigator

- Before the start of a Phase I study, the Sponsor must indemnify the Investigator (and any CRO providing the Investigator) against any loss incurred by the Investigator (including the cost of legal representation) as a result of claims arising from the study, except to the extent that such claims arise from the negligence of the Investigator, in respect of which the Investigator remains responsible, as between the Investigator and the Sponsor
- For these purposes the Investigator is the person responsible for the conduct of a study at a trial site and, if the study is conducted by a team of individuals, the Principal Investigator

Insurance or indemnity of the Investigator (Contd)

- In the case of Phase I trials, the right of the volunteer to claim compensation from the Sponsor is not affected because, as described in paragraph 2 above, the Sponsor's undertaking to pay compensation is given on a "no fault" basis.
  It arises wherever the volunteer can show that the volunteer suffered injury through participation in the trial, even if the injury was due to the negligence of a person other than the Sponsor

Insurance or Indemnity of the Investigator (Contd)

- However, having paid such compensation, the Sponsor is free to seek full indemnity or (depending upon the circumstances) a contribution from any person whose negligence caused the injury

Clinical Research – Main Risks

- Injury (physical and psychological) to participants from poorly designed or executed research
- Breach of privacy and confidentiality in relation to inappropriate research methodologies and publication practices
- Breach of rights and dignity of participants in relation to consent
- Lack of compliance with legislation and regulations
- Damage to good-name and reputation

Clinical Research – Main Risks (contd)

- Inappropriate usage or wastage of resources
- Financial impropriety and inequity in support and funding
- Variance in the standards of the conduct of research
- Breach of indemnity or insurance requirements
- Absence of a learning and research culture

Inclusion of the GCP system in the Pharmaceutical Affairs Act and establishment of the compensation system for health damage

- 1989 GCP standards when conducting clinical studies (trials) subject to Pharmaceutical Affairs Act, the sponsor was requested (administrative guidance) to take steps to provide compensation and insurance for subjects, and interested parties followed those requests

Inclusion of the GCP system in the Pharmaceutical Affairs Act and establishment of the compensation system for health damage

- It became essential to insert in consent forms and explanatory statements provisions for “treatment and compensation” in the event a subject’s health is damaged

Inclusion of the GCP system in the Pharmaceutical Affairs Act and establishment of the compensation system for health damage

- Based on the above provisions, interested parties promised (free) treatment and compensation and, at the same time, requested non-life insurance companies to create indemnity insurance policies that they then took out

Typical example of a “treatment and compensation for health damage” provision

The following is an example of a treatment and compensation for health damage provision:

- “Please consult your primary doctor immediately if you develop symptoms during this trial that you did not have before. Appropriate treatment and appropriate measures shall be taken if you suffer an adverse effect or other health damage during or after participation in this trial. You may also receive compensation according to the type and degree of health damage.

Typical example of a “treatment and compensation for health damage” provision

- However, please be aware that you may not receive compensation if it is found that you did not follow your primary doctor’s instructions or that the health damage was due to your own carelessness.”

Aims of guidance

The aims of guidance, which has been developed by the Association of the British Pharmaceutical Industry ABPI, the BioIndustry Association (BIA) and the Clinical Contract Research Association (CCRA) in consultation with the Department of Health and the National Research Ethics Service, are:

- To provide authoritative recommendations to clinical trial sponsors, clinical research organisations and ethics committees on the level of insurance and other aspects of insurance cover for industry sponsored Phase I clinical trials;

Aims of guidance

- To assure volunteers in clinical trials and ethics committees that adequate insurance is in place for industry sponsored Phase I clinical trials; and
- To accelerate the ethics committee review process, enabling clinical trials to start more quickly, and thereby enhancing the early stage clinical development environment in the UK, but without compromising the protection of volunteers

ABPI Clinical Trial Compensation Guidelines (1991)

Under the Guidelines (section 1.2), the sponsor should pay compensation:

- … when, on the balance of probabilities, the injury was attributable to the administration of a medical product under trial or any clinical intervention or procedure provided for by the protocol that would not have occurred but for the inclusion of the patient in the trial…

ABPI Clinical Trial Compensation Guidelines (1991) (contd)

- Compensation should only be paid for the more serious injury of an enduring and disabling character (including exacerbation of an existing condition) and not for temporary pain or discomfort or less serious or curable complaints.
- Where there is an adverse reaction to a medicinal product under trial and injury is caused by a procedure adopted to deal with that adverse reaction, compensation should be paid for such injury as if it were caused directly by the medicinal product under trail…

ABPI Clinical Trial Compensation Guidelines (1991) (contd)

The amount of compensation paid should be appropriate to the nature, severity and persistence of the injury and should in general terms be consistent with the quantum of damages commonly awarded for similar injuries by an English Court in cases where legal liability is admitted.

ABPI Clinical Trial Compensation Guidelines (1991) (contd)

Compensation may be abated, or in certain circumstances excluded, in the light of the following factors (on which will depend the level of risk the patient can reasonably be expected to accept):

- The seriousness of the disease being treated, the degree of probability that adverse reactions will occur and any warnings given;
- The risks and benefits of established treatments relative to those known or suspected of the trial medicine

Present Status of Compensation

Insurance

- There are three major types of insurance that pharmaceutical companies currently buy

- The first is **comprehensive liability insurance**, which is bought by foreign pharmaceutical companies and some major Japanese pharmaceutical companies

- This provides adequate coverage for clinical trials in addition to product liability for over-the-counter drugs and things such as insurance against fire at plants

Present Status of Compensation (contd)

- The second type is **healthy subject compensation insurance**, which is insurance for clinical trials conducted on healthy people
- It provides relief up to after effects impediment grade 14 in addition to death
- In the case of the elderly and subjects who lack the ability to work because of a disability or other cause, the amount of compensation cannot be determined by focusing on the ability to work (or degree of loss thereof). Therefore, the time has come to think of a way to determine the amount of compensation in those kinds of situations

Present Status of Compensation (contd)

- However, as a third type, some pharmaceutical companies have introduced a compensation system for clinical trials on patients that uses the **adverse drug reactions injured party compensation system**
- Insurance companies sell this type of insurance based on user requests

Comprehensive Liability Insurance

Certificate of Insurance Coverage

Period: 1st March, 2013-1st March, 2014

Covered Perils Comprehensive General Liability

1), 2) Products, 3) Fire Legal, ～6)

Comprehensive Liability Insurance (contd)

- Clinical Testing Liability and Experimental Testing of New Drugs Endorsement/Compensation in Clinical Trials
- Endorsement (The Indemnity provided by this policy shall apply to legal liability and compensation for bodily injury to third parties in clinical trials conducted by or on behalf of the Insured)
- Limit of Liability;…

Healthy Subject Compensation Insurance

Certificate of Product Liability Insurance Coverage (Schedule)

- Insured: ABC Co. Ltd.
- Term: Midnight on 1st April 2013 to Midnight on 31st March 2014
- Amount payable: Bodily injury liability per person: 100 million yen; per accident: 300 million yen(3.2 million USD)*;
  during the insurance term: 300 million yen
- Deductible: Per accident: 500,000 yen(5,263 USD)
- Notes: Clinical Trial Liability Insurance Rider

*US dollar/JPY exchange rate: US$1 ≒95 yen

Healthy Subject Compensation Insurance

- Per accident, during insurance term: 300 million yen (coverage for bodily Injury liability per accident, payment within the limit during the insurance term)
- Coverage limit per victim: as shown on reverse (no exemption from responsibility)
  25th February 2013

- Fire Insurance Company

Patient Subject Compensation Insurance (contd)

Certificate of Product Liability Insurance Coverage

- Policy Owner: XYZ Co. Ltd.
- Insured: XYZ Co. Ltd.
- Term: Midnight on 1st January 2013 to Midnight on 31st December 2015

Patient Subject Compensation Insurance (contd)

Coverage limit: Bodily injury liability per person: 100 million yen (1.1 million USD) ; per accident: 500 million yen (5.3 million USD); during the insurance term: 500 million yen

Deductible: Bodily injury liability per accident: 1 million yen (10,526 USD)

Patient Subject Compensation Insurance (contd)

Notes: Investigational drug code: PP-001; investigation drug rider ancillary; clinical trial compensation liability insurance ride ancillary Death: 20 million yen (0.2 million USD)

After effects impediment grade 1: 70 million yen (0.7 million USD)

After effects impediment grade 2: 50 million yen (0.5 million USD)

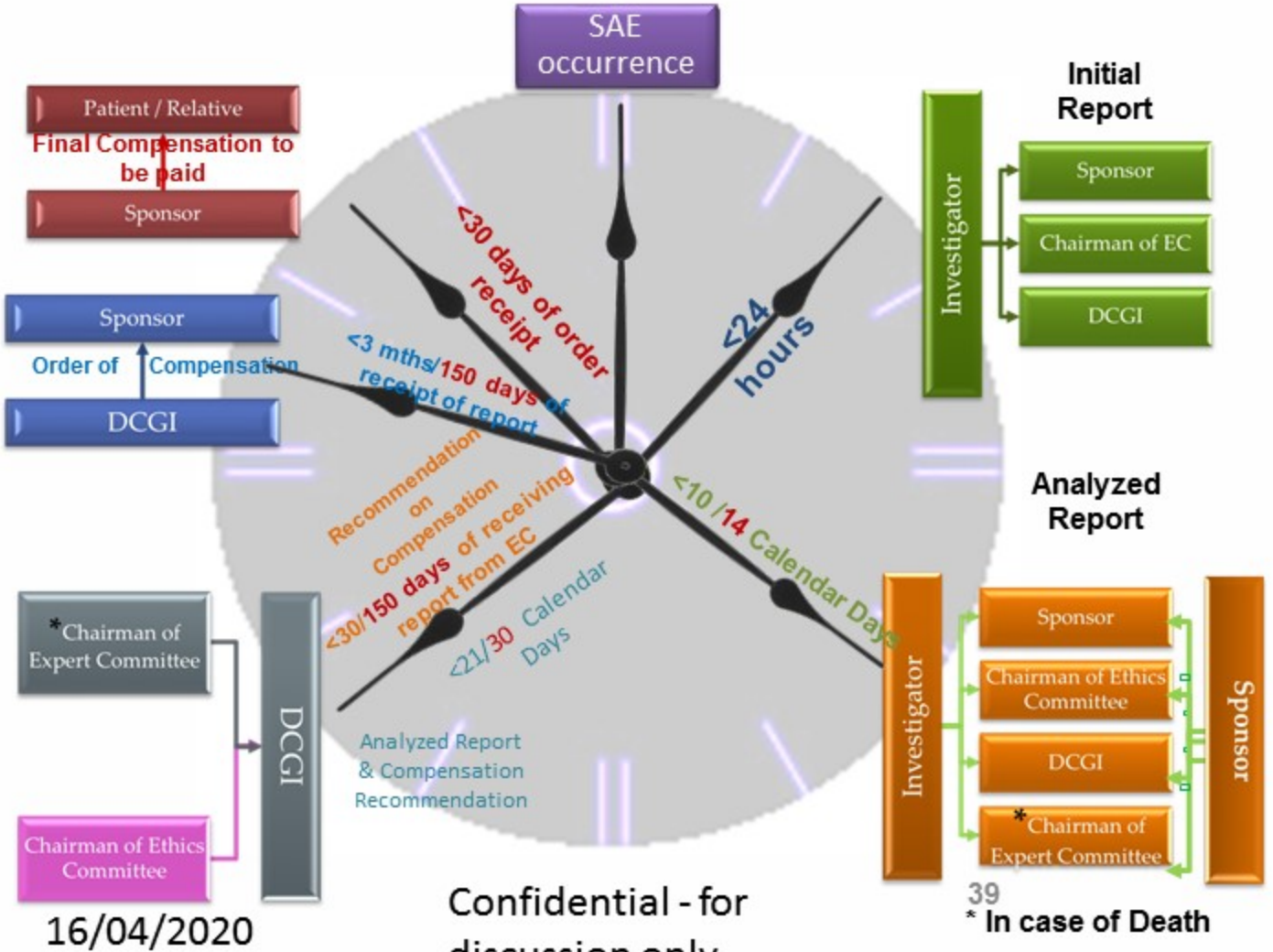
25th November 2012

- ZZZ Marine Insurance Company

Reporter note:
Since after effects impediment grades 1 and 2 are the only ones covered by the insurance, it is clear that only compensation equivalent to the adverse drug reaction compensation system is being considered.

Compensation Laws in India

New SAE Reporting Process in India



Rule 122 DAB- Compensation rules in India

G.S.R. 53(E)

- In case of injury, Subject shall be provided free **medical management** as long as required
- In case of CT related injury or death subject is entitled for financial **compensation** as per order of DCG(I)
- The expense on medical management and financial compensation shall be borne by the **Sponsor**

Rule 122 DAB- Compensation rules in India (contd)

G.S.R. 53(E)

- Sponsor shall give an **undertaking** along with the CT application to provide compensation in case of CT related injury or death
- In case of **failure to provide** medical management and/or compensation
  - CT can be suspended /cancelled
  - Sponsor can be restricted from conducting future CTs

What is CT related injury or Death?

G.S.R. 53(E)

- Adverse effect of investigational product(s);
- Violation of the approved protocol, scientific misconduct or negligence by the Sponsor or his representative or the investigator;
- Failure of investigational product to provide intended therapeutic effect;
- Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;
- For injury to a child in–utero because of the participation of parent in clinical trial;
- Any clinical trial procedures involved in the study

Amendment in Informed Consent Form

G.S.R. 53(E)

- Essential elements of ICF have been amended to include statements that -
  - in the event of injury, free medical management as long as required
  - in case of CT related injury or death, compensation
- The Format of ICF have been amended to include -
  - Address
  - Qualification and Occupation
  - Annual income of the subject and Name & address of his nominee
- Mandatory for Investigator to hand over a copy of duly filled ICD to the subject or his/her attendant

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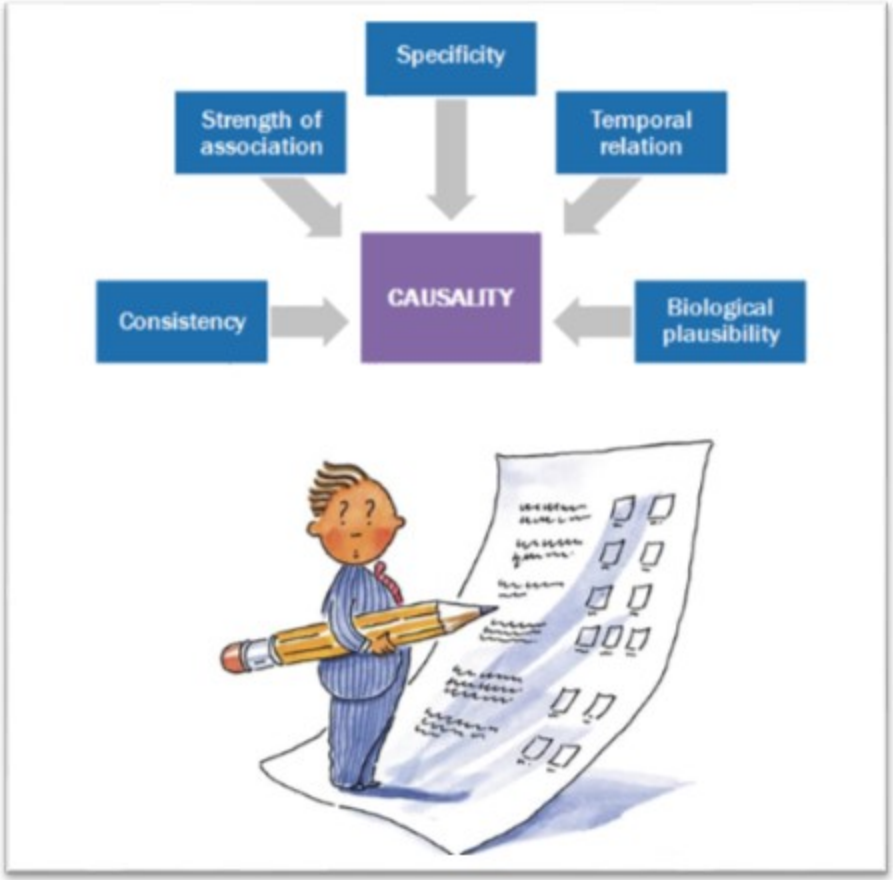
Causality Assessment

The evaluation of the likelihood that a medicine was the causative agent of an observed adverse event



Execution Steps for Compensation in India

- Licensing authority primarily responsible for the causal assessment of injury/death and compensation amount to be paid for it to trial participant
- In case of occurrence of serious adverse event (SAE), the Expert Committee communicates its recommendation about causality and quantum of compensation to the licensing authority, and then, the licensing authority shall pass the final order

Execution Steps for Compensation in India (contd)

- The sponsor needed to compensate the participant as per order of licensing authority. In case of failure to comply with the order, licensing authority may take necessary action as per rule, including suspension or cancellation of the clinical trial and/or restricting sponsor including his representative(s) to conduct any further clinical trials in India

Execution Steps for Compensation in India (contd)

- As per rule 122 DAB of Drugs and Cosmetics Rules 1945, this is the responsibility of the sponsor to compensate financially in case of clinical trial-related injury/death as per the order of DCGI based on recommendation of Expert Committee
- In case of SAE other than death, the cause of injury and amount to be given to participant is finalized by the DCGI as per the report submitted by Investigator, Sponsor, and Ethics Committee

Formula In Case Of Death

Compensation = (B x F x R)/ 99.37

Where,

B = Base amount (i.e. 8 lacs)

F = Age Factor (based on Workmen Compensation Act)

R = Risk Factor of the subject at the time of enrolment in the clinical trial between a scale of 0.5 to 4 as under:

- 1 .0.50 terminally ill patient (expected survival 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

Formula In Case Of Death (contd)

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

To simplify

Age	Risk factor	Compensation
> 65 yrs	4	32 Lacs
< 16 yrs	4	73.59 Lacs
>65 yrs	0.5	4 Lacs
< 16 yrs	0.5	9 Lacs

Responsibilities-Investigator

- Responsible for the conduct of the trial according to the protocol, GCP Guidelines, Regulations and Standard Operating Procedures
- Ensure that adequate medical care is provided to the participant for any adverse events.
- Report all serious and unexpected adverse events to the Sponsor within 24 hours and to the Ethics Committee that accorded approval to the study protocol within 10 working days of their occurrence

Responsibilities-Ethics Committee

- Safeguard the rights, safety and well being of all trial subjects, particular care to protect the rights, safety and well being of all vulnerable subjects
- Conduct ongoing review of trials to ensure adherence to protocol and protection of subjects
- Stop the trial if in their opinion the subjects are at risk of injury or death
- If an ethics committee refuses approval, it must record the reasons in writing. If it revokes an approval, the same must be communicated to DSCO

Powers-Ethics Committee

- Decide on every proposal giving:
  - Approve the proposed study
  - Suggest changes prior to approval
  - Reject the proposal
- Review the study periodically to ascertain that the study adheres to the conditions of approval and that subjects' rights are protected.
- Take appropriate action in case of default
- Take cognisance of any complaints from any stake holder, investigate and take appropriate action

Powers-Ethics Committee (contd)

- Review all non compliances, suggest remedial action and ensure that it is taken
- Some non compliances may require stoppage of the trial or removal of a patient from the trial
- Ensure that PI and trial staff adhere to regulatory guidelines

Powers-Ethics Committee

- Review all serious and unexpected adverse events, ensure their reporting as per schedule
- Analyse all SAEs for causality (Naranjo or WHO algorithm)
- Recommend reimbursement/free medical treatment and compensation for trial related injuries
- Ensure that subjects are paid the ordered reimbursements/compensation

Conclusion

Compensation is excluded in certain circumstances, including those where injury was caused by another licensed medicinal product which was administered as a comparison with the product under trial, or where placebo has failed to provide a therapeutic benefit

Compensation should not be paid, or should be abated, to the extent that the injury has arisen through a significant departure from the agreed protocol, or through the wrongful act or default of third party, including the doctor's failure to deal adequately with an adverse reaction, or through contributory negligence by the patient