Indian Society for Clinical Research

ISCR comments/suggestions on
Draft Drugs and Cosmetics(Amendment) Bill, 2015

S.No	Page no / Section / Subsection	Comments / Suggestions	Justification
1.	Pg # 2/ 2. Long title/Amendment of the long title	The title focuses only on import, manufacture, distribution and sales of Drugs, cosmetics and medical device, we recommend to add 'exports' also in the definition	Since in last one decade the exports from India has increased many folds, the focus of regulators should be more on exports as well. In last 2 years many Indian companies have faced challenges from authorities of various geographies and there are questions on the regulatory framework as well.
2.	Pg #3/7, section 3(c) / definition of bioequivalence study	Bioequivalence study is defined as a comparison to "refernce formulation", however, "reference formulation" has not been defined in the Act	Reference formulation needs to be defined as formulation of the drug approved by Central Licensing Authority. Central Licensing Authority needs to publish the list of such reference formulations as and when the drugs are approved by the authority
3.	Pg #3/7, section 3(g) / definition of clinical trial	Section defines clinical trial and this definition is not consistent with Rule 122DAAA To add word quality after the word efficacy in the definition	Both definitions need to be aligned Since the definition of CT also includes BA/BE studies objectives mentioned towards end of the definition should also include "quality" after efficacy word
4.	Pg #4 /7, section 3(j) / definition of drug	Reference to point no. (iii) - addition of the statement may convey a need for obtaining permission of excipents used for first time in the products. To omit subclause no. (iii) Clarification required on sub clause (iv) of the definition Reference to sub-section (2) needs confirmation, what does it mean?	

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5.	Pg #5/section 3/ subsection (q)/ definition of investigational new drug	The definition only refers to New 'Chemical' entity, our suggestion is to add 'new biological entity' as well.	Since in the modern era referring only to chemcial entities will be inappropriate.
6.	Pg #5/section 3/ subsection (x)/ definition of new drug	Definition of New Drug is not consistent with Rule 122E	Both definitions need to be aligned to have consistency
7.	Pg #7/Chapter 1A, section 4A(3)/ period of new drug	The period for which a new drug shall be considered as a new drug has not being defined	While Sch. Y does define the duration of 4 years for which a new drug shall be deemed as new drug, it may be good to incorporate the same in the bill
8.	Pg #7/Chapter 1A, section 4B/ injury or death in the course of a clinical trial	This part of the bill should cross refer the related rules (e.g. Rule 122DAB) and in that rule the objective definition of Clinical Trial Related Injury should be specified. For example the injury can be defined in various categories per the professional judgment of the treating physician (PI) There is no provision for the sponsor and other organizations involved in clinical research to appeal to a board of experts, and discuss on scientific grounds in case of disagreement relating to causality of serious adverse events or amount of compensation determined by the Licensing Authority For determination of relatedness of injury or death to clinical trial, it is not clear which "authority" is referred- whether it is DCGI or some other authority. It is recommended to clearly state the concerned authority responsible for determining relatedness	For the word Injury in above sections: Clinical Trial related injury needs a more objective definition which would be uniformly understood by all stakeholders. This will provide for expedited compensation and will benefit patients in case of SAE leading to injury and to nominee in case of death We urge that an opportunity be given to the experts from the sponsor organization to also present their assessment before arriving at a final decision as they would have the most in depth information about the investigational product. We would also recommend that determination of causality and any process relating to the final assessment in respect of whether a serious adverse event has/has not been caused by an

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			investigational drug be included in the legislation rather than being included as a rule which may be varied from time to time by successive governments, so as to provide a reasonable degree of certainty in respect of the process.
9.	Pg #7 /Chapter 1A, section 4C / medical treatment and compensation	The words 'caused due' in above section should be replaced with 'related' Mentions Legal Heir whereas, current gazette mentions nominee [nominee also mentioned in the current prescribed ICF template]	This will align the causality analysis being done by experts committee where the final opinion of either 'related' or 'not related'to the clinical trial is stated Documentation required to establish legal heir is very different from that of nominee
10.	Pg #7 /Chapter 1A, section 4D / Deferment of clinical data	Authorities may ……. "For approval of clinical trial" – should this read as "approval of the drug for marketing?" Waiver for medical devices not addressed	Clinical trial of medical devices should also be waived if there is sufficient data to support the safety and performance of the devices for unmet medical need for life threatening or irreversibly deliberating diseases or condition
11.	Pg #8 /Chapter 1A, section 4F / Functions and responsibilities of EC	The text "~~internal audit reports furnished by the Sponsor~~" can be deleted because it is not clear whether this can be done or not and if done, whether or not this would be a GCP violation Authority to the ECs to revoke approval of the trial at the site: Criteria need to be defined when they should suspend the study and what scientific evidence they should review.	Sponsor audit reports are not provided to Ethics Committees. Refer ICH E6 section 5.19.3 Auditing Procedures (d) To preserve the independence and value of the audit function, the regulatory authority(ies) should not routinely request the audit reports. Regulatory authority(ies) may seek access to an audit report on a case by case basis when evidence of serious GCP non-compliance exists, or in the course of legal proceedings.

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12.	Pg #9 /Chapter 1A, section 4G (1)(2)(3) / action against EC	On cancelation or suspension of EC there should be clear provision from CLA to immediately transfer all other CLA approved clinical trial to another EC within the same city to ensure continuity and to safeguard already enrolled patients. There should also be a provision of sharing such information with all other sponsors immediately after cancellation Incorporate in Rule 122DD the equivalent of "US FDA Guidance for IRBs, Clinical Investigators, and Sponsors Considerations When Transferring Clinical Investigation Oversight to Another IRB"	Continuance of all other trials is very important since the trials are not only approved by EC but is also approved by DCGI, the conduct at that center might be of concern to CLA but safeguarding patient interest should be of prime importance. This does not address the question of what would happen to the study/ies which are overseen by the discontinued EC. The language could be modified as "in case the EC ceases to exist because of suspension/cancellation by the regulatory authorities or due to other reasons, then the trial/s overseen by that EC may be monitored by another competent registered EC *<limits to lay down criteria like within certain geographical premises can be specified>*"
13.	Pg#9/Chapter 1A, section 4 H / Inspection by drug control officer	**Inspection by regulatory authority:** While it is imperative for regulatory authorities to be able to inspect the ongoing clinical trials at any time, this needs to be balanced with the demand of time of the investigators who are also practicing clinicians. Any unannounced inspection may impact their ability to carry out their regular clinical duties. The CDSCO has issued excellent guidelines on inspection of clinical trials and these guidelines need to be followed by all the inspectors in word and spirit.	We would urge that the investigators are given adequate notice for the inspections and unannounced inspections are conducted on a "for cause" basis. We would also urge that with reference to sub-clause 2 of this section, the words "or matters relating thereto" be more clearly defined so as to ensure that this power is exercised in a judicious and predictable manner

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14.	Pg#9/Chapter 1A, section 4-I / Disclosure of name, address etc	Clearly define the expectation from each entity, eg. A sponsor or a CRO may not have personal information of paricipants. Disclosure of personal details of participants in the clinical trial to the Drugs Control Officer where necessary only (eg: subject compensation in case of clinical trial related injury or death) may be acceptable. However, a clause towards keeping confidentiality of clinical trial participants (personal details and disease condition related information) will make it more robust in terms of adherence to Ethical principles of Biomedical research by ICMR and widely followed standards (ICH-GCP). This was also stressed by the Supreme Court.	As per GCP's principals of privacy and confidentiality, investigator can not share patient's personal information with sponsor Following sentence may to added to the existing paragraph. **"All stakeholders including Drugs Control Officer should maintain the confidentiality of clinical trial participants in adherence to Ethical principles of Biomedical research issued by ICMR and as per ICH-GCP."**
15.	Pg#9/Chapter 1A, section 4J / Maintenance of records etc.	The period for which data pertaining to clinical trial needs to be stored by any person, sponsor, clinical research organisation or any other organisation or investigator conducting a clinical trial or his agent holding a permission under this Chapter is not specified	Data in respect of clinical research is voluminous and while we fully support the need for this data to be maintained by those mentioned in the proposed section, we believe that the practical issues in respect of the maintenance of such data indefinitely need to be considered. Accordingly, we would urge you to consider including a reasonable time frame for the maintenance of data in respect of this section. It is recommended that the CDSCO issue specific guidance documents for Industry and Researchers in this regard., and which may be included in the prescribed rules. It will be good if these requirements are aligned to established international norms.

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16.	Pg # 10/Chapter 1A, section 4K / Penalty for conducting clinical trial etc.	This may potentially impact stakeholders who may conduct a clinical trial/academic research study (eg: with drug which is not defined as new drug as per the bill) in approved/unapproved indication, without approval from all concerned authorities. **Penal Provisions under the bill:** **While the amendment does specify penal provisions for the regulated, there are no penalties defined for corruption or complacency by regulatory officials, dereliction of duty or non-performance and no recourse prescribed against charges or claims that are frivolously made. It is unclear how determinations of guilt are to be made and the forum and procedure to be adopted for such determinations to be made / appeal mechanism available. The penal provisions set out in the bill need to be reviewed in order to ensure that they may be tenable in law and the process for determination of penalties of any nature, including the inclusion of appeals and alternate dispute resolution mechanisms (such as mediation/arbitration and the like), should be considered to be included. The bill also does not specify which violation of the law will lead to imprisonment – even minor mistake in documentation can also be interpreted as violation of the law. These need to be clearly defined in the Act and not left to interpretation, discretion of presiding regulatory authorities. The bill thus needs to be more balanced and fair towards all stakeholders involved.**	**May we point out that from the perspective of ensuring that the medical fraternity and all pharmaceutical industry and other organizations in India continue to maintain an interest in conducting clinical research in India, to ensure that new drugs are developed to ultimately safeguard the Indian population and its health and well being, the penal provisions are bound to seriously discourage the conduct of clinical research in India. We therefore urge a reconsideration of this section.** **An appeal process/redressal mechanism should be mentioned or defined appropriately**. All the procedures under this section must follow principles of natural justice and the principles of "*audi alteram partem*" must be followed before prosecution is initiated

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17.	Pg#11/Chapter 1A, section 4-O and 4P/ Penalty for violation of conditions of permission and repeated offence	The penal provision is very broad and loosly defined, a deviation can happen but if safety measures are in place, the entity should not be convicted with imprisonment unless it has affected patient safety. Penalties like the ones set forth in this section of Bill needs to be defined more clearly including the right to appeal/redressal mechanism and process for same. The Bill 'as is' could lead to potential misuse /abuse. Clarity required on "violation of the conditions of permission", and about the redressal/appeal mechanism available to concerned persons/organizations and stakeholders in clinical trials.	Eg. An approval comes with a condition of 50% govt. sites and if unfortunately one of the govt. site is not able to enroll any patients, such a situation can be misinterpreted as contravention of conditions of permission. The scope should be brought down to specific violations which are intentional and/or concerning patient safety **'Section 4-O and 4-P' should be deleted**, till such time the clarity is brought regarding the 'conditions' through amendments to relevant D&C Rules and justifying the actions and punishment versus the respective violations.
18.	Pg#11/Chapter 1A, section 4Q / Penalty for failure to provide compensation	An investigation /appeal / redressal mechanism is missing **leading to potentially unfair implementation** when the compensation payment is delayed due to valid or justifiable administrative /scientific review reasons.	**Clear terms and conditions/exceptions/acceptable explanations for the delay, needs to be defined in the Rule 122 DAB of Schedule Y**. The existing rules (including the latest released amendment in December 2014, effective after 6 months) do not provide clarity on this
19.	Pg#12/Chapter 1A, section 4R/Penalty for contravention of any provision of this chapter	In the statement starting with, 'whoever initiates… please add 'himself or by any other person on his behalf'	This is to maintain consistency with all other sections of this chapter.

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20.	Pg#12/Chapter 1A, section 4S/ Consfication of stock, medical device or cosmetics	It is not clear in the section if the contravention by one of the investiagator will lead to confsication of stocks at that particular location or stocks of that drug or cosmetic from all patricipating sites.	A blanket provision can jeopardize the trial at other locations and can impact patient saftey if whole stocks are confiscated and no access given to patient already on the drug
21.	Pg#12/Chapter 1A, section 4T / Cognizance of offence	Provision makes it possible that a prosecution to be initiated on the complaint of "any recognised consumer association	This clause should be deleted as the person participating in clinical trial is not a "consumer" as per the provisions of Consumer Protection Act and the consumer association do not have any locus standi in the matters of prosecultion related to Clinical Trials.
22.	Pg#19/Chapter IIA/ section 7E(b)/Spurious Medical Device	The statement is not very clear, can be replaced by- Purports to be manufactured by a manufacturer who is not involved at all in the manufacturing process as prescribed in the definition of 'Manufacturer' of this act	The scope of this statement is not clearly coming out and may lead to misinterpretation
23.	Pg#2//Section 3 of Principal Act:	Term "New Medical Device" has not been defined.	New Drugs is defined. New Medical Devices Term is used but not defined. It should also be defined.
24.	Pg#2//Section 3 of Principal Act:	Definition of Biologic Missing	No explanation or definition of Biologicals, Bio-similars has been provided. Biological are incorporated under the scope of "New Drug" definition thus restricting the scope of new biological beyond the existing category.

General Comments:

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- The rule defines Drugs and Devices differently and the penalties are also relaxed on devices which is inappropriate as it assumes that adverse events caused due to misuse of devices / non –adherence to regulatory requirements for a device would have less severe consequences as against drugs..
- It's not very clear from the act that who will be convicted for specific violations. All parties involved cannot be blindly convicted for everything.
- Protocol deviations are inevitable, people cannot be convicted for every deviation. Only serious and intentional non-compliance should be considered for penalization.
- There is no provision for prohibition on unethical and outside – label promotion of drugs .

- While the powers of Drugs Inspectors (referred to as DCO/MDO in the bill), as well of the Central Drug Authority (CDA) and DCG(I) have been substantially increased, there are no provisions introduced to improve the functioning of the regulatory agencies. For example:
    - There is no requirement for any internal operating procedures for the licensing authority specified in the Act.
    - There is no requirement for periodic reporting of performance of the licensing authority to the CDA specified.
    - There are no performance criteria defined for the licensing authority.
    - There is no definition of the qualifications and experience of senior officials of the licensing authority or the non-ex-officio members of the CDA.
    - The Act provides no mandate for public transparency of regulatory processes and performance of the regulator.
- There is also no mandate in the bill for the ongoing training and skill development of regulatory officials in India.
- A vast number of Sections within the Bill, set out that processes/procedures/proceedings will be 'prescribed'. Presumably, this prescription would be in the form of rules to be set out in Schedule Y of the Act. It is imperative, that the rules, which are formulated are not only tenable in law, but aligned with the existing provisions of the Act and the newly proposed provisions