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Supplementary Table. Evolution of post-trial access in Indian ethical guidelines

Year of guidelines publication	Name of guideline and publishing agency	Whether post- trial access or synonyms mentioned or otherwise. If mentioned, the exact wording along with section
1980	Policy statement on ethical considerations involved in research on human subjects, Indian Council of Medical Research	None
2000	Ethical Guidelines for Biomedical Research on Human Subjects, Indian Council of Medical Research	None
2006	Ethical Guidelines for Biomedical Research on Human Subjects, Indian Council of Medical Research [9]	I. INFORMED CONSENT PROCESS 12. Benefit sharing in the event of commercialization VII. POST - TRIAL ACCESS The Helsinki Declaration of the World Medical Assembly (WMA), 2000 states that at the end of the trial every participant should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study. This led to a lot of debate globally on account of lack of even basic drugs in most of the developing countries. The Declaration of the WMA in 2004 reaffirmed "its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review."

		Therefore, whenever possible I\EC should consider such an arrangement in the a priori agreement. Sometimes more than the benefit to the participant, the community may be given benefit in indirect way through improving their living conditions, establishing counseling centers, clinics or schools, and giving education on maintaining good health practices. For smaller scale or student projects post trial benefit to the participants may not be feasible but keeping in mind the post trial responsibility conscious efforts should be made by the guides and the institution to initiate steps to continue to support and give better care to the participants. **I. DRUG TRIALS** iii. After the clinical trial is over, if need the drug is found effective, it should be made mandatory that the sponsoring agency should provide the drug to the patient till it is marketed in the country and thereafter at a reduced rate for the participants whenever possible. A suitable a priori agreement should be reached on post trial benefits. **II. VACCINE TRIALS** iv. Post trial access to the vaccine should be available to the control group. But if the vaccine is for pediatric age group and by the time the study gets over the children in the control arm may cross the age when the vaccine is supposed to be protective. In such instances the control arm could be some other alternative vaccine for that pediatric age group although this does not restore clinical equipoise. EC may examine the feasibility and ethical aspects on a case-to-case basis. v. Post trial access to the vaccine should be given first to the community from which the participants were drawn. **V. DNA AND CELL-LINE BANKING / REPOSITORY** As tissue banking concerns research at a later time, the ethical issues pertain to consent requirements for the banking and further uses of tissue and DNA samples, their control and ownership, and the benefit sharing to the individual or community. General Principles An Ethics Committee exclusive to the Repository, the Repository Ethics Committee constituted as per the guidelines in the Chapter on Ethics Review Mechanism, should play an important role in looking at the

		issues related to informed consent, privacy and confidentiality, risk-benefit analysis, benefit sharing, maintain linkages with other biobanks and repositories while adhering to the basic principles of bioethics viz. Autonomy, Justice, Beneficence and Non-maleficence.
2016	The Drugs and Cosmetics Act and Rules (1940, 1945) Amended up to 31 Dec 2016 Ministry of Health and Family Welfare, Department of Health [15]	None
2017	National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, Indian Council of Medical Research [10]	**Section - Post research access and benefit sharing (Section -2.11)** The benefits accruing from research should be made accessible to individuals, communities and populations whenever relevant. Sometimes more than the benefit to the individual participant, the community may be given benefit in an indirect way by improving their living conditions, establishing counselling centres, clinics or schools, and providing education on good health practices. 1 Efforts should be made to communicate the findings of the research study to the individuals/communities wherever relevant. 2 The research team should make plans wherever applicable for post-research access and sharing of academic or intervention benefits with the participants, including those in the control group. 3 Post-research access arrangements or other care must be described in the study protocol so that the EC may consider such arrangements during its review. 4 If an investigational drug is to be given to a participant post-trial, appropriate regulatory approvals should be in place. 5 The EC should consider the need for an *a priori* agreement between the researchers and sponsors regarding all the points mentioned above. 6 In studies with restricted scope, such as student projects, post study benefit to the participants may not be feasible, but conscious efforts should be made by the institution to take steps to continue to support and give better care to the participants. 3.1.2 Contemporary ethical issues in biomedical and health research Among the contemporary issues recently under debate are the use of underprivileged and vulnerable groups as participants, post-trial access of research benefits to participants and their communities, research on emerging technologies, etc

		Box 5.1 Essential and additional elements of an informed consent document v. post research plan/benefit sharing, if research on biological material and/or data leads to commercialization. 6.10.4 The EC should carefully review post-trial access to the medication, especially if it is beneficial to the participant. **Box 7.5 Precautions to be taken when a placebo is used 5.** Ensure transition to standard of care/active medicine for study participants after research is completed, including post-trial arrangements for implementing any positive trial results. 7.7.1 If feasible, post-trial obligations should be emphasized with the sponsor. 7.12.10 Where possible, for example, if the drug is found useful, standard of care is not available or regulatory permissions are in place, the EC should ensure post-trial access of the IP for the participants. 7.14.4 A placebo may be used as comparator when the response to a diagnostic test is being assessed using subjective evaluation criteria, for example, skin changes in a skin prick test or for the assessment of tolerability. There have to be clear justifications in the protocol for the use of a placebo and no irreversible harm should occur to the participant. Post-trial access to the standard of care diagnostic test must be assured. 7.14.5 Safety follow-up of patients in these trials should not be limited to the duration of the diagnostic procedure but may be extended for a longer period according to the pharmacokinetic and pharmacodynamic properties of the diagnostic agent. 7.19.8 A post-trial access plan must be in place for patients who show benefit from an IP. In case it is a placebo controlled trial, those participants who have been in the placebo group may be offered post-trial access to the IP if found effective in other patients. 8.7.2 The involved stakeholders must make every effort to provide post-research public health interventions, post-research use of the findings, or sustainability of the public health action.

		12.6 Post-research benefit Sponsors and researchers should strive to continue to provide beneficial interventions, which were part of the research initiative even after the completion of research and till the local administrative and social support system is restored to provide regular services.
2017	National Ethical Guidelines for Biomedical Research Involving Children, Indian Council of Medical Research [11]	-Benefit sharing, if research on biological material and/or data may lead to commercialisation.
2017	National Guidelines for Stem Cell Research, Department of Biotechnology, Govt of India [17]	-if commercialization brings any benefits, say financial, efforts should be made to pass on the same to the donor/community wherever possible. - It is expected that a proportion of the benefit accruing from commercial use of donated tissue/cells will be returned to the community (the word "community" here refers to all potential beneficiaries including patient/s, which has directly or indirectly contributed to the product) as per the norms.
2019	New Drugs and Clinical Trials Rules [16]	**Point 2- Under definitions** (cc) Post-trial access" means making a new drug or investigational new drug available to a trial subject after completion of clinical trial through which the said drug has been found beneficial to a trial subject during clinical trial, for such period as considered necessary by the investigator and the Ethics Committee **Rule 27** Post-trial access of investigational new drug or new drug. Where any investigator of a clinical trial of investigational new drug or new drug has recommended post-trial access of the said drug after completion of clinical trial to any trial subject and the same has been approved by the Ethics Committee for clinical trial, the post-trial access shall be provided by the sponsor of such clinical trial to the trial subject free of cost (i) if the clinical trial is being conducted for an indication for which no alternative therapy is available and the investigational new drug or new drug has been found to be beneficial to the trial subject by the investigator; and

		(ii) the trial subject or legal heir of such subject, as the case may be, has consented in writing to use post-trial investigational new drug or new drug; and the investigator has certified and the trial subject or his legal heir, as the case may be, has declared in writing that the sponsor shall have no liability for post trial use of investigational new drug or new drug. Point 3- Under Responsibilities The sponsor shall provide post-trial access of the investigational drug by giving the drug free of cost to the trial subject as per directions of the Central Licencing Authority in special circumstances on the recommendations of the investigator and the ethics committee and written consent of the patient in accordance with rule 27.
2020	National Guidelines for Ethics Committees reviewing Biomedical and Health Research during COVID-19 pandemic [12]	**Under point 2- General Ethical issues** 2.8 - Post research access and benefit sharing 2.8.1 Efforts be made to communicate the research findings to the individuals/communities. 2.8.2 EC should consider the need for an *a priori* agreement between researchers and sponsors regarding post-research access of the community to successful interventions and benefit sharing if relevant 2.12 Role of Agencies/ Sponsors & Governance of Research: 2.12.5 Central regulatory authority to undertake expeditious review process for clinical trials for new drugs/ compassionate use and ensure safety/efficacy monitoring processes. 2.12.7 Facilitate post-trial access of the successful investigational drug/ vaccine free of cost to the trial participants till the same is available in the market. Table 3: Elements of an ICD **Additional elements (optional)** v. Post-research plan/benefit sharing
2023	Policy statement for the ethical conduct of Controlled Human Infection Studies (CHIS) in India, Indian Council of Medical Research [14]	7.12. Post-Study Access/ Benefit Sharing/ Publication -There may or may not be clear and direct benefits to research enrolling for CHIS. However, in case there are any benefits accruing from a study that may have relevance to participating individuals or communities, it is ethically and morally imperative to make those benefits available to the participants. Annexure 3 – Checklist for Ethics Committee - Has post-trial access to treatment for the placebo group been considered?

		7.12 Participants should be provided with detailed information about the rationale and nature of the study, including the potential risks and benefits, expected endpoints, treatment plan, duration of infection clearance and measures to minimize risks and post-trial provisions. An assessment of the level of deliberate infection with expected and unexpected outcomes, its reversibility and a comprehensive risk mitigation plan must be in place. Table 2: Elements of Informed Consent Form Post-study plan/ benefit sharing/ dissemination/ publication of results/ long term follow-up
2023	Ethical guidelines for application of Artificial Intelligence in biomedical research and healthcare, Indian Council of Medical Research [13]	None
Note: *CHIS: Controlled Human Infection Studies; DNA: Deoxyribonucleic acid; EC: Ethics Committee; ICD: Informed Consent Document; IP: Investigational Product*		