Global Policy Hackathon - Policy Overview - Indian region

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1. Introduction

Our motivation behind the scope of our analysis was to provide a comprehensive overview of the shipping policies in India. The kinds of samples in the purview of this policy analysis include Genetically Modified Organisms (GMOs), microorganisms, nucleic acids, proteins and cultures, human samples and Living Modified Organisms (LMOs). We have compared and analysed Import, Export and Domestic shipping policies.

Our methodology included a systematic and critical review of the history of shipping policies both within and outside the Indian region over a span of three decades that formed the foundation for our understanding of regulatory bodies as well as facilitate comparison of shipping policies. Finally, we also analysed the supply chain model of vaccines to get a birds eye view of policy relaxations given ensuring their rapid movement which guided our recommendations to facilitate better implementation.

2. History of Policies concerning the shipment of biological materials within and outside the Indian region

To gain an overview of the shipping policies regarding biological materials, we began with a literature review that spans 3 decades. The ensuing two subsections would delineate policies for non-human and human samples along with an elaborate discussion on the guidelines stated in the same.

2.1 Policies concerning non-human samples (Genetically Modified Organisms, microorganisms, nucleic acids, proteins and cultures)

India recognised the need to maintain separate guidelines for shipping biological materials way back in 1989 (just three years after US passed the Coordinated Framework for the Regulation of Biotechnology), where it stipulated the "Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells" Act. This act was passed in "*exercise of the powers conferred by the Environment Protection Act, 1986*" to the Department of Biotechnology (DBT),

Government of India (GoI) and stands applicable to "*manufacture, import and storage of micro-organisms and gene-technological products*". Noteworthy, this act defines the contextual use of the following terms - *biotechnology, cell hybridization, gene technology, genetic engineering and microorganisms*, thus spanning the spectrum of non-human biological materials that could be handled and shipped. It is to be noted that the above act remains applicable in cases of domestic sale, export, import, indigineous production, packaging, and storage of the non-human biological samples such as Genetically Modified Organisms (GMOs), microorganisms, nucleic acid, proteins and cultures.

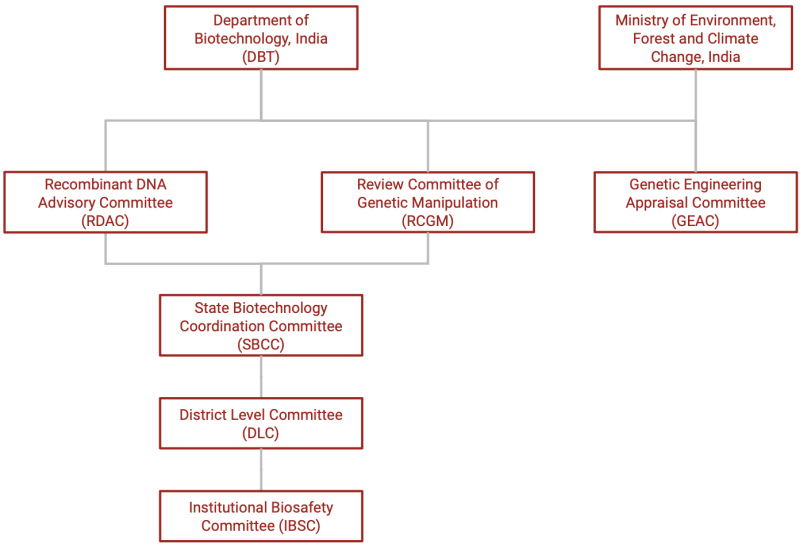

Fig 1. Hierarchy of competent authoritative bodies for non-human sample handling in India

The act assigns authorities with distinct and differential responsibilities, thereby decentralising power from the apex regulatory body which is the DBT for non-human samples handling to the Institutional Biosafety Committee (IBSC) present in every biological research-undertaking institution dealing with human and non-human biological samples across India. Intermediate bio-safety regulatory bodies such as RBAC, GEAC, RCGM are prescribed to review the latest developments in each of the fields in biology and (i) recommend guidelines and regulations in that space to the Department of Biotechnology (DBT), (ii) approve activities involving the manufacture and use considering environmental and health hazards and (iii) inspect, investigate and take punitive action in case of violence of the stipulated provisions. Fig. 1 shows the hierarchy of competent authoritative bodies for non-human sample handling in India, as defined by the 1989 Act.

RCGM, in its capacity as the intermediate working body, has the mandate to bring out manuals of guidelines specifying procedure for regulatory processes with respect to activities involving GMOs for research use, had approved simplification of the procedures and guidelines on shipment of non-human samples in 2015 (dated 22.09.2015) by providing additional authorization to IBSCs for approving "*exchange, import and export of regulated biological materials up to prescribed quantities*". Under this simplification, exchange/import/export of polynucleotides (of natural or synthetic or recombinant origin), proteins (including pure plant protein), non-living plant material, GE microorganisms and cell lines that could be handled at BL 1 containment and model organisms were clearly mentioned along with the relevant guidelines based on quantities involved for the individual research purpose. In 2020 (dated 17.01.2020), RCGM simplified the above guidelines further to "*facilitate conduct of preclinical and safety studies and the product development at GMP facilities for biological drug development*" and provided extended authority to IBSCs in this regard.

In 2017, RCGM, recognising the advancements made in the field of Recombinant DNA technology, published a guideline titled Regulations and Guidelines for Recombinant DNA Research and Biocontainment. This guideline was an extension and consolidation of the earlier guidelines concerning recombinant DNA technology, namely - Recombinant DNA Safety Guidelines, 1990; Revised Guidelines for Safety in Biotechnology, 1994; Revised Guidelines for Research in Transgenic plants. This guideline covers regulation of biosafety with regards to handling and storing microorganisms, animals, plants, insects and microorganisms during import/export, research, disposal, and emergency. The regulatory aspect involved both precise guidelines in terms of protocols and infrastructural measures that needed to be taken by the institutes. The guideline stipulates the same approval agencies for the movement of GE organisms, non-GE hazardous microorganisms and products and the vectors of diseases alike the 1989 Act.

However, the 2017 Regulations for Recombinant DNA research sheds extensive light on the shipment protocols to be followed, in accordance with Section 18 of The Foreign Trade (Development & Regulation) Act, 1992 No. 22. For instance, import of GM plants and planting materials has been stated to require a permit to be issued by the Director, National Bureau of Plant Genetic Resources, New Delhi (NBPGR) of the Indian Council of Agricultural Research (ICAR). The permit is then issued subject to the issue of import authorization letter by the RCGM, where it is requisite to clearly specify the scope of the import and required safety measures to be adopted during R&D work. The import consignment would then enter through the New Delhi Airport where customs shall verify the documents and hand it over to

NBPGR. NBPGR then would verify the contents and the accompanying documents (Import permit, Phytosanitary Certificate, Supplier Declaration that the GM material does not contain any embryogenesis deactivator gene). NBPGR is also tasked to test for the absence of diseases, pests and other undesirable material, absence of embryogenesis deactivator gene and for the presence of the declared transgene. Subject to satisfactory outcome of the tests, NBPGR would then hand over the consignment to the importer. Parts of the material (5% or 5 to 50 seeds whichever is less) will be kept at NBPGR in a double lock system in the presence of the importer, which will act as source material in case of any legal dispute.

Concerning export of non-human samples, especially that of GM plants and planting material, besides being regulated by the Environment Protection Act, 1986 and The Foreign Trade (Development & Regulation) Act, 1992, attracts the provisions of Biological Diversity Act, 2002 which states the access and use of biological resources in India. It stipulates the *Advance Informed Agreement* procedure of the Cartagena Protocol to be followed that applies to the first intentional transboundary movement of LMOs for intentional introduction into the environment of the party of import.

2.2. Policies concerning human samples

The Ministry of Health and Family Welfare (MOH&FW) under the Government of India issued a guideline for the transfer of human biological material in 1997 titled Guidelines of Transfer of Biological Material. The materials that fall under this category include organs and parts of organs; cells and tissue; subcellular structures and cell products: blood; gametes (sperm and ova); embryos and fetal tissue; wastes (urine, faeces, sweat, hair, epithelial scales, nail clippings, placenta etc.); and cell lines from human tissues. By the guidelines,

1. Exchange of material for therapeutic purpose to patients does not require authorisation
2. Authorisation is not required when the institute participating in collaboration with foreign institute is under World Health Organization (WHO), Indian Council of Medical Research (ICMR), Council of Scientific and Industrial Research (CSIR) or such government overseen bodies
3. For private institutes, medical colleges and other educational and research institutes under the University Grants Commission (UGC), proposal for movement of human biological samples is to be submitted to the ICMR for obtaining an endorsement from the Health Ministry Screening Committee (HMSC), for which ICMR is the Secretariat.

The ICMR sets up the committee with experts from relevant fields for discussing proposals on a case by case basis before making a decision. It is to be noted that HMSC was constituted by GoI way back in the early 1980s to "*screen and approve the international collaborative proposals in the field of biomedical health research*".

The Committee comprises distinguished representatives from the Ministry of Health & F.W. (Department of Health, Family Planning, NACO, AYUSH and Directorate General of Health Services); Ministry of External Affairs; Ministry of Finance; Department of Biotechnology; Department of Science and Technology; Directorate General of Armed Forces and Medical Services and is chaired by the Secretary, Department of Health Research (DHR), MOH&FW, GoI.

It is noteworthy that ICMR has signed Memorandum of Understanding (MoUs) or Letters of Intent (LoIs) or given joint statements with several countries across the world and whenever there is a transfer of human biological material from India to the foreign lab, or vice-versa, the 1997 guidelines impose a submission of duly signed Material Transfer Agreement that contains the following information: nature, number and quantity (% wise) of material to be sent; purpose/need of transfer; type of investigation(s) to be done utilizing the material; institution(s)/scientist(s) to whom material is to be sent along with their addresses.

However, in 2016 a gazette notification from the Ministry of Commerce and Industry regarding the import/export policy for Human Biological Samples for commercial purposes nullifies the requirement of any approval for the transfer of human biological samples as long as the institute/agency involved in the movement submits an undertaking to follow the WHO/DGFT (Directorate General of Foreign Trade) laid guidelines regarding handling, shipping, packaging and disposal; along with a document containing the sample details.

Shipping/Packaging: For both human and non-human biological samples, the shipping and packaging policies in India follow the 2015-2016 WHO guidelines for Transport of Infectious Substances. The guidelines are listed for infectious substances (category A, B, exemptions), biological products, GMOs, medical and clinical wastes. The guideline specifies that all biological samples need to be assigned UN numbers based on their type and follow shipping/packaging regulations based on the UN number. The following are the UN numbers for infectious agents.

- Infectious substances category A, affecting humans: UN 2814
- Infectious substances category A, affecting animals: UN 2900
- Infectious substances category B: UN 3373
- Exemptions: No UN category

It also includes the regulatory body based on mode of transport, whose regulations need to be followed for determining whether the mode of transport is applicable, and if yes, what are the shipping and packaging procedures. For India, the major modes of international transport include air and ship which are regulated by International Civil Aviation Organisation (ICAO) and International Maritime Organisation (IMO) respectively.

In 2018, India joined the Australia group, an International informal arrangement that aims to minimise the proliferation of chemical and biological weapons, established in 1985. The Australia group holds a control list on dual use items, which need to follow the guidelines as stipulated in the Guidelines for Transfers of Sensitive Chemical and Biological Items, 2015. It hence aims to achieve its goal of regulating bioweapons by laying out clear provisions for export licensing measures for items in the control lists.

2.3 Table of Policies

Policy Name	Country/ Region	What biological materials?	What kinds of shipping?	Limits	Relevant policy bodies	Other notes	Link to details of policy
Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells (1989)	India	GMOs, microorganisms, nucleic acids, proteins and cultures	Import, Export and Domestic	Power was concentrated at RCGM	DBT, RCGM, GEAC	Limitations led to revisions in 2015 and 2020, to distribute power to IBSC	[1]
Coordinated Framework for Regulation of Biotechnology (1986)	USA	Recombinant DNA Derived products including GMOs, Chemically synthesised antigens, Monoclonal Antibodies, Cell Cultures, Organisms and Vectors	Import, Export and Domestic	Not applicable (NA)	FDA, FSIS, APHIS, EPA	NA	[2]

Regulations and Guidelines for Recombinant DNA Research and Biocontainment (2017)	India	GMOs, microorganisms, nucleic acid, proteins and cultures	Import, Export, and Domestic	The kinds of shipping and their relevant protocols were unclear for biological samples other than plants	DBT, RDAC, ICAR, NBPGR	NA	[3]
Working Safely with Potentially Hazardous Biological Materials, (2015)	USA	Infectious materials	Import, Export and Domestic	NA	CDC, NIH	NA	[4]
Guidelines of Transfer of Biological Material, (1997)	India	Human samples	Import, Export and Domestic	The gazette notification that was passed mentions that the nullification is for commercial purposes, but includes research laboratories/institutes in the applicable bodies, leading to lack of clarity. In such cases, nullification may lead to undesirable outcomes due to the lack of proper oversight.	ICMR, HMSC	A gazette notification was passed in 2016 that nullified authorisation for movement of human samples	[5]
Transport of Infectious Substances, (2015-2016)	Member countries of WHO	Human and non-human samples	Import and Export	NA	WHO and relevant bodies present in each country overseeing	The guideline specifies that all biological samples need to be assigned UN numbers based on	[6]

					biosafety	their type and follow shipping/packaging regulations based on the UN number	
The Foreign Trade (Development & Regulation) Act, 1992 (Section 18)	India	Genetically Modified Food, Feed, Genetically Modified Organism (GMOs) and Living Modified Organisms (LMOs)	Import	NA	DBT, GEAC, RCGM	The import of GMOs/LMOs will be governed by the provisions of the Environment Protection Act, 1986 and Rules 1989	[7]
Biological Diversity Act (2002)	India	Human and non-human samples	Export and Domestic	NA	National Biodiversity Authority (NBA)	Biological resource(s) occurring in India or knowledge associated thereto for research or for commercial utilisation or for bio-survey and bio-utilisation should not be obtained without prior approval of NBA	[8]
European Biological Resource Centers Network Information Resource (2013)	Members of European Union	Human and non-human samples	Export, Import and Domestic	NA	EBRC	Specifies the guidelines for shipping, packaging for different transport modes	[9]
Guidelines for Transfers of Sensitive Chemical and Biological Items (2015)	Members of the Australia Group	Human and Animal Pathogens; Toxins	Export	NA	Australia Group, BTWC, National Government agencies	India joined the Australia group in 2018	[10]

3. Comparison with other regions

To gain an idea on where India stands in terms of bio-policy in the global field, we looked into the shipping policies of countries, namely the United States of America, Germany and Australia, that were from three different continents. The following table summarizes the comparison:

	US	Germany	Australia
Dignitary body overseeing requests	National Institute of Health Quarantine Permit Service Office (NIH QPSO)	There are no import/export permits required for well declared biological samples. An end user capability declaration is required in all cases.	Biosecurity Import Condition Systems (BICON)
Materials considered in request	Biological products, diagnostic or infectious materials	All biological samples that do not fall under dual use items regulation	Toxic substances, Infectious substances, GMOs
Bodies issuing permits	Import/transfer permit: Center for Disease Control and Prevention (CDC) Export: Department of Commerce For import/export concerning domesticated plants/animals: US Department of Agriculture For import/export concerning fish and wildlife: US Fish and Wildlife Service Regulation	Federal Office for Economic Affairs and Export Control	Import: Department of Agriculture, Water and the Environment Biological Imports Program Export: Defense of Strategic Goods and Technology
Packaging guidelines	Department of Transportation (DOT), Federal Aviation Authority (FAA) International Air Transport Association (IATA)	International Civil Aviation Organisation (ICAO), International Maritime Organisation (IMO), International Carriage of Dangerous Goods by Rail (RID), European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR)	National Transport Commision (NTC), Office of Gene Technology Regulator (OTGR)

Based on our efforts, we realised that India was not lagging behind in terms of updating its policies for biological shipping at the global front. The implementation of the 1989 Act serves as a great example for this. However, there exist lacunae in the Indian policies which will be discussed in section 6.1.

4. Methods of Research

Our modus operandus involved the following sequence of events:

1. As our team members got familiar with the regulatory bodies in India such as the DBT and ICMR during our iGEM participation in 2019, we searched the relevant policies on their websites and came across the 1989 Act and 1997 rules concerning non-human and human biological materials, respectively.
2. In addition, the RCGM repository entailing the rules, acts and guidelines passed by the Department of Biotechnology so far helped us gain access to a lot of relevant policies required for this hackathon.
3. Furthermore, to compare and contrast the biosafety and shipping policies in India with other regions of the world, we chose a representative country from 3 different continents - USA from the American region, Germany from the European region and Australia from the Australian region.
4. Our team also looked into the supply chain model of vaccines to understand the policy relaxations given by the GoI for ensuring their rapid movement from which we got inspiration for prospective changes in the implementation level.

5. Case study of policy relaxations for SARS-CoV-2 research in India

The COVID-19 pandemic has brought about an enormous impact on the policies that govern the shipment of samples across and within the Indian borders. With GoI's strong commitment to furnish an *enabling ecosystem* for research to develop diagnostic tests, therapeutics and vaccines for COVID-19. In endeavouring this, a sharing mechanism for biological/clinical samples and data between institutions and researchers was imperative and was realized by the setting up of 17 biorepositories across India. The Office Memorandum dated 07.06.2021 titled the "*Standard Operating Procedures for exchange of infectious biosamples/biospecimens from biorepository*" recognizes these biorepositories and have given rise to the production of two indigenously developed vaccines, Covishield and Covaxin. India was self-reliant of its

vaccines and was able to export vaccines to many needy countries in the South East Asian region. Had not these biorepositories been identified and established, the enormous research carried out from India on SARS-CoV-2 research and development of tests, therapeutics and vaccines would not have been possible in the last two years. As a result, India is able to administer 7-10 million doses of vaccines each day, thanks to the efficient supply chain that was established as a result of this sharing mechanism. We believe that such a mechanism could serve as a positive precedent for policy changes, thus expanding this successful model to research on other biological samples.

6. Way Forward

6.1 Analysis

The following are the limitations we could identify from the policies governing handling of biological samples in the Indian region (refer to Table of Policies for the policies we have studied).

- Based on the Guidelines of Transfer of Biological Material Policy in 1997, and the update to it in 2016, all human samples can be freely imported/exported/transferred within the country, as long as the institutes/agencies submit a document with the details of the samples along with a declaration saying they would follow WHO/DGFT guidelines, *for commercial purposes*. However, the agencies that could make use of this update include research laboratories and institutes. Hence, there seems to be a conflict regarding to whom the updated notification applies to.
- In addition, although India was able to codify policies/guidelines for biotechnology and genetic engineering/technology way back in the 1990s, the policy language is vaguely defined towards distinct shipment protocols to be followed for each kind of biological sample. More focus has been shed on the biosafety and biocontainment aspects and not for sharing and shipping of such samples across and outside the Indian region. It was only after the onset of the pandemic, India realized this lacuna and established biorepositories and a sound sharing mechanism along with mention of SoPs for movement of SARS-CoV-2 related samples. We anticipate and believe that this model could be extended to other biological samples by amending the 1989 Act and 1997 Rules, thus expanding their purview.
- India's role as a member of the Australia Group in 2018 implies that it is liable to follow the guidelines as specified by the Guidelines for Transfers of Sensitive Chemical and Biological Items, 2015. However, in the Indian policies, no mention has been made with regards to this, and the

policies such as the 1989 Act and 1997 rules have not been updated to demarcate the biological materials that fall under the category of controlled dual use items. Not doing so might lead to a lapse in following defined precautionary measures to prevent bioweapons proliferation.

Considering synthetic biology, India is yet to formally come up with its national strategy on it — both policy and regulatory. Regulatory bodies are yet to form India's policy and regulatory framework focusing on defining what constitutes the science of synthetic biology; what kinds of research and development priorities will be made for the public sector; what will be the guidance for the private sector in synthetic biology research in the future that considers all relevant policy frameworks. This is directly reflected in the shipping policies of samples associated with synthetic biology work.

The Act passed in 1989 touches upon the following areas *biotechnology, cell hybridization, gene technology, genetic engineering and microorganisms.* There is a lacunae for constructive shipping policies tailored to the needs of synthetic biology work since there is a fundamental lack of understanding as to what synthetic biology constitutes. This translates to stakeholders having to navigate different policy frameworks since, in some cases, the application of their samples do not fall into the purview of any shipping policy. This is true both at the national and global front, based on our research in the USA, Germany and Australia.

6.2 Proposal

Our proposal involves using the supply chain model of vaccine distribution as a precedent for policy changes. The way forward is to include shared facilities that serve multiple stakeholders together.

At a policy level this would include

- *Making* provisions and identifying overlaps in policy specific to samples for synthetic biology work in both the private and public sectors.
- *Recognising* and *including* the end user in the policy framework as stakeholder for synthetic biology samples/work.

At an implementation level this would include -

- Biorepository capacity building across the nation to include synthetic biology samples, as extension of the biorepositories created for the pandemic purpose (Office Memorandum, DBT,

dated 07.06.2021 titled the "*Standard Operating Procedures for exchange of infectious biosamples/biospecimens from biorepository*")

- Establishment of Biofoundries - places for distributed manufacturing of biological parts to accelerate, automate and streamline research and innovation. Streamlining and building of pipelines has a direct effect on policy frameworks since regulatory bodies would have to accomodate efficient shipping protocols based on use cases of biological parts. This would eventually lead to consolidation of shipping of biological parts within the country in a regulated manner and recognition of synthetic biology within the policy framework
- Integration of biorepositories and biofoundries with national and international regulations

Fig 2. A threefold implementation solution to ease shipping of synthetic biology components in India

Based on our research, we figured that Indian researchers, institutes and agencies, would have to shuffle through a lot of websites and guidelines to understand which regulations apply to their biological material, and what dos and don'ts they would have to follow to responsibly ship their materials. So we put the 'hack' in this hackathon and came up with a website, an all purpose guide for biological shipping in India. We hope that this would serve as a ground material for not just those looking for policy details, but also as a foundation for understanding lacunae and bridging gaps in existing policies.