Blood Safety in India:

Regulatory Mapping and Analysis

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I. Introduction

Access to safe blood is considered one of the most vital components of modern-day healthcare. In India, issues related to access and safety of blood have emerged time and again. While at some places, collected blood is available in excess and unused blood needs to be discarded, at other places there is a scarcity of safe blood.[1] And wherever it is available, there are concerns regarding its safety.

The Supreme Court, in 1996, issued several directions to ensure blood safety, which included setting up the National Blood Transfusion Council (NBTC) and State Blood Transfusion Councils (SBTC), mandating licensing of blood banks, framing an immediate as well as long term plan for blood safety, and passing separate legislation for regulating blood processes.[2] While other directions have been implemented, no action has been taken with respect to implementing a long term plan for blood safety and having a separate legislation in place, and the issues with respect to blood safety persist. A matter before the Gujarat High Court in 2012 brought to light a case in which 23 minor children were found HIV positive due to negligence on the part of a single government hospital during blood transfusion.[3] Even now, many blood banks continue to run without following appropriate safety standards, particularly, with respect to the testing of collected blood for Transfusion Transmissible Infections (TTIs).

The current pandemic too highlighted complications related to blood and blood transfusion services (BTS). The supply chain of blood, particularly for patients who need regular transfusions, was impacted.

These issues point towards a larger gap in the current regulatory framework around BTS. The inherent risks of blood and the complexity of providing adequate, timely and equitable access to safe blood products require an organized national or regional blood regulatory system. Within that system, a competent blood products regulatory authority assures that appropriate standards are met to produce blood products and monitoring of blood safety.[4]

While unsafe blood is a matter of concern for everyone, it has more effect on people who need blood transfusion regularly like thalassemia patients. One such patient group-Thalassemia Patients' Advocacy Group (TPAG) has been working on the cause of Blood Safety since 2017. One of the objectives of their Blood Safety Mission is to study regulatory gaps with respect to blood safety.

To this end, TPAG approached the Vidhi Centre for Legal Policy to map the current regulatory framework with respect to blood safety in India and its comparison with international best practices, and highlight the gaps, if any.

As part of this study, Vidhi has reviewed statutes, rules, regulations, executive orders/notifications, guidelines, policies, reports, judgments, and literature related to the regulatory aspect of blood safety in India. A mapping of this legal framework can be found as an Annexure to this report. While we have attempted to cover the entire regulatory landscape related to blood, this by no means should be considered exhaustive.

Since one of the objectives of this study is to analyse India's blood regulatory framework against global standards, we have used the World Health Organisation's (WHO) Assessment Criteria for National Blood Transfusion System for this purpose. As a limitation of this study, we have analysed India's regulatory framework only against six criteria and their associated indicators out of a total of fourteen criteria set out in the tool. These six criteria are directly related to the regulatory aspects of BTS.

The gaps that have emerged out of this analysis have been highlighted along with recommendations for the way forward in the concluding chapter.

[1] Kevin James Shreya Shrivastava, 'Every Drop Matters' The Hindu (13 February 2019) <https://www.thehindu.com/opinion/op-ed/every-drop-matters/article26261466.ece> (last accessed 20 October 2020)
[2] Common Cause v. Union of India, 1996 SCC (1) 753
[3] Ravjibhai Ramabhai Sondarwa & ors. v. State of Gujarat & ors., 2012 SCC Online Guj 3767.
[4] World Health Organisation, Assessment Criteria for National Blood Regulatory Systems (2012) <https://www.who.int/bloodproducts/NationalBloodRegSystems.pdf?ua=1> (last accessed 27 October 2020)

II. Blood Safety

Blood safety is a dynamic concept which changes with advancements in technology as well as with the discovery of new infections and viruses. Thus, while there need to be some basic regulatory checks and set standards to guarantee the safety and quality of blood, they should be ever evolving.

In contrast, India is saddled with a pre-independence legislation, with fragmented and complicated structures in place for Blood Safety. Blood is considered a 'drug' under the Drugs and Cosmetics Act, 1940 (D&C Act)[5] and thus, by default, the regulation of blood banks falls under the domain of the Drug Controller-General of India (DCGI) just like any other manufacturer or storer of drugs. The Central Drugs Standard Control Organisation (CDSCO), at the apex of which is the DCGI, primarily comprises officers and staff with technical expertise in pharmaceuticals, rather than blood and blood products.

Further, the Drugs and Cosmetics Rules, 1945 (D&C Rules) lay down the requirements for the collection, storage, processing and distribution of whole human blood, human blood components by blood banks and manufacture of blood products[6] as well as the requirements for the functioning and operation of a blood bank and for preparation of blood components.[7]

BTS were initially housed under the Directorate General of Health Services (DGHS) until they were shifted to the National Aids Control Organisation (NACO) after its formation in 1992.[8]

A Supreme Court judgment in 1996 in *Common Cause v. Union of India*[9] marked a milestone in the history of blood safety in India. This judgment made the regulatory process stringent by making the licensing of blood banks mandatory. It also led to the setting up of the technical expert bodies-the NBTC and SBTCs. NBTC is housed under NACO and is the apex policy making body for issues pertaining to blood and plasma. However, NBTC does not find any mention in the D&C Act or the Rules. As a result, standards for Blood Banks and BTS published by NBTC are not enforceable. They are used only as a guiding document by State Health Authorities, Licensing Authorities, the administrations of hospital-based blood banks and blood banks run by charitable organisations to understand the basic standards required to operate a blood bank in the most efficient way and provide quality service delivery.[10] NBTC also issues non-binding guidelines on various aspects of BTS from time to time.

After the 2017 Amendment to the D&C Rules, SBTCs now find mention in the D&C Rules, to the extent that blood banks run by registered voluntary or charitable organisations must be recognised by SBTCs before organising a donation camp.[11]

Even after several amendments to the D&C Rules, particularly regarding BTS and almost 25 years after the *Common Cause* judgment, India's regulatory landscape in terms of blood safety is still not satisfactory as compared to international standards and global best practices. We will be looking at regulatory mapping around BTS using the lens of blood safety in this chapter. We will compare it with international best practices in the following chapter.

Elements of Blood Safety

The safety of blood transfusion services must be ensured at the stage of collection, after collection and before transfusion, and during transfusion. As a result, there are three important elements of blood safety that need to be ensured:

1. Safe Donor
2. Safe Blood

[5] Section 3(b)(i): All medicines for internal or external use of human beings or animals and all substances intended to be used for or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in human beings or animals, including preparations applied on human body for the purpose of repelling insects like mosquitoes.
[6] Part XB, D&C Rules
[7] Schedule F, Part XIIB, D&C Rules
[8] National Aids Control Organisation, Blood Transfusion Services (BTS) <http://naco.gov.in/blood-transfusion-services> (last accessed 27 October 2020)
[9] 1996 SCC (1) 753
[10] National Aids Control Organisation, 'Standards for Blood Banks and Blood Transfusion Services' (2007) <http://naco.gov.in/sites/default/files/Standards%20for%20Blood%20Banks%20and%20Blood%20Transfusion%20Services.pdf> (last accessed 27 OCtober 2020)
[11] Schedule F XIIB, Heading II-Blood donation camps

3. Safe Transfusion

We will be capturing and analysing in detail the regulatory landscape and safeguards around each of these three elements in the following sections.

Safe Donor

As a first step towards blood safety, selecting a healthy and safe donor is the most vital step. This is to ensure that unsafe blood is prevented at the stage of collection itself. As recommended by the WHO, voluntary non-remunerated altruistic donors are the safest.[12] To understand how blood safety is ensured at this stage, it is important to look at the provisions regarding donor selection under the current framework.

The D&C Rules define "donor as a person who voluntarily donates blood after he has been declared fit after a medical examination, for donating blood, on fulfilling the criteria given hereinafter, without accepting in return any consideration in cash or in-kind from any source but does not include a professional or a paid donor."[13]

As per the criteria for blood donation referred to in the above definition, no person can donate blood and no blood bank can draw blood from a person, more than once in three months. The donor needs to be in good health, mentally alert and physically fit and should not be an inmate of a jail, have multiple sex partners or be a drug-addict. Further, the donor also needs to fulfil requirements-the donor should belong to a specified age group, have a minimum specified weight, with blood pressure and haemoglobin within the specified range, should be free from acute respiratory diseases, skin diseases and those transmissible by blood transfusion. There are periods of deferment for people under certain circumstances, for example, women who had abortions are deferred to donate blood for 6 months. Persons who have received blood transfusions themselves cannot donate blood for 6 months after their last transfusion. Further, persons suffering from specified diseases including cancer, leprosy etc. are barred from donating blood.[14]

After the *Common Cause* Judgment[15] professional donors have been banned in India. As a result, one of the conditions for obtaining a license to run a blood bank is that the licensee shall neither collect blood from any professional donor or paid donor nor shall they prepare blood components and/or manufacture blood products from the blood drawn from such a donor.[16]

Donor Selection

In addition to the criteria for blood donation given under the Rules, NBTC's Standards for Blood Banks and BTS also include standards for Donor Selection. These standards focus on donor recruitment and retention, information to be supplied to the donor, pre and post-donation counselling and referrals, medical history of the donor and criteria for blood donation that build on what is already prescribed in the Rules. However, as stated above, these standards are non-binding.

The NBTC recently issued uniform Guidelines for Blood Donor Selection and Blood Donor Referral in 2017. These guidelines also emphasise the recruitment and retention of voluntary non-remunerated donors. They lay down a step-by-step process for donor selection with important details like donor consent mechanisms, pre-donor counselling, donor's health questionnaire, information about tests that will be conducted on the donated blood, post-test counselling if blood is tested positive for TTIs, and referrals if needed based on the test results. These guidelines are followed across Blood Banks as per our conversations with a Blood Bank personnel based in Delhi. However, they are not formally part of the conditions that must be met to obtain a licence as a blood bank and thus, they are non-enforceable in nature.

Replacement Donations

Though regular voluntary non-remunerated blood donation is encouraged globally as well as in India, replacement donation is very common in India. In the case of replacement donation, relatives of patients in need of blood are asked by hospitals to arrange for the same expeditiously. This blood is not

[12] WHO Expert Committee on Biological Standardization Sixty-seventh report, 'Guidelines on management of blood and blood components as essential medicines' (2017) <https://www.who.int/bloodproducts/brn/ManBloodEM_GL_WHO_TRS_1004_web_Annex_3.pdf?ua=1> (last accessed 27 October 2020)

[13] Rule 122EA(g), Part XB

[14] Schedule F Part XIIB, D&C Rules

[15] 1996 SCC (1) 753

[16] Rule 122-P, D&C Rules

used for the patient herself but is intended as a replacement for the blood that is actually used. A lot of times, replacement donors are represented as voluntary donors. Currently, hospitals in India depend heavily on replacement donations for their blood supply, which in effect creates more risks insofar as the prevalence of TTIs in donated blood is concerned. As per a study conducted in 2017, replacement donation constituted a major source of blood supply in hospital-based blood transfusion services and the prevalence of TTIs was higher among them in comparison to first-time voluntary donors. Out of a total of 850 first-time donors, voluntary donors were 109 (12.82%) and replacement donors were 741 (87.18%). Prevalence of TTIs among voluntary donors was very low. All donors were seronegative for HIV and malaria. Prevalence of HBV, HCV, and syphilis was higher in replacement donors.[17]

While the National Blood Policy states that no hospital should depend on replacement donors and that replacement blood donation should be gradually phased out, none of the rules, standards or guidelines currently focus on reducing or eliminating replacement donation. The Operational Guidelines for the Voluntary Blood Donation Programme released by the NBTC state that voluntary blood donation organisations should urge lawmakers to enact legislation, where necessary, to prohibit the practice of paid or family replacement donation.[18]

In 2017, the Maharashtra SBTC issued a circular to blood banks across Maharashtra, directing them to stop replacement blood donation and instead achieve 100% voluntary blood collection for patients, on the condition that their No Objection Certificate (NOC) would be revoked if they did not improve the situation. Particularly, hospitals were asked to conduct more blood camps instead of asking for replacement donations. Hospitals, however, find it easier to put the responsibility to get donors on patients' relatives instead of organising blood donation camps, which involve more effort.[19]

Blood Donation Camps

Under the D&C Rules, only a licensed designated Regional Blood Transfusion Centre, a licensed Government blood bank and the Indian Red Cross society were initially allowed to organise blood donation camps.[20] Since private hospital blood banks were barred from organising camps, they were compelled to opt for replacement donations.

After the 2017 Amendment to the D&C Rules, licensed blood banks run by registered voluntary or charitable organisations recognised by their respective State or Union territory Blood Transfusion Council, and private hospital blood banks have been allowed to organise blood donation camps.[21] However, blood banks, particularly, hospital-based blood banks, continue to resort to replacement donations even now.

Safe Blood

The next important step post collection of blood is to ensure that the collected blood is safe from any TTIs by way of testing. As per the WHO, obtaining data on testing of donor blood is critical in getting a global picture of the blood safety situation.[22]

Ensuring blood safety at this stage has two important elements - first, the TTIs for which blood is tested and second, the technology used for testing.

While the current regulatory framework focuses on the former, there is no specific mandate with respect to the latter. As per the testing requirements given under the D&C Rules, it is the responsibility of the licensee to ensure that the whole blood collected, processed and supplied conforms to the standards laid down in the Indian Pharmacopoeia and other tests published, if any, by

[17] Singh PJ, Bhatt H., 'Is there a need to phase out replacement blood donors by voluntary blood donors in hospital-based blood transfusion services?' (2017) 6(2) Iraqi J Hematol <https://www.researchgate.net/publication/320284433_Is_there_a_need_to_phase_out_replacement_blood_donors_by_voluntary_blood_donors_in_hospital_based_blood_transfusion_services> (last accessed 27 October 2020)

[18] National Aids Control Organisation, 'Voluntary Blood Donation Programme- An Operational Guideline' (2007) <http://naco.gov.in/sites/default/files/voluntary%20blood%20donation.pdf> (last accessed 28 September 2020)

[19] Jyoti Shelar, Blood banks told to stop replacement donation The Hindu (12 July 2017) <https://www.thehindu.com/news/cities/mumbai/blood-banks-told-to-stop-replacement-donation/article19260234.ece> (last accessed 28 September 2020)

[20] Schedule F XIIB-II Blood donation camps, D&C Rules

[21] Drugs and Cosmetics (Eighth Amendment) Rules, 2017.

[22] World Health Organisation, 'Global Status Report on Blood Safety and Availability' (2016) <https://apps.who.int/iris/bitstream/handle/10665/254987/9789241565431-eng.pdf;jsessionid=A9220FB295EE1E763AC7322F87AE8675?sequence=1> (last accessed 28 September 2020)

the Government. It is further prescribed that the samples of every blood unit should be tested by the licensee, before use, for freedom from HIV 1 and HIV II antibodies. Each blood unit should also be tested for freedom from Hepatitis B surface antigen, Hepatitis C Virus antibody, VDRL and malarial parasite.[23]

The products manufactured from blood also need to conform to the standards specified in the Indian Pharmacopoeia and where standards of any product are not so specified, the standard for such product may conform to the standard specified in the United States Pharmacopoeia or the British Pharmacopoeia. The final products also need to be tested for freedom from HIV I and HIV II antibodies, Hepatitis B surface antigen and Hepatitis C Virus antibody.[24]

The Rules further specify that Written Standard Operating Procedures (SoP) need to be maintained by all Blood Banks, which shall include all steps to be followed in the collection, processing, compatibility testing, storage and sale or distribution of blood and preparation of blood components. The SoP should include criteria used to determine donor suitability, blood collection procedure, including in-process precautions, all tests and repeat tests performed on blood and blood components during processing, and pre-transfusion testing.[25] While the Rules prescribe the board outline of the SoP, the details are left to the discretion of Blood Banks. Further, these SoPs need to be made available to the personnel such as medical officer, blood bank technicians, registered nurses, and technical supervisor for use in the concerned areas. However, there is no mandate to make them available to the donors and patients availing BTS.[26]

Testing Technologies

The D&C Act regulates testing kits/reagents to be used for blood screening by means of the Medical Devices Rules, 2017. Some commonly adopted technologies as approved by the CDSCO for TTI testing are enzyme-linked immunosorbent assay (ELISA), or nucleic acid testing (NAT). However, there is no mandate under the Act or the Rules with respect to what technology should be adopted for testing, and it is left to the discretion of individual blood banks.

NAT has lately emerged as one of the most effective screening methods to enhance blood safety given its efficacy in detecting TTIs.[27] NAT has been made mandatory for blood testing in the United States and European Union, however, in India, it is neither mandatory nor widely adopted given its high cost.[28]

Under the current framework, blood banks can adopt any testing technologies they prefer. They are allowed to charge a processing fee depending on the specialised tests/technology they are adopting. For example, blood banks using NAT may charge up to INR 1200 per whole blood unit, whereas those using IV Generation ELISA may charge INR 50 each for HIV and HBsAg, and INR 150 for HCV as per NBTC's Guidelines on Recovery of Processing Charges for Blood and Blood Components.[29]

While the current framework provides flexibility to blood banks to adopt testing technologies as per their affordability and convenience, this leads to non-uniformity in the safety of blood across India. Blood banks with small workloads (5-10 donors/day) compromise safety by using rapid tests, which are associated with a delay of over 1 week in antibody detection.[30]

Licensing of Blood Banks

One major regulatory check towards ensuring blood safety at this stage is the licensing of blood banks under the D&C Act. Licensing was made mandatory in 1996 after the SC judgment in *Common Cause*.[31] For a blood bank to get a license, the application must be made at the state level to the Licensing Authority. The licensing authority must verify the

[23] Schedule F Part XIIB, Heading I, Item K, D&C Rules
[24] Schedule F PArt XIIB, Heading III, Item G, D&C Rules
[25] *Ibid*
[26] *Ibid*
[27] Shyamala V., 'Factors in enhancing blood safety by nucleic acid technology testing for human immunodeficiency virus, hepatitis C virus and hepatitis B virus' (2014) 8(1) Asian J Transfus Sci <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3943137/> (last accessed 27 October 2020)
[28] Gupta S, Popli H., 'Regulation of Blood and Blood products in India, USA and EU' (2018) 6(2) International Journal of Drug Regulatory Affairs <http://ijdra.com/index.php/journal/article/view/246> (last accessed 27 October 2020)
[29] See: http://naco.gov.in/sites/default/files/Guidelines%20on%20recovery%20of%20Processing%20Charges%20for%20Blood%20%26%20Blood%20Components.pdf
[30] Chandrashekar and Kantharaj, 'Legal and ethical issues in blood transfusion, (2014) 58(5) Indian Journal of Anaesthesia <https://www.researchgate.net/publication/270005602_Legal_and_ethical_issues_in_safe_blood_transfusion> (last accessed 27 October 2020)
[31] 1996 SCC (1) 753

information provided and will cause the manufacturing and testing capabilities of the establishment to be inspected. If satisfied that the bank will be in a position to fulfil the requirements under the Rules, it will forward the application to the Central License Approving Authority i.e., the Drug Controller. The Drug Controller, after causing the inspection of the establishment by an Inspector accompanied by an expert in the field if necessary, and on being satisfied that the applicant can fulfil the requirements prescribed, may grant the license.

However, there are several issues with this system. The dual licensing system for grant or renewal of license has made the licensing process very tedious and slow with no prescribed time limits. The requirements for blood banks, which form the basis for granting licenses, are not updated rationally. The Inspectors who oversee inspecting establishments for manufacturing and testing are not experts in the field. There is also no mandatory mechanism to audit licensed blood banks.

Safe Transfusion

Appropriate clinical use of blood is an important aspect of blood safety just like the previous two elements. This is to reduce unnecessary exposure of patients to allogeneic blood with its attendant risks while ensuring judicious utilization of a scarce resource.[32] WHO, in its Guidelines on the management of blood and blood components as essential medicines, emphasises the importance of an appropriate blood transfusion system consisting of care centres (hospitals, surgical centres and outpatient facilities; and sometimes ambulances) that utilize blood and blood components for the treatment of patients. Such centres need to have a variety of transfusion-related responsibilities, which include storing blood and blood components appropriately, developing appropriate procedures for further processing of the blood and blood components prior to transfusion, appropriate pre-transfusion testing of patients and cross-matching to ensure compatibility of the blood component to be transfused, maintaining appropriate records to ensure that blood components can be traced to their recipients and from recipients back to their donors, reporting adverse events and reactions etc. Member countries can build their Transfusion Guidelines based on these.

However, as per WHO's 2016 Global Status Report on Blood Safety and Availability, fifty-four countries reported not having such national guidelines, or their status was unknown. Although 126 countries reported the existence of national transfusion guidelines, that does not indicate whether they were effectively implemented.[33]

In India, while NBTC has issued guidelines related to different aspects of BTS, there are no transfusion triggers[34] or national guidelines with respect to the safe transfusion of donated blood in a patient. The D&C Act or the Rules do not have any provisions with respect to informing those receiving transfusion about the blood being transfused.[35]

Haemovigilance Program

The CDSCO updates on its website's public notices with respect to drug related adverse reactions. However, there was no mechanism in place until 2012 to particularly trace any adverse reactions in the blood transfusion chain. In 2012, the National Institute of Biologics (NIB) and the Indian Pharmacopoeia Commission jointly launched the Haemovigilance Program of India. It is a set of surveillance procedures covering the whole transfusion chain from the collection of blood and its components to the follow-up of its recipients. It is intended to collect and assess information on unexpected or undesirable effects resulting from the therapeutic use of labile blood products and to prevent their occurrence and recurrence.[36]

However, this is an independent program primarily limited to voluntary reporting of serious adverse reactions in recipients. Thus, it does not have any

[32] World Health Organisation, 'Global Status Report on Blood Safety and Availability' (2016) <https://apps.who.int/iris/bitstream/handle/10665/254987/9789241565431-eng.pdf;jsessionid=A9220FB295EE1E763AC7322F87AE8675?sequence=1> (last accessed 28 September 2020)

[33] *Ibid*

[34] The point at which the risks associated with low hematocrit or hemoglobin levels outweigh the risks of adverse reactions associated with a blood transfusion.

[35] Chandrashekar and Kantharaj, 'Legal and ethical issues in blood transfusion' (2014) 58(5) Indian Journal of Anaesthesia <https://www.researchgate.net/publication/270005602_Legal_and_ethical_issues_in_safe_blood_transfusion> (last accessed 27 October 2020)

[36] National Institute of Biologicals, 'Haemovigilance Programme of India <http://nib.gov.in/haemovigilance.html> (last accessed 27 October 2020)

regulatory control mechanism under the current framework.

III. India's Regulatory Landscape vis-a-vis International Standards

In 2010, the World Health Assembly passed a resolution urging member states "to take all the necessary steps to update their national regulations on donor assessment and deferral, collection, testing, processing, storage, transportation and use of blood products, and operation of regulatory authorities. This was to ensure that regulatory control in the area of quality and safety of blood products across the entire transfusion chain meets internationally recognized standards."[37]

In 2011, the WHO adopted Assessment Criteria for National Blood Regulatory Systems with the intention to help member states to identify gaps and priorities when developing capacity building programmes and support the introduction of regulation of blood products.[38]

We have used the following six criteria out of a total of fourteen criteria of the WHO Assessment tool to analyse India's regulatory framework against international standards:

1. National regulatory system
2. National regulatory authority
3. Licensing or registration of blood establishments
4. Approval of blood and blood components
5. Regulatory inspections and enforcement activities
6. Vigilance systems

We will be applying the required indicators of each of these criteria to the Indian framework in the following sections.

1. National Regulatory System

1.1. A comprehensive legal (statutory) basis exists for establishment of a regulatory system applicable to blood, blood components, plasma-derived products, associated substances, and medical devices including in-vitro diagnostics.

1.1.1. Provisions for the main regulatory functions can be identified and are up to date.

The regulatory functions are fragmented and not clearly identifiable under the D&C Act and the corresponding rules. While some regulatory functions are assigned to the Drug Controller under the Rules, other functions are merely in the form of non-binding guidelines assigned to the NBTC.

[37] Resolution WHA63.12
[38] World Health Organisation, Assessment Criteria for National Blood Regulatory Systems (2012) <https://www.who.int/bloodproducts/NationalBloodRegSystems.pdf?ua=1> (last accessed 27 October 2020)

1.1.2. The regulations or their adaptations take into consideration developments in the field of blood and related technologies.

While there are frequent developments in the field of blood and related technologies, the D&C Rules are not frequently updated. The Rules were last updated in 2017 only in the context of blood donation camps, storage centres, and sharing of blood between blood banks.

1.1.3. Regulations have been established and are available; they are intelligible to those that need to comply with or enforce them, and the ways of communication used are adequate.

While some aspects of regulations are covered under the D&C Rules, most of it is available in the form of non-binding guidelines issued from time to time by the NBTC. Hence, the regulations are available in a fragmented manner.

1.1.4. Legislation exists that defines therapeutic products for human use to be regulated, and establishes standards of quality, safety and efficacy for:

a. blood, blood components and plasma-derived products.

The D&C Act defines therapeutic products for human use to be regulated. The D&C Rules lay down requirements for the collection, storage, processing and distribution of whole human blood, human blood components by blood banks and manufacture of blood products.[39]

b. associated substances and medical devices including in-vitro diagnostics.

Medical Devices Rules, 2017 passed under the D&C Act regulate medical devices and IVDs. Further, Schedule M III (Quality Management System –for Notified Medical Devices and In-vitro Diagnostics) of D&C Rules applies to Blood and blood collection bags.

1.1.5. Legislation exists that provides a legal basis for the responsible NRA to perform the essential functions

The D&C Act gives power to the Drug Controller to license blood banks. However, the apex policy body NBTC, which frames technical standards and guidelines for BTS has not been provided with statutory powers under the Act.

1.1.6. Legislation enables the appropriate institutions to issue regulations.

The D&C Act does not give enabling powers to the technical expert body NBTC to issue regulations.

1.2. The legislation assigns the enforcement of regulations regarding the products covered in 1.1 to one or more responsible regulatory authorities.

1.2.1. The competent authorities involved in the regulatory system for blood, blood components, plasma-derived products, associated substances, and medical devices including in vitro diagnostics are clearly identified and can be named for each of the regulatory functions.

CDSCO, headed by the Drug Controller, performs regulatory functions for all these products.

Although NBTC is a more competent authority for blood products, it does not have any regulatory functions under the D&C Act.

1.2.2. The responsibilities, functions and the organization of each of these authorities are clearly defined, in particular as regards the scope of the regulation (regulatory functions) they have under their control.

Yes, to the extent that the D & C Rules set out the responsibilities and functions of the Drug Controller, which exercises authority in relation to pharmaceutical products, medical devices, as well as

[39] Part XB, D&C Rules

blood and blood products. The Rules do not lay down the functions for the NBTC or SBTCs.

1.2.3. The activities of the various authorities involved are coordinated and supervised by an administrative mechanism

CDSCO does not involve the NBTC in the licensing process.

2. National Regulatory Authority

2.1. There is independence of the regulatory authority in decision-making.

2.1.1. A clear division of roles and responsibilities is implemented between the NRA, blood establishments, manufacturers and distributors, reflecting independence of the regulatory system.

Yes, to the extent that the Drug Controller is recognised as the NRA. No formal role for the NBTC is envisaged in relation to blood establishments, manufacturers and distributors.

2.1.2. Accountabilities for decision-making are clear

Licensing Authority and the Central License Approving Authority have to give reasons in writing for rejecting an application for license or renewal of license.

However, there is no time-limit imposed on them for taking the decision.

2.1.3. Internal policy on potential conflicts of interest for staff exists.

No information is available

2.1.4. NRA management and assessment activities (including use of expert committees) never include representatives from manufacturers or licence holders.

No information is available

2.1.5. A code of conduct for regulatory staff exists

No information is available

2.2. The NRA has adequate resources to carry out its functions properly and to enforce regulatory functions.

2.2.1. An adequate number of trained staff and budgetary provisions exist for all essential functions.

Not in a position to assess independently as far as BTS and blood products go but India has been facing a chronic shortage of drug inspectors since years.[40]

2.2.2. All staff members have appropriate qualifications to conduct regulatory activities and are provided with timely, relevant and regularly updated training.

Rule 122G of the D&C Rules prescribes that the operation of Blood Bank and/or processing of whole human blood for components shall be conducted under the active direction and personal supervision of competent technical staff consisting of at least one person who is a whole-time employee and who is Medical Officer.

However, no special cadre of inspectors with specific qualifications is appointed under the D&C Act to carry out inspection of blood establishment.

2.2.3. Tasks and responsibilities of staff members are well defined.

No information is available

[40] Abhay B. Kadam, Karen Maigetter, Roger Jeffery, Nerges F. Mistry, Mitchell G. Weiss, Allyson M. Pollock, 'Correcting India's Chronic Shortage of Drug Inspectors to Ensure the Production and Distribution of Safe, HighQuality Medicines (2016) 5(9) IJHPM <https://www.ijhpm.com/article_3190_1895d7ae0048fe698a79fac6f50d77b3.pdf> (last accessed 27 OCtober 2020)

2.2.4. Mechanisms are in place to ensure that those performing regulatory functions have sufficient and current expertise in specialized areas.

The Drug Controller does not have sufficient or current expertise related to blood and blood products.

NBTC is the expert body on this subject.

2.2.5. Policies and procedures exist for recruitment and selection of external experts and the management of expert advisory committees, including potential conflict of interest.

The D&C Rules prescribe that before a licence is granted or renewed, the Licensing Authority or the Central Licence Approving Authority shall cause the establishment in which a Blood Bank is proposed to be operated/whole human blood for components is processed/ blood products are manufactured, to be inspected by one or more Inspectors, appointed under the Act and/or along with the Expert in the field concerned.[41]

However, no information is available regarding policies and procedures for recruitment and selection of external experts.

2.2.6. An agreement between the NRA and external experts defining roles and responsibilities is established.

No information is available

2.3. Transparency and accountability are ensured.

2.3.1 Legally specified, confidential and trade secret information is available for internal use and decision-making. However, all other information is publicly available and kept up to date.

No information is available

2.3.2 Listing of authorized products and companies is made available where needed.

The details regarding blood products, their manufacturing companies, and the registration certificate and import license of these companies are available on the CDSCO website.[42]

2.3.3 Information on sanctions, recalls and public health warnings is publicly available

There are adverse drug reaction related notifications available on the CDSCO website.

Further, in case of recall, "the State Licensing Authority needs to communicate to stop the usage of the drug immediately in case of Class –I recall as per the Guidelines for Recall & Rapid Alert System through the fastest mode of communication such as by mass media through newspapers, TV and in the departmental web portal. Most appropriate methods are to be used which may include issuance of notices, circulating letters to all State Licensing Authorities by whichever possible mechanism to ensure that the fastest mode of transmission is used. It is preferred that information is given by SMS or through the website to the public and the regulatory mechanism shall try to reach that level."[43]

3. Licensing of blood establishments

3.1. Legislative authority exists to require registration and/or licensing of blood establishments, and for enforcement power.

3.1.1 Legislation and/or regulations exist that require a blood establishment that

[41] Rule 122I, Part XB, D&C Rules

[42] Blood Product Data 2018 to till Date (30 May 2018) (Registration Certificate and Import Licenses) <https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=MjA5NA⇒ (last accessed 24 October 2020)

[43] Central Drugs Standards Control Organisation, 'Guidelines for Recall & Rapid Alert System (Including Biologicals & Vaccines)' (2017) <https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/biologicals/17RecallRapid.pdf> (last accessed 24 October 2020)

intends to collect, test, process, store, manufacture, distribute, import or export blood and blood components to be authorized, accredited, registered or licensed by the designated NRA.

Yes, under Rule 122F of the D&C Rules.

3.1.2 The NRA has the authority to take regulatory action (e.g., revoke, suspend the licence) if the establishment does not comply with regulatory requirements.

Yes, under Rule 122O of the D&C Rules.

3.2. A licensing and/or registration system is established and operational for blood establishments.

3.2.1. Activities that are decentralized or delegated to other agencies or authorities follow the standards, guidelines and procedures as agreed by the central regulatory authority, and a reporting mechanism is established between the responsible authorities.

The Licensing Authority at the state level follows standards and guidelines published by the NBTC, which is not the central regulatory authority.

There is a reporting mechanism set out in the Rules, where the Licensing Authority at the state level gives its report to the Central License Approving Authority for granting blood bank license to an establishment.

3.2.2. Required registration and/or licence applications are assessed by the NRA based on written guidelines.

The D&C Rules do not mandate the Central License Approving Authority to follow any guidelines while assessing applications.

3.2.3. A list of all licensed and/or registered blood establishments is maintained and made available where needed.

Yes, the most updated list available on the CDSCO website is from 2015.[44]

Further, the NBTC website also has a search-engine, which allows to find blood banks across states and districts.[45]

3.2.4. Advice for applicants is available on the content, format, requirements and procedures to follow in order to submit a required registration and/or application for an establishment licence.

The CDSCO provides guidance of this nature for drugs and medical devices. However, no guidance document is available for blood banks specifically.

3.3. Significant changes to an establishment licence and/or registration are submitted and assessed by the NRA prior to implementation.

3.3.1. Changes are assessed based on the type of change.

No information is available

3.4. Compliance with the principles of good manufacturing practice (GMP) is assessed as part of the establishment licensing and/or registration process.

[44] List of Licensed Blood Banks in India (February 2015) <https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=Mzcw> (last accessed 24 October 2020)

[45] <http://nbtc.naco.gov.in/bloodBank/findblood/> (last accessed 24 October 2020)

3.4.1. Compliance with applicable principles of GMP is a condition for maintaining an establishment licence and/or registration and for approval of significant changes.

Yes, the D&C Rules specify that the GMP/ Written Standard Operating Procedures need to be maintained by all Blood Banks, which shall include all steps to be followed in the collection, processing, compatibility testing, storage and sale or distribution of blood and/or preparation of blood components.[46]

3.4.2. National GMP and good distribution practice (GDP) principles are published and are consistent with or based on recognized standards for the manufacturing and distribution of blood and blood components.

National GMP and GDP principles are not published.

Blood banks have to maintain and follow GMP/Standard Operating Procedures. They may utilise current Standard Operating Procedures, such as the Manuals of the Directorate General of Health Services or other organisations or individual blood banks' manuals subject to the approval of the State Licensing Authority and Central Licence Approving Authority.[47]

3.4.3. Periodic inspections according to GMP and GDP principles are carried out for supervision of blood establishments. For inspections carried out abroad:

a. there is an agreement with other NRAs for exchange of inspection reports and/or certificates; or

No information is available.

b. a list of reference countries and/or agencies whose certificates and decisions are accepted exist; or

Yes, if drug manufacturers have market approval from specific countries, they are exempted from obtaining a license in India.

However, there is no information on how this is implemented in the context of blood and blood products.

c. site inspections are carried out abroad.

While there are provisions under the D&C Act for the inspection of drug manufacturing sites abroad, no specific information is available on how it is carried out for blood establishments.

3.5. QMS requirements are established for all functions performed by blood establishments.

3.5.1. The essential components for a QMS are covered.

The D&C Rules do not prescribe any QMS requirements for blood banks.

The Standards for Blood Banks and Blood Transfusion Services published by the NBTC recommend that blood banks should establish and maintain a quality assurance system based on any current international standard. They also prescribe the essential components of the Quality Assurance System.

3.6. Assessment of compliance with standards regarding donor selection criteria and testing of donations is part of the establishment licensing and/or registration process (alternatively this requirement can be met under Core function - Approval of blood and blood components).

[46] Schedule F Part XIIB, Heading I Item G, D&C Rules

[47] *Ibid*

3.6.1. Compliance with national standards is a condition for maintaining an establishment licence.

No

3.6.2. National standards are published and are consistent with or based on recognized standards for blood and blood components.

National Standards published by the NBTC are non-binding in nature.

An independent assessment will have to be carried out to see whether they are consistent with or based on recognised standards.

3.6.3. Inspections are carried out for checking compliance with these national standards.

Inspections are carried out to check if the establishment will be in a position to fulfill the requirements given under the D&C Rules, but the Standards published by the NBTC are not a part of the Rules formally.

3.6.4. Defined procedures are in place for taking action in instances of any nonconformity.

Yes, there are procedures to suspend or cancel licenses in case of breach of a condition of license.

4. Approval of blood and blood components (product and/or process approval)

4.1. Legal provisions exist for a system to ensure quality, safety and efficacy of blood and blood components.

4.1.1. An approval system is required that includes any imported products.

Yes

4.1.2. The NRA has the authority to issue an approval, to suspend it and to withdraw it if the product is considered unsafe or does not comply with regulatory requirements

Yes

4.2. A system for ensuring quality, safety and efficacy of blood and blood components is established and operational.

4.2.1. The capability exists to perform science-based risk assessments and risk management.

No

4.2.2. Specifications related to quality, safety and efficacy of blood and blood components are defined and under the supervision of the NRA.

While some of the specifications are prescribed under the D&C Rules, details are laid down in the non-binding Standards and Guidelines issued by the NBTC.

4.2.3. The critical standards for product manufacturing are legally binding and include donor selection, laboratory testing, component preparation, storage, issuance, tracking, tracing, record keeping, and safe disposal of units not meeting specifications for use in transfusion.

No, they are not legally binding, to the extent that they have not explicitly been incorporated in the D & C Rules.

4.2.4. Plasma for fractionation meets internationally recognized standards.

An independent assessment by experts will be needed to determine this.

4.3. Donor selection and deferral criteria are established as

appropriate to the intended use of the component.

4.3.1. Donor selection and deferral criteria (temporary and permanent deferrals) take into account the health of the donor and the safety and suitability of the donation consistent with current science.

Yes, these are specified under the D&C Rules, as discussed in Part II.

4.3.2. Mechanisms for regularly reviewing and updating the donor selection and deferral criteria are in place and take into consideration the development of issues that might have a negative impact on the quality and safety of blood and blood components, e.g., epidemiological situation or emerging diseases.

The D&C Rules Rules are not reviewed and updated regularly. However, the NBTC issues guidelines taking into consideration the development of issues that might have a negative impact on the quality and safety of blood and blood components. For instance, the NBTC issued National Guidance on Blood Transfusion Services in India in light of COVID-19 Pandemic.[48]

4.4. Transmissible-disease testing requirements are established as appropriate to the intended use of the component.

4.4.1. Mechanisms for regularly reviewing (e.g. by qualified experts in epidemiology) and updating the testing requirements are in place.

The D&C Rules prescribe the TTIs for which blood needs to be tested before transfusion. Further, the CDSCO approves the tests that could be used to determine the prevalence of TTIs in blood. However, no formal provisions are in place mandating that a particular test needs to be adopted by blood banks, or that the testing requirements need to be reviewed.

NBTC has the expertise to update its guidelines related to testing including TTIs. However, no information is available on how frequently this power is exercised or a review is undertaken.

4.4.2. Epidemiological data regarding the prevalence and incidence of infectious disease markers in blood donors are available and regularly updated.

No information is available.

4.5. Labelling requirements are established.

4.5.1. Each blood component has a unique and clear identifier and is fully traceable.

Yes

4.5.2. Original labelling and significant amendments are submitted to the NRA and assessed prior to implementation.

The licensing authority needs to be intimated and permission needs to be obtained for making any changes in labelling of drugs.

4.6. An approval system for blood and blood components is operational.

4.6.1. Assessment exists that includes relevant aspects of quality, safety and where applicable efficacy of blood and blood components.

Yes

4.7. Appropriate assessment expertise is available.

[48] <https://nidm.gov.in/covid19/PDF/covid19/Ministries/Ministry%20of%20Health%20and%20Family%20Welfare/145.pdf> (last accessed 27 October 2020)

4.7.1. Access to experts with relevant qualifications and experience (internal and/or external) is assured for assessment of blood and blood components (preclinical, clinical and quality data).

The CDSCO can co-opt subject experts to determine whether a pharmaceutical product is safe and efficacious.

Further, the D&C Rules provide that the Drug Inspector, while inspecting the establishment may be accompanied by an expert in the field if necessary.[49]

5. Regulatory inspections and enforcement activities

5.1. Legal provision exists to inspect premises where regulated activities are performed in order to assess and enforce compliance with the applicable laws, regulations and standards.

5.1.1. A mandate exists for inspections by the NRA and enforcement of compliance with principles of GMP, GDP and other standards.

Yes, the D&C Rules contain provisions that allow inspections by the drug inspectors to check compliance with regulatory requirements prescribed under the Rules.

5.1.2. Applicable standards and practices are defined in legal provisions.

Some requirements are specified in the D&C Rules, however, standards published by the NBTC are not backed by a statute, rules or regulations.

5.1.3. The NRA has the authority to take enforcement action against the accountable companies or persons that are not in compliance.

Yes, there are procedures to suspend or cancel licenses in case of non-compliance.

5.1.4. The NRA has the authority to sample products, manufacturing materials and records if necessary.

Yes

5.1.5. The NRA has the authority to recall products.

Yes

5.1.6. Provisions exist for conflict of interest and confidentiality.

Yes, the inspectors appointed under the D&C Act need to be independent of any manufacturers.

5.2. Inspection and enforcement systems are established and operational.

5.2.1. Established policies and programmes exist for conducting inspections of all regulated activities.

Yes

5.2.2. An inspection plan exists with adequate human and financial resources for conducting inspections at appropriate intervals.

No

5.2.3. The NRA maintains files of each inspection, including the inspection report and final decisions taken.

Yes

5.2.4. There is an established process for appropriate regulatory action to address

[49] Rule 122-I, D&C Rules

inspectional findings (e.g., recall of products, amended licences).

Yes

5.2.5. If the mechanism is adopted, provisions exist for acceptance of external inspectorates according to internationally recognized standards.

No. Inspectors appointed under the D&C Act can be accompanied by experts in the field if desired.

5.3. Inspectors with appropriate expertise and qualifications are available.

5.3.1. Inspectors have the appropriate expertise and training to conduct inspections of blood establishments and manufacturers and distributors of plasma-derived products.

No.

5.3.2. Training of inspectors includes specific aspects related to the activities of relevant establishments.

No information is available

5.4. A quality management system is implemented that is consistent with international principles for pharmaceutical and related inspectorates.

5.4.1. Written procedures exist for conducting inspections (inspection manual) and following-up on deficiencies and/or violations.

No information is available.

5.5. A recall system exists with mechanisms to ensure the proper disposition of blood, blood components, plasma-derived products, associated substances, and medical devices including in-vitro diagnostics.

5.5.1. Policy and procedures for a recall system including product disposition exist.

Yes[50]

5.5.2. The recall system is based on defined action and documented communication to the appropriate level of the distribution system.

Yes[51]

5.5.3. A feedback mechanism exists to confirm that appropriate action (including destruction when necessary) has been taken at all appropriate levels.

Follow-Up Action of Recalled Goods is undertaken, which consists of a check on the effectiveness of the recall, an investigation of the reason for the recall and remedial action taken to prevent a recurrence of the defect.[52]

5.5.4. Full lot traceability is in place.

This assessment is outside the scope of this paper.

6. Vigilance Systems

6.1. Legal provisions for a national vigilance system exist.

[50] Central Drugs Standards Control Organisation, Guidelines for Recall & Rapid Alert System (Including Biologicals & Vaccines) <https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/biologicals/17RecallRapid.pdf> (last accessed 24 October 2020)

[51] *Ibid*

[52] *Ibid*

6.1.1. The NRA has a legal mandate and enforcement power for mandatory reporting elements of the national vigilance system.

No. The Hemovigilance Program of India has been launched by the Indian Pharmacopoeia Commission in collaboration with NIB. It is a voluntary program.

6.1.2. The NRA has the authority to specify reporting of adverse events (AEs) and adverse reactions (ARs) within the national vigilance system.

NRA exercises this power independent of the National Vigilance System.

6.1.3. Authority exists to require the marketing authorization holder to perform a specific study of safety and/or effectiveness in the post-marketing period.

Yes

IV. Conclusion

There are two key issues with India's blood regulatory framework that emerge from this analysis. First, the Indian regulatory system relies on the outdated architecture of the D&C Act without taking into consideration rapid changes in the field of blood safety. As the analysis in Part III demonstrates, the regulation of blood suffers from the same deficiencies as the pharmaceutical regulatory framework, characterised by a lack of resources, clearly defined regulatory processes, and weak powers.

Second, CDSCO, being the regulatory authority for all drugs including blood and blood products does not have the relevant expertise in this field. While the expert technical body NBTC has been set up following Supreme Court directions in this regard, it is not formally incorporated in the D&C Act or the corresponding D&C Rules. The NBTC acts as the apex policy body with respect to blood transfusion services, however, there is uncertainty about the binding nature of guidelines and standards issued by the NBTC and SBTCs. This non-binding nature appears to have contributed to a lot of varying practices regarding blood safety, including donor selection and pre-transfusion testing, as we have pointed out in the earlier half of this paper.

Some specific issues have also emerged with respect to the measures taken towards blood safety. To ensure safe blood, blood banks must be required to observe rigorous rules regarding donor selection. However, it appears that the more formal criteria are to be found primarily in non-binding standards/guidelines, not in the requirements for licensing of blood banks. While professional donors have been legally banned in India, a large pool of blood in India is still donated by replacement donors instead of voluntary donors. Despite regulatory amendments that now allow a wider range of institutions including hospitals to organise blood donation camps, most hospitals continue to resort to replacement donation by friends or families of patients. This increases the chances of Transfusion Transmitted Infections (TTIs) as voluntary non-remunerated donors are considered the safest. Further, no specific tests are mandated by the current regulatory framework to test donated blood for TTIs. Blood banks adopt different technologies as per their convenience and infrastructure, which leads to non-uniform standards of blood safety across India.

To enhance blood safety, replacement donations should not merely be discouraged but it should be a pre-condition for granting blood banks a no-objection certificate. Centralised collection and testing of blood banks with well-defined transport infrastructure and regional storage centres will also go a long way towards ensuring blood safety. This will ensure uniform testing standards across India along with a central repository of voluntary regular donors who are the safest.

As a way forward towards reforming the regulatory architecture, India needs to update its blood regulatory framework regularly with respect to newer developments regarding both TTIs and testing technologies to detect them. Further, technical expert bodies NBTC and SBTSc should be given a formal role in the blood regulatory framework by involving them in the licensing process, and formally incorporating the guidelines and standards issued by them in the D&C Rules, making them binding in nature.

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