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A REVIEW ON ETHICAL AND LEGAL ASPECTS ON BLOOD AND BLOOD PRODUCTS IN INDIA AND AUSTRALIA

PRIYA DARSINI G*, KOUSHIK Y AND RAMA RAO N

Pharmaceutical Regulatory Affairs, Chalapathi Institute of Pharmaceutical Sciences (Autonomous), Lam, Guntur, Andhra Pradesh, India

***Corresponding Author: Priya Darsini Gorantla: E Mail: preethigorantla022@gmail.com**

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ABSTRACT

Blood and blood products are valuable assets that give life to others. Although we have great break thoughts and invention in science and technology, but we cannot produce blood, so there is no substitute for human blood. We still do not have a clear, well defined and rigorous regulatory framework to regulate blood products. Fragility can result from the inability of governments to enforce laws, regulations and guidelines, and personnel who may be unaware of or unable to follow quality control and/or good manufacturing practices. The availability of safe blood and safe blood products is critical to several varieties of modern health services, including some surgeries, cancer treatment, chronic medical conditions, trauma care, organ transplantation and delivery, ultimately improving the lives of the millions of patients who need transfusions for every year. This review summarizes the ethical and legal aspects of blood and blood product regulation in India and Australia.

Keywords: Australia, Blood, Ethical and Legal aspects, India

INTRODUCTION

Blood may be a rescue liquid organ. Blood is a mixture of cellular elements; colloids associate degreed crystalloids **[1]**. Blood and blood merchandise is treasured commodity which offers lifestyles to every other person **[2]**. The fundamental additives of blood are

platelets, white blood cells, red blood cells and plasma. A blood product is any restoration and healing substance, which include complete blood and distinct blood additives for transfusions and plasma-derived healthy product and they are derived from human blood **[3]**. The blood element manufacture / availability and usage of blood components are extraordinarily limited. For quality, protection and efficacy of blood and blood merchandise, properly ready blood centre with enough infrastructure and educated manpower is a crucial requirement **[4]**. The supply of secure blood and blood merchandise is crucial for various current healthcare offerings which include a few surgeries, treatments, clinical situations etc. **[2]**. Legal issues play a vital role in providing a framework and shaping the structure of the blood, while ethical issues pave the way for quality **[5]**.

Ethical and legal principles governing blood and blood products in India

The regulatory authority of India is the Central Drugs Standard Control Organization (CDSCO) which is going by the Drugs Controller General. National AIDS Control Organization (NACO) goes about as an ally of the Ministry of Health and Family Welfare to Indian blood transfusion services **[2]**. Human blood is falls under the definition of 'Drug' and blood banks and blood transfusion service are regulated or subjected under the Drugs & Cosmetics Act and its rules. To work on the guidelines of Blood and blood constituents, the Government of India has authorized a thorough enactment to guarantee better quality control framework for the assortment, testing and circulation of blood and blood constituents **[6]** Clinicians must be trained for effective clinical use of blood. To achieve the highest level of safety, good manufacturing practice requirements and implementation of quality assurance systems must be followed **[4]**. Some of the examples of blood products that are manufactured in India are Human Prothrombin Complex-500 IU, Human Albumin 20g/100 ml, Anti-haemophilic Factor IX IP- 250 IU, 500 IU, 1000 IU and Anti-inhibitor Coagulant Complex- EP 500 IU **[7]**.

Human Albumin 20g/100 ml (AlbuMax)

AlbuMax is a sterile highly purified albumin protein solution prepared from human plasma obtained from healthy volunteer donors and it does not contain preservatives. This product is manufactured by an Indian biopharmaceutical organization specializing exclusively in Plasma Proteins and specialized therapies i.e. PlasmaGen BioSciences. Used in the treatment of

hypovolemic shock, hypoproteinemia, hemorrhagic shock, and plasma exchange dialysis. Stored at 2°C - 25°C and it is also protected from light and shelf life is approximately 36 months **[8]**.

APPROVAL OF DRUG IN INDIA

CDSCO is an Indian regulatory agency with access to and primarily focused on the safety and efficacy of domestic medicines. Blood and blood products are classified as biologics, which are regulated by the Drug and Cosmetics Act of 1945 **[10]**.

If an Indian company wishes to manufacture / import a new drug, it must submit Form 44, also submit the data and apply for approval by the Drugs Controller General of India (DCGI). In order to demonstrate its efficacy and safety to Indians, clinical studies must be conducted in accordance with the guidelines given and reports of such clinical studies must be submitted in a specific format **[11]**. The licensing authority may take specific steps and another provision that states that new drugs approved in other countries and used for several years may be exempt from clinical trials **[12]**.

Stages of approval

1. Require Clinical study application to assess safety and effectiveness
2. Approval Requirements for Approval of New Drugs.
3. Changes post-approval for biologics: documentation of quality, safety and effectiveness.
4. Preparation of Quality Information for Submission for approval of the new drug

Most countries use the CTD format. As a result, CDSCO has also decided to apply the CTD format to the technical requirements for registration of pharmaceutical products for human use **[14]**. The new drug approval process in India is a very complex process that must meet the essential requirements along with the FDA's NDA. The need for this work is to investigate and document the requirements of the new drug approval process in India, with a focus on clinical trials, according to the Government of India's Drug Control Department **[12]**.

Indian clinical trial applications must be submitted to DCGI along with chemical, manufacturing, control and animal study data. The date of the study protocol, the investigator's brochure and informed consent documents should also be attached. A copy of the application must be submitted to the ethics committee, and clinical trials must be approved by DCGI and the ethics committee **[9]**. After clinical trial approval, applicants can conduct Phase I, II, and III studies to determine safety, effectiveness, and side

effects. Once the clinical trial is complete, a new drug registration will apply. In addition to safety and efficacy information, we need comprehensive information about the status of pharmaceutical markets in other countries.

The application can be reviewed within approximately 12-18 months. If a company is allowed to distribute and commercialize a product after NDA approval, it is considered in a Phase IV study investigating new uses or new population, long-term impact, etc. **[13]**.

The application form applies for a license to manufacture blood products on application form 27-C. The license is issued on Form 28-C and can be renewed on Form 26-G. License fee of six thousand rupees and inspection fee of fifteen hundred rupees for each same inspection or for the purpose of renewing the license. The original Form 28-C or Form 28-E license, or the renewed Form 26-G or Form 26-I license, is valid for five years from the date of grant or renewal unless suspended or cancelled early **[15-16]**. The NRA (National Regulatory Authority) has the authority to grant, suspend, and withdraw approval if the product is determined to be unsafe or does not meet regulatory requirements.

Ethical and legal principles governing blood and blood products in Australia

Therapeutic goods administration (TGA) is the regulatory body of Australia. Under the Therapeutic Goods Act 1989, Blood, blood components and blood products are regulated **[17]**. Australia has a safe and sustainable supply of blood and blood products **[18]** and National Blood Authority (NBA) is the one which manages and coordinates the supply of blood and blood products and services on behalf of all Australian governments and includes extensive assessment processes for new products **[19-20]**. The Australian Red cross Blood service (ARCBS) plays a key role in ensuring Australians in providing access to blood and blood products to meet the needs of Australians. The main regulation of Australia's TGA is when the blood is collected and manufactured from Australian donors it should meet the most stringent safety and quality requirements **[21]**.

Some of the examples of blood products that are manufactured in Australia **[22]**:

- Albumin (Albumex)- 20% 10ml, 4% 50ml
- Emicizumab (bi-functional monoclonal antibody) (Hemlibra)- 30mg/1ml, 60mg/0.4ml
- Factor VIII (plasma derived - domestic) (Biostate)- 250 IU, 500 IU

Human albumin (4%) solution for infusion (Albumex 4)

Albumex 4 is a clear, slightly viscous liquid which is almost colorless, yellow, amber or green and is prepared by a combination of the Cohn cold-ethanol fractionation process and chromatographic techniquesand it contains no preservatives. It is produced from human plasma donated by a voluntary, non-refundable donor in New Zealand. It can be stored below 30^0C (Do not freeze) and protected from light and shelf life is about 48 months (4years). It is used for the treatment of Hypovolaemia, plasma exchange and patients with multiple organ failure or leaky small blood vessels **[23]**.

APPROVAL OF DRUG IN AUSTRALIA

Under the Therapeutic Goods Act 1989, Blood, blood components and plasma derivatives are regulated. Blood defines as whole blood which is collected or extracted from human donors and where as Blood components refers to therapeutic components that are manufactured from blood and does not include products which are derived through fractionation process of plasma **[17]**. The Australian regulatory body which is responsible for regulating therapeutic goods including prescription medicines, vaccines, sunscreens, vitamins and minerals, medical devices, blood and blood products is TGA. In general, the standard drug approval process takes about 240-260 business days **[24]**.

Stages of approval

1. Pre-submission phase (50 business days)
2. Submission phase (20 business days)
3. Assessment phase (80-20 business days)
4. Decision phase (10 business days)

During the Pre-submission phase prior to submission, the applicant submits a Pre-Submission Planning Form (PPF) to TGA 26 months before submission. TGA logs the PPF and starts processing after the first day of every month and then it will issue a planning letter to the applicant, including submission milestones, feedback, and specific conditions and in Submission phase before 15th day of month applicant submits formal submission dossier and payment for 75% of evaluation fees and the TGA review the process of submission and determines whether it follows according to the Australian Regulatory guidelines for Prescription Medicines (ARGPM) and it is accepted for evaluation and TGA issues a notification letter about its decision to the applicant. In the assessment phase, Evaluation process into two rounds. During the first round TGA reviews through the primary and secondary assessment units and conjure questions and related issues the consolidated response to the applicant and

response timeline for applicant is about 20-40 business days and response period start either 30 or 60 days nominated in PPF. Then the applicant responses to the TGA mentioned issues then the evaluation proceeds or the evaluation ends.

In the second round assessment phase response and final evaluation report of TGA is completed and the applicant can review the report and make changes based on the recommendations. Then the process is followed by Expert advisory review phase which takes about 5-10 business days in which the TGA representative appeal advice from three committees and they are advisory committee on prescription medicines (ACPM), Pharmaceutical subcommittee (PCS) and from advisory committee on the safety of medicines (ACSOM) which is optional. During the decision period, the TGA delegate's review and decision-making process takes place. A decision is being prepared and the remaining 25% will be paid to the applicant. If the decision is denied, the applicant has 90 days to appeal the decision. During the post-decision period, the final regulatory body of the TGA which prepares the Australian Public Assessment Report (AusPAR) and drafts the applicant's AusPAR C-I-C. The documents are then published on the official TGA website and followed by listing in the Australian Registry of Therapeutic Products (ARTG) **[25]**.

CONCLUSION

Since the development of blood and blood products is a series of processes, their ratification requires fixed and consistent regulation. Authorities need to ensure that these regulations are strictly adhered to in order to minimize the time and cost of developing blood and blood products. CDSCOs and TGAs also have their own strict regulations on blood products. This includes regulations, guidelines, and other measures aimed at increasing blood availability.

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