AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Regulatory requirements on parenteral dosage forms as per CDSCO in India comparison with south Africa

Ashok Kumar P*, Preethi B, Nithyashree M, Navya H C, Srujana G, Poornima CS

Department of Regulatory Affairs, Sree Siddaganga College of Pharmacy, 1st Left Cross, 3rd Block, Mahalakshmi Nagar, Near Railway Gate, 80 feet Road, Batwadi, Tumkur-572103. Karnataka (India)

ABSTRACT

Parenteral products are currently widely utilized in emergency situations since they provide the highest bioavailability. Parenteral product legislation is crucial as non-sterile, non-pyrogenic products can provide a serious health risk to patients, potentially leading to death. The Central Drugs Standard Control Organization (CDSCO) in India and South African health products regulatory authority (SAHPRA) in South Africa have specified different dosage formats, and this review offers a comparative examination of those requirements. This review explores critical aspects including governing legislation, clinical trial requirements, good manufacturing practices (GMP), quality control, packaging and labelling standards, import and export regulations and recent reforms. As indicated above comparative analysis of regulation and registration process for parenteral dosage from will be valuable regulatory point of view as well as business development point. With this viewpoint industry can unify dossier application in better method, which would aid in lowering time for product to go in market.

Keyword: Parenteral products, CDSCO, SAHPRA, GMP.

*Corresponding Author Email: ashokkumarscp@gmail.com

Received 12 August 2024, Accepted 19 September 2024

Please cite this article as: Kumar A *et al*., Regulatory requirements on parenteral dosage forms as per CDSCO in India comparison with south Africa. American Journal of PharmTech Research 2024.

INTRODUCTION

Parenteral dose forms, which avoid the gastrointestinal system, are sterile preparations meant to be administered via injection, infusion, or implantation.

They are generally sterile and pyrogen free preparation.

Small Volume Parenteral	Large Volume Parenteral
≤ 100ml volume	> 100ml volume

Routes of administration:

Intravenous (IV), Intramuscular (IM), Subcutaneous (SC), Intradermal (ID).

Types of parenteral preparation:

Solution, Suspension, Emulsion, Powder for injection, lyophilized powder for injection, Infusion fluids[1].

In an individual who are unable to take their medication orally, parenteral formulation is the recommended method of delivery. This injection functions as a particular dosage type that is given via a different route than the gastrointestinal tract. Compared to oral use, they have a quicker start of effect because they are directly absorbed into the circulation. Most medication absorption occurs through blood arteries. The intravenous (IV) route is commonly employed in emergency medical circumstances since it is the quickest means to deliver medication to peripheral tissue. When a patient's body absorbs medication more quickly and effectively, these quantities may be recommended. When a medication enters the patient's digestive system, it becomes useless and can be used in this situation. Parenteral products that are liquid-containing are delivered by sterilizing small biopharmaceutical containers and then filling them with the sterile parenteral products. In the medical field, these sterile liquids include IV medications, diagnostic samples, and other liquids. In addition, saline bags, and sterile water diluents are included. They also consist of external water utilized in tube nourishment solutions that do not come into contact with the patient's blood, reconstitution of powdered medications for direct delivery by IV or IM injection, and saturated carrier solutions for short-term usage. It is anticipated that the parenteral pharmaceutical and medical market will expand yearly on a global scale.

Significance:

Global regulatory bodies have set standards and specifications for the creation, production, and promotion of parenteral goods. The GMP guidelines' even stricter criteria are in line with the GMP requirements for parenteral products, particularly in the aseptic area. Regulatory bodies specify

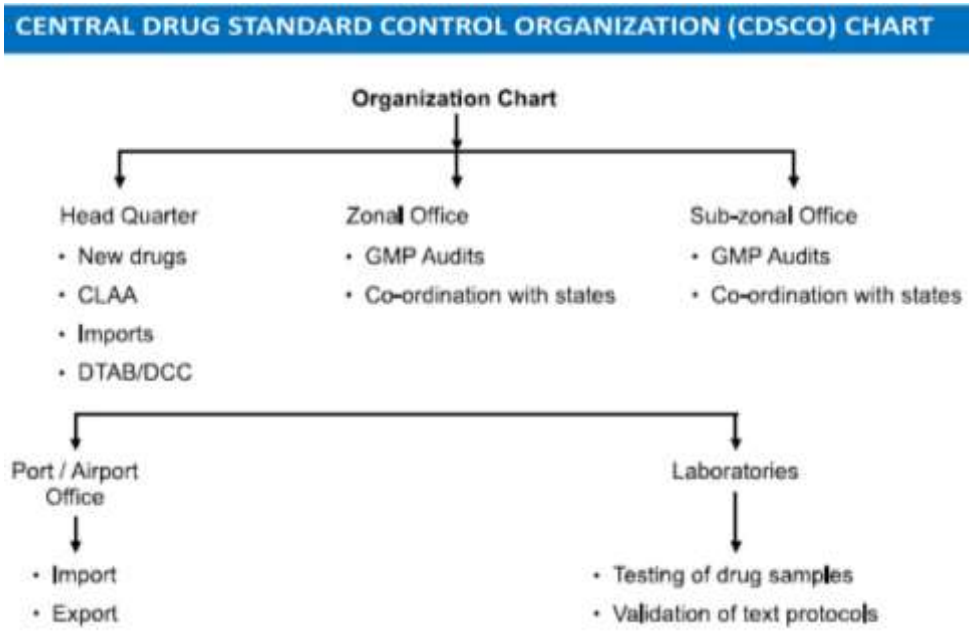
precise requirements for stability testing, preparation guidelines, and validation for parenteral goods in order to guarantee that important details are met. These items have very stringent standards for the formulation additives, containers, and closure mechanisms that are designated. If any particular pharmaceutical product has been marketed for at least 40 years and is still available with the same composition, indication, dosage form, amount, and expiration period, it will be regarded as a branded formulation. This could be a requirement for waiving drug regulation for products made in nations like India[2].

Overview of CDSCO in India:

The Central Drugs Standard Control Organization (CDSCO) is India's national regulating authority for cosmetics, pharmaceuticals, and medical devices. It performs a comparable function to the FDA in the United States and the EMA in the EU.

Key information regarding CDSCO:

CDSCO, headquartered in New Delhi, operates 9 zonal offices, 7 sub-zonal offices, 18 port offices, 7 central laboratories, and 6 small labs throughout India.



It is run by the Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India.

CDSCO is in charge of licensing medications, conducting clinical trials, establishing drug standards, monitoring the quality of imported drugs, and working with state drug regulators.

It grants permits for specialist pharmaceuticals such as blood products, IV fluids, vaccinations, and sera in collaboration with state authorities.

CDSCO is divided into eight divisions: BA/BE, New Drugs, Medical Devices and Diagnostics, DCC-DTAB, Import and Registration, Biologicals, Cosmetics, and Clinical Trials.

The Drug Controller General of India (DCGI) is responsible for regulating pharmaceuticals and medical devices under CDSCO, with advice from the Drug Technical Advisory Board (DTAB) and Drug Consultative Committee (DCC).

- To conduct business with CDSCO in India, manufacturers must choose an Authorized Indian Representative.
- CDSCO ensures the safety, efficacy, and quality of pharmaceuticals and medical devices in India by overseeing and enforcing the pharmaceuticals and Cosmetics Act[3].

Overview of SAHPRA in South Africa:

The South African Health Products Regulatory Authority (SAHPRA) regulates medications, medical equipment, radiation-emitting devices, radioactive nuclides, and complementary medicines in South Africa. Key points concerning SAHPRA:

Mandates and Functions:

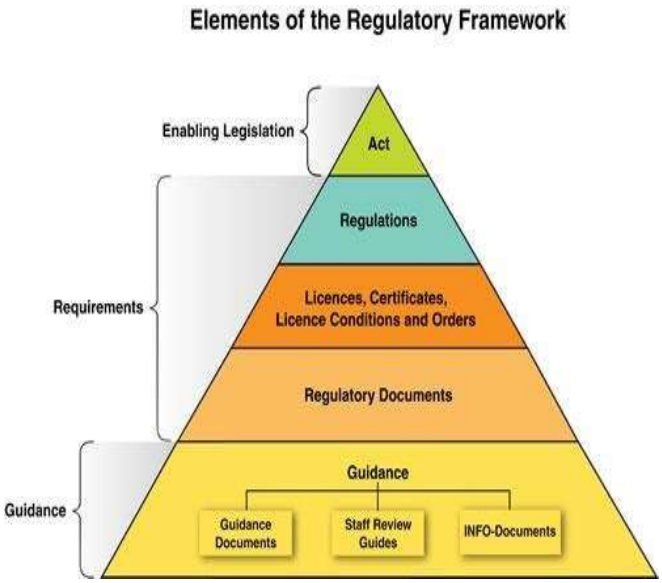
- SAHPRA was formed in 2018 to replace the Medicines Control Council (MCC) and the Directorate of Radiation Control.
- It is run by the National Department of Health and reports to the National Minister of Health through its Board.

- The Medicines and Related Substances Act (Act No. 101 of 1965) and the Hazardous Substances Act (Act No. 15 of 1973) establish SAHPRA's authority.
- Its primary functions are to monitor, evaluate, investigate, inspect, register, and manage health products to assure their safety, efficacy, and quality[4].

Regulatory Oversight:

- SAHPRA oversees clinical trials, complementary medicines, medical equipment, in vitro diagnostics, radiation control, and the licensing of makers, wholesalers, and distributors of pharmaceuticals.
- It strives to gradually actualize the right to healthcare by ensuring that South Africans have access to safe, effective, and high-quality health goods.
- SAHPRA takes a risk-based approach to its regulatory review process and is trying to improve regulatory performance and responsiveness.

Elements of the regulatory framework:



Elements of the regulatory framework[5].

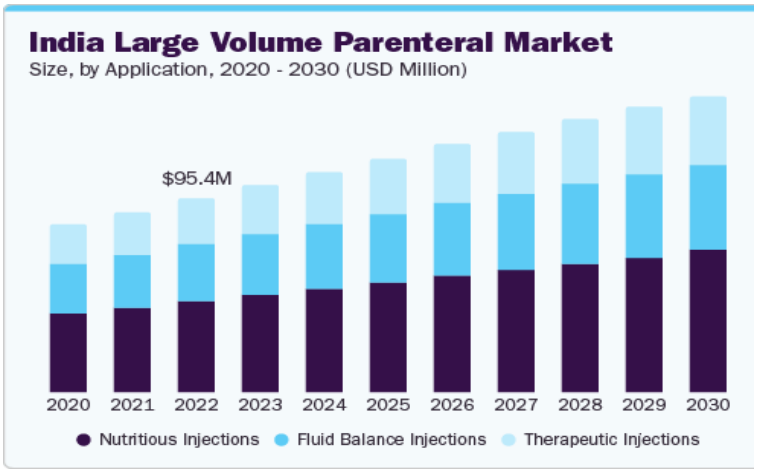
Some key differences between India and southafrica in their regulatory frameworks includes:

- Based on their constitutions, both nations have legal systems that protect the rule of law.
- India has adopted a more aggressive strategy for large-scale financial reforms, whereas South Africa is taking a more measured approach.
- When it comes to regulating a combination of monopolies and markets, India's telecom regulatory system is more complicated and developing than that of other nations, such as the United States and the United Kingdom.

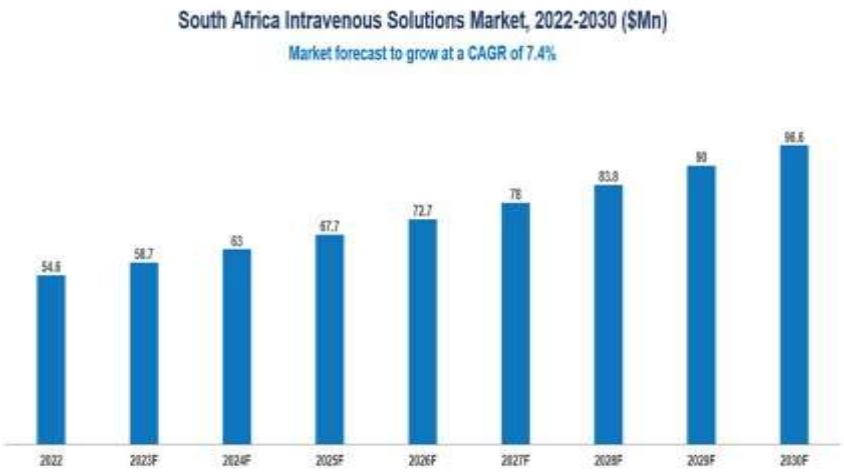
- The laws in India and South Africa diverge when it comes to the transparency of Members of Parliament's personal interests.
- Although the speed and methods may differ, both nations' regulatory systems have developed to support the rule of law and promote progress despite facing issues like poverty, violence, corruption, and underdevelopment.

Parenteral markets scenarios in South Africa and India differ greatly in terms of size, growth rates, and underlying factors:

The parenteral market in India is expected to expand at a compound annual growth rate (CAGR) of 6.6%, from roughly $1,165.4 million in 2024 to $2,203.7 million by 2034.and The only large volume parenteral market in India was estimated to be worth USD 95.4 million in 2022, and between 2023 and 2030, it is projected to develop at a compound annual growth rate (CAGR) of 5.3%. The strong pharmaceutical industry, the rise in chronic illness rates, and the growing need for sophisticated drug delivery devices such prefilled syringes are the main drivers of this expansion. Fresenius Kabi AG and Parenteral Drugs (India) Ltd. are two significant companies in this sector[6].



The parenteral market in South Africa, on the other hand, is smaller but expanding significantly, especially for intravenous (IV) solutions. Based on a compound annual growth rate (CAGR) of 7.4%, the market is expected to reach $96.6 million by 2030 from its estimated $54.6 million in 2022. Palliative care advances, the growing geriatric population, and the increase in non-communicable diseases are the main drivers of growth in South Africa. Adcock Ingram Holdings Ltd. and Fresenius Kabi AG are important participants[7].



Quality standards for parenteral in India and South Africa:

In India:

The Central Drugs Standard Control Organization (CDSCO) regulates the quality standards for parenteral (injectable) products. The standards are designed to ensure the safety, efficacy, and quality of these products. Here are the key aspects of the quality standards for parenteral preparations as per CDSCO:

Pharmacopeial Standards:

Parenteral products must comply with the standards set by the Indian Pharmacopoeia (IP), which includes specifications for sterility, pyrogenicity, particulate matter, and other critical quality attributes.

- For products intended for export, compliance with other pharmacopoeias like the United States Pharmacopoeia (USP) or the European Pharmacopoeia (EP) may also be required.
- **Sterility**: Parenteral products must be sterile. Sterility testing is mandatory to ensure that the product is free from viable microorganisms.
- **Pyrogenicity**: The product must be free from pyrogens, which are substances that can cause fever when injected. Testing for bacterial endotoxins or performing the rabbit pyrogen test is required.
- **Particulate Matter**: Parenteral products must be free from particulate matter that could pose a risk to patients. Limits are set for both visible and sub-visible particles.
- **pH and Osmolarity**: pH and osmolarity of the product must be within the specified limits to ensure compatibility with the body's fluids and to avoid irritation or other adverse effects.

- **Container Integrity:** containers used for parenteral products (vials, ampoules, etc.) must maintain their integrity to prevent contamination and ensure product stability.
- **Stability Testing**: Stability studies must be conducted to establish the product's shelf life and storage conditions, ensuring that the product maintains its quality, safety, and efficacy over time.
- **Good Manufacturing Practices (GMP)**: Manufacturers must follow the guidelines outlined in the Schedule M of the Drugs and Cosmetics Rules, which includes GMP for the manufacturing of sterile products.
- **Labeling**: The labeling must include clear instructions for use, storage conditions, expiry date, and any precautions or warnings necessary for safe administration.
- **Bioequivalence and Bioavailability**: For generic products, bioequivalence studies may be required to ensure that the product performs in the same manner as the original.
- **Product Approval**: Any new parenteral product must be approved by CDSCO before it can be marketed. This involves submitting a detailed dossier, including quality data, clinical trial data (if applicable), and information on the manufacturing process.
- These standards are in place to protect public health by ensuring that parenteral products meet the necessary safety and quality requirements before they reach the market.

In South Africa:

The quality standards for parenteral (injectable) products are regulated by the South African Health Products Regulatory Authority (SAHPRA). SAHPRA ensures that all medicines, including parenteral products, meet specific safety, efficacy, and quality standards. Here are the key aspects of the quality standards for parenteral preparations in South Africa:

- **Pharmacopeial Standards**: Parenteral products must comply with the standards set by recognized pharmacopoeias, such as the British Pharmacopoeia (BP), United States Pharmacopoeia (USP), European Pharmacopoeia (EP), or the International Pharmacopoeia.
- These standards cover critical quality attributes such as sterility, pyrogenicity, particulate matter, and chemical purity.
- **Sterility**: Parenteral products must be sterile to prevent infections. Sterility testing is mandatory and must comply with international guidelines.
- **Pyrogenicity**: The product must be free from pyrogens, which can cause fever when injected. Testing for bacterial endotoxins or performing pyrogen tests is required to ensure this.

- **Particulate Matter**: Injectable products must be free from particulate matter. There are specified limits for both visible and sub-visible particles to prevent complications upon administration.
- **Container Integrity**: The integrity of the container (vial, ampoule, etc.) is critical to prevent contamination and ensure the product's stability. Testing for container closure integrity is required.
- **pH and Osmolarity**: The pH and Osmolarity of the product should be within acceptable ranges to ensure compatibility with the body's fluids and to avoid irritation or adverse reactions.
- **Stability Testing**: Stability studies must be conducted to establish the shelf life and recommended storage conditions of the product. These studies ensure that the product remains safe and effective throughout its shelf life.
- **Good Manufacturing Practices (GMP)**: Manufacturing facilities must comply with SAHPRA's guidelines for Good Manufacturing Practices (GMP). These guidelines cover aspects like facility cleanliness, personnel hygiene, and equipment validation to ensure the consistent quality of sterile products.
- **Bioequivalence and Bioavailability**: Generic parenteral products may need to undergo bioequivalence studies to ensure that they are therapeutically equivalent to the innovator products.
- **Labelling and Packaging**: The labelling must include comprehensive information such as the product name, concentration, instructions for use, storage conditions, expiry date, and any warnings or precautions.
- **Product Registration**: Before a parenteral product can be marketed in South Africa, it must be registered with SAHPRA. The registration process requires the submission of a detailed dossier, including data on quality, safety, efficacy, and manufacturing processes.
- **Post-Market Surveillance**: Once the product is on the market, ongoing monitoring (pharmacovigilance) is required to track any adverse effects or quality issues.
- These standards are aligned with international norms to ensure that parenteral products in South Africa are safe, effective, and of high quality[8].

The approval process for new drugs differs significantly between CDSCO in India and SAHPRA in South Africa:

CDSCO (India):

- **Application Submission**: Requires Form 44 for new drug applications, including comprehensive data on Chemistry, Manufacturing, Control (CMC), clinical trials, and non-clinical studies.
- **Review Process**: Applications undergo preliminary evaluations, followed by assessments from Subject Expert Committees (SEC). On-site inspections may be required before final approval.
- **Post-Approval**: Post-approval studies may be mandated to monitor long-term safety and efficacy[9].

SAHPRA (South Africa):

- **Application Submission**: Involves a detailed dossier submission, including clinical trial data, CMC, and pharmacovigilance plans.
- **Review Process**: Applications are reviewed by a dedicated committee, and SAHPRA may request additional information or conduct inspections.
- **Post-Approval**: Emphasizes on going safety monitoring and may require risk management plans[10].

Both authorities prioritize safety and efficacy but differ in documentation specifics and review mechanisms.

COMPARISON OF REGULATORY REQUIREMENTS 0F PARENTERALS IN INDIA WITH SOUTH AFRICA:

Regulatory aspect	CDSCO (India)	SAHPRA (South Africa)
Regulatory body	Central drugs standard control organization (CDSCO)	South African health product regulatory authority (SAHPRA)
Governing legislation	Drugs and cosmetics act, 1940	Medicines and related substances act, 1965
Product registration	Requires a new drug application (NDA) or abbreviated NDA for generics (extensive documentation required including drug master file (DMF), stability data, and clinical trial data.	Requires a new drug application (NDA) or abbreviated NDA (similar documentation to CDSCO INCLUDING stability data, GMP certification.
Clinical trial requirements	Approval required from CDSCO and ethics committee follows good clinical practice (GCP) guidelines separate approval for each phase of trials.	Approval required from SAHPRA and ethics committee must adhere to south African GCP guidelines all phases of clinical trials must be registered with SAHPRA.
Good manufacturing practice (GMP)	Adheres to schedule M of the drugs and cosmetics act regular inspection and compliance audits by CDSCO.	Adheres to GMP guidelines as per South African regulations (Regular inspections and compliances audit by SAHPRA.
Quality control and testing	Requires compliance with Indian pharmacopoeia (IP) standards mandatory sterility, pyrogen and stability testing.	Requires compliance with South African pharmacopoeia or recognized international standards mandatory sterility, pyrogen, and stability testing.
Labelling requirements	Must include drug name, compositions, batch number, manufacturing and expiry date, storage conditions etc. Specific requirements for injectable.	Must include drug name, composition, batch number, manufacturing and expiry date, storage condition, etc. labels must be in English and meet SAHPRA's labelling guidelines
Packing requirements	Compliance with schedule P of the drugs and cosmetics act (includes requirements of tamper-evident packaging and light-resistant containers)	Compliance with SAHPRA's guidelines for parenteral packaging (requirements for tamper-evident packaging and protection against contamination)
Pharmacovigilance	Mandatory reporting of adverse drug reactions (ADRs) to the pharmacovigilance program of India (PvPI) (regular safety updates required)	Mandatory reporting of adverse drug reactions (ADRs) to SAHPRA (continuous post marketing surveillance and safety updates)
Import and export regulations	Import license required under form 10/10A (export regulated under the export and import policy of India)	Import license required from SAHPRA (export regulated under south Africa trade loss and international agreements
Registration timelines	Average of 6-12 months for product registration depending on the complexity of the application	Average of 12-18 months for product registration; timelines can vary depending on the type of product
Fees	Fees vary based on type of application (new drug, generic, etc) (additional fees for clinical trials and GMP inspections)	Fees are tiered based on the type of application (new drug, generic, etc) (additional fees for clinical trials, inspections and post marketing surveillance)
Ethical review	Ethics committee approval required for all clinical trials (adheres to ICMR ethical guidelines)	Ethics committee approval required for all clinical trials (adheres to national and international ethical standards)

Intellectual property (IP)	Patent protection for pharmaceuticals under the Indian patents act, 1970 (data exclusivity not explicitly provide)	Patent protection under the patents act, 1978 (limited provisions data exclusivity)
Recent reforms	Recent updated to streamline drug approval processes and enhance pharmacovigilance	Recent focus on harmonizing with international standards and enhancing drug safety monitoring

This above table provides a high-level overview of the similarities and differences in a regulatory requirement of parenteral dosage form between India and South Africa[11].

CONCLUSION:

The regulatory standards for parenteral dosage forms in India and South Africa demonstrate a dedication to drug safety, efficacy, and quality. India's CDSCO requires extensive paperwork, including precise pharmacological data and bioequivalence studies, as well as adherence to good manufacturing procedures (GMP). The approval procedure is systematic, although the duration varies depending on the complexity of the application. In contrast, South Africa's SAHPRA uses a similar approach, stressing the submission of a Common Technical Document (CTD) and stability data. Both regulatory agencies seek to align standards with international principles, thereby enabling market access while promoting public health. This comparative research emphasizes the need of continued coordination and alignment between regulatory frameworks in improving the efficiency of drug approval processes in both nations.

ACKNOWLEDGEMENT:

The author wish to thank the management and faculty of Sree Siddaganga college of Pharmacy, Tumkur-572103, Karnataka, India for providing facilities to carry out this research

REFERENCES:

1. Shah Z, Maitreyi Z, Shrikalp D. A Comparative Study on Regulatory Requirements for Pharmaceutical and Biological Product registration in ASEAN and Asia Pacific Region for Parenteral Dosage Form. International journal of drug regulatory Affairs. 2024June;12(2):27-36.
2. Availablefrom:https://ijdra.com/index.php/journal/article/view/669.
3. Central Drugs Standard Control Organization (Import & Registration Division) Guidance Document.
4. Document No. IMP/REG/200711.
5. Central Drugs Standard Control Organization. (n.d.). About CDSCO. Retrieved from CDSCO Official Website: https://cdsco.gov.in
6. South African Health Products Regulatory Authority. (n.d.). About SAHPRA. Retrieved from SAHPRA Official Website: https://www.sahpra.org.za/
7. Key elements of regulatory frameworks. Available from:
8. URL: https://images.app.goo.gl/ZzYqorhTNcdJEuQZ7
9. India Large Volume Parenteral Market Trends. Available from:
10. URL:https://www.grandviewresearch.com/industry-analysis/india-large-volume-parenteral-lvp-market.
11. South Africa Intravenous Solutions Market Analysis. Available from:

12. URL: https://www.insights10.com/report/south-africa-intravenous-solutions-market-analysis/
13. SAHPRA, "Good Manufacturing Practices (GMP) Guidelines," South African Health Products Regulatory Authority, South Africa. Available from :(https://www.sahpra.org.za/guidelines).
14. Central Drugs Standard Control Organization (CDSCO), "New Drug Approval Process," CDSCO, India. Available from: (https://cdsco.gov.in).
15. South African Health Products Regulatory Authority (SAHPRA), "Guideline for the Registration of Medicines," SAHPRA, South Africa. Available from:(https://www.sahpra.org.za).
16. Central Drugs Standard Control Organization (CDSCO), "Drugs and Cosmetics Act, 1940 and Rules, 1945," CDSCO, India. Available from :(https://cdsco.gov.in).
17. South African Health Products Regulatory Authority (SAHPRA), "Medicines and Related Substances Act, 1965 (Act 101 of 1965)," SAHPRA, South Africa. Available from :(https://www.sahpra.org.za).

AJPTR is

- **Peer-reviewed**
- **bimonthly**
- **Rapid publication**

Submit your manuscript at: editor@ajptr.com