PATH workshop
AFSA-IABS Conference

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Disclaimer

The content of this presentation is for informational purpose only. This shall not be treated as an official interpretation of Indian Pharmacopoeia (IP) standard or relied on to demonstrate compliance with IP requirements.

Bacterial Endotoxin Test-Indian Pharmacopeia perspectives

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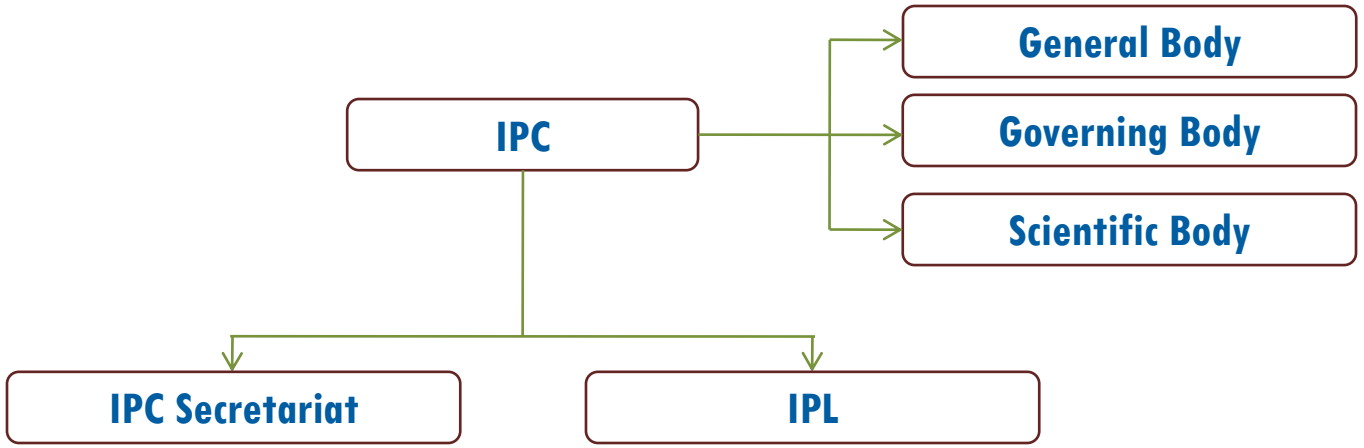
Indian Pharmacopoeia Commission (IPC)

- The Govt. of India has created a separate, dedicated, autonomous institution-Indian Pharmacopoeia Commission (IPC) in 2009-to deal with matters relating to timely publication of the Indian Pharmacopoeia (IP) which is the official book of standards for drug included therein, in terms of the Second Schedule to the Drugs and Cosmetics Act, 1940.

- IP specifies the Standards of Quality (identify, purity and strength) of the drugs imported, manufactured for sale, stocked or exhibited for sale or distributed in India.

- IPC has a three-tier policy formulation and execution setup comprising of the General Body, Governing Body and Scientific Body with experts drawn from various Science & Technology areas.



Mandates of IPC

- To publish new edition and addenda of the IP at regular intervals.
- To publish the National Formulary of India (NFI).
- Certification and distribution of IP Reference Substances (IPRS) and Impurity Standards.
- National Coordination Centre (NCC) for Pharmacovigilance Programme of India (PvPI)
- To establish working relations with National and International Institutes.
- To organize educational programs, skill development and research activities.

Indian Pharmacopoeia

Indian Pharmacopoeia-

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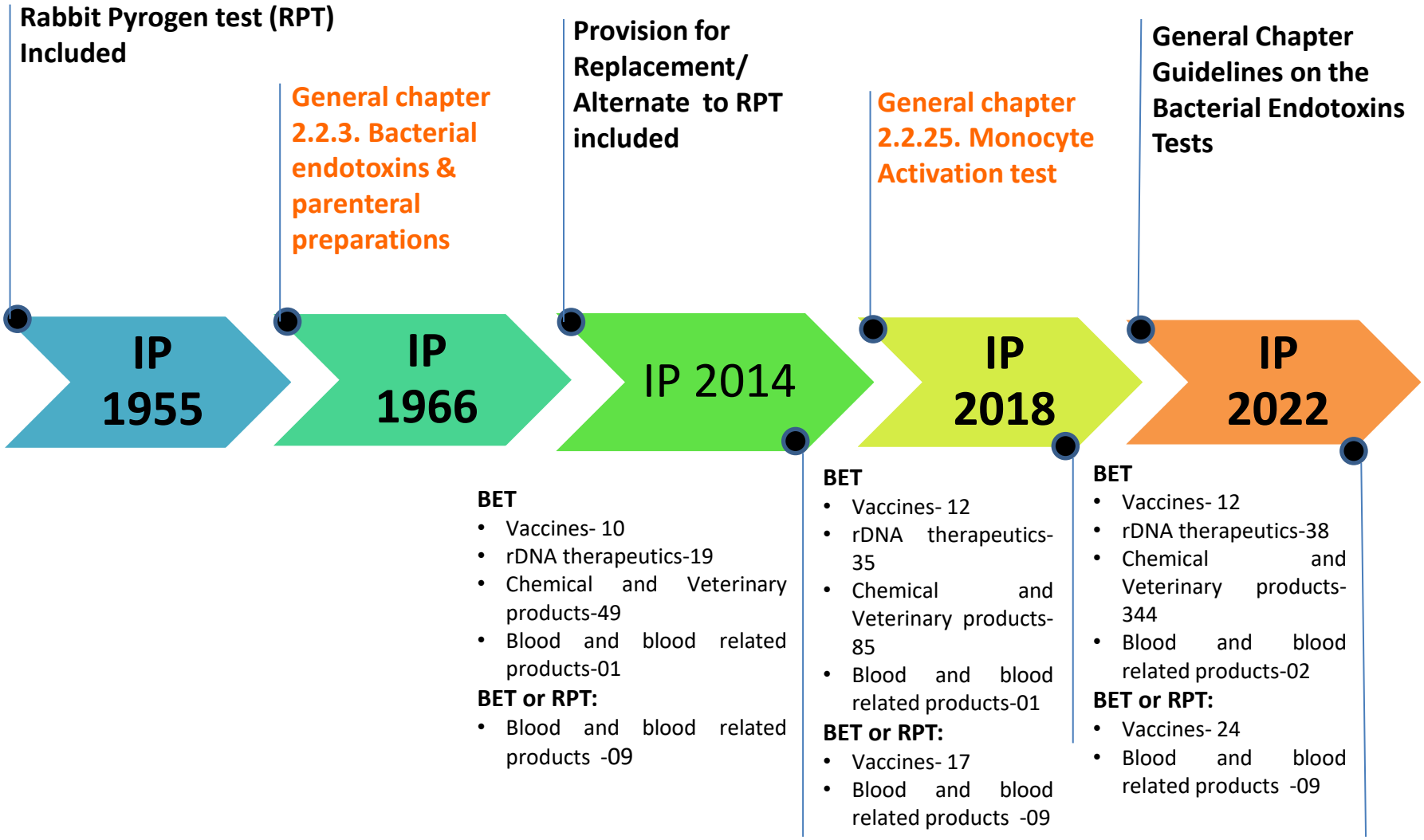
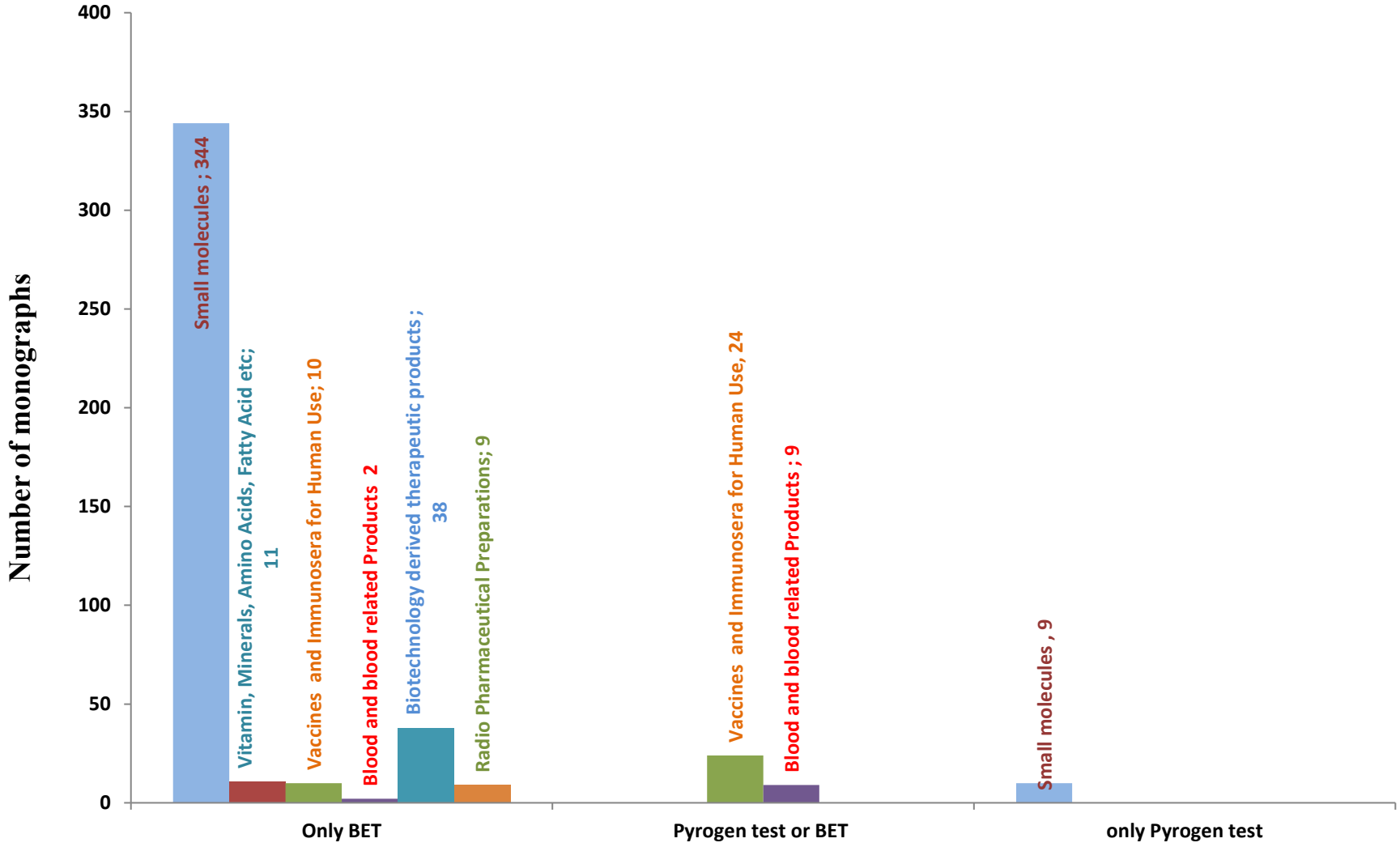
- Official book of standards for drug included therein, in terms of the Second Schedule to the **Drugs and Cosmetics Act, 1940**

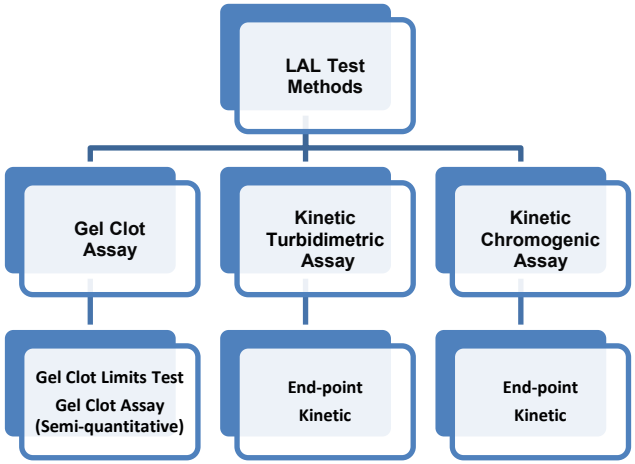
Pyrogenicity test in Indian Pharmacopoeia



IP 2022: Pyrogenicity testing status



IP 2022: 2.2.3. Bacterial Endotoxins



Parenteral formulations: Bacterial endotoxin test (BET) using LAL reagent

Few Vaccines for human use and Blood and Blood related products: Alternative approach as 'Pyrogen test or BET, if justified and authorized by NRA

2.2.3 Guideline on the Bacterial Endotoxins Test

- Chapter for information
- Alternate test method
  - ✓ Laboratory may choose alternate method
  - ✓ Fully validated
  - ✓ equivalent or better than pharmacopoeial method
  - ✓ approval of regulatory authority

IP 2022: 2.2.8. Pyrogens

Only Rabbit pyrogen test (RPT)

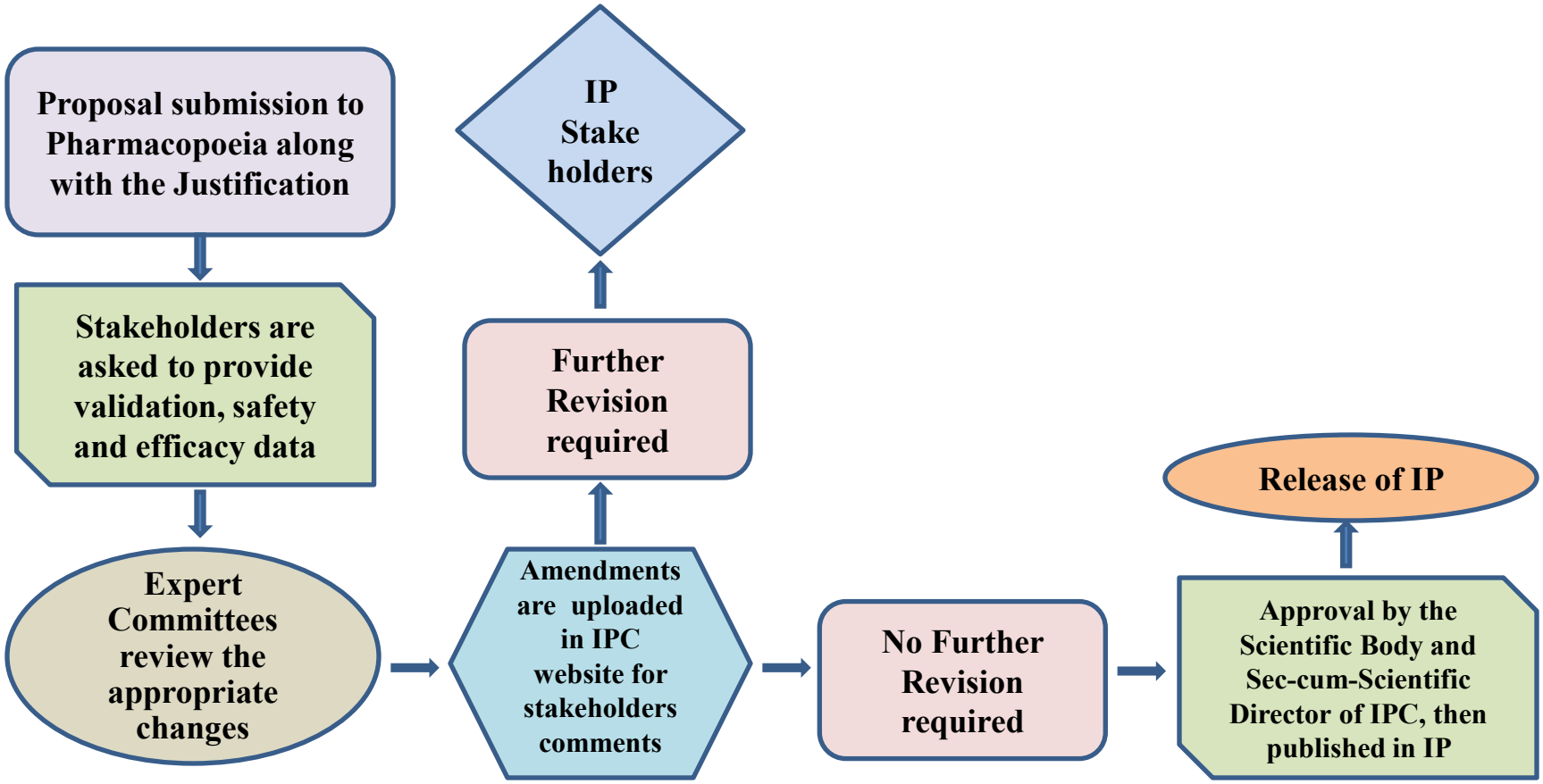
-06 individual monographs

-03 general requirements

RPT or BET- Vaccines for human use

Blood & Blood related products

Process for incorporating new methods in IP



Alternatives to animal methods- IPC's approach

IPC adopts any one or all of the following strategy in implementing alternatives to animal methods

- **Comparability and applicability of suitable non-animal** method/test in place of current *in vivo* method/test
- **Alternative approaches** based on scientific literature, retrospective data (ex: ATT & TABST), GMP and Pharmacovigilance in place etc
- Implementation of **consistency approach**
- **International harmonization** of regulatory requirements-WHO TRS and other pharmacopoeia
- **Expert opinion:** IPC has constituted a separate expert working group for 'Alternatives to Animal Methods'

Regulatory & Harmonization Aspects

Indian Pharmacopoeia (IP 2022	Unites states of Pharmacopoeia (USP-NF 2025)	European Pharmacopoeia 11.8	Japanese Pharmacopoeia 18th Edition
2.2.3. Bacterial Endotoxins	<85>BACTERIAL ENDOTOXINS TEST	2.6.14. Bacterial Endotoxins	4.01 Bacterial Endotoxins Test
2.2.33. Guidelines on the Bacterial Endotoxin Tests	⟨1085⟩ Guidelines On The Endotoxins Test	5.1.10. Guidelines For Using The Test For Bacterial Endotoxins	-
-	⟨86⟩ Bacterial Endotoxins Test Using Recombinantreagents	2.6.32. Test For Bacterial Endotoxins Using Recombinant Factor C	<G4-4-180> Bacterial Endotoxins Test and Alternative Methods using Recombinant Protein-reagents for Endotoxin Assay

*Legal requirement in India as per Drugs & Cosmetics act & rules there under

Harmonization & PDG

- Pharmacopoeial Discussion Group (PDG), brings together the Indian Pharmacopoeia (IP) European Pharmacopoeia (Ph. Eur.), the Japanese Pharmacopoeia (JP) and the United States Pharmacopeia (USP), with the World Health Organization (WHO) as an observer.

- IP aligns its general chapters and monographs with globally harmonized texts whenever feasible.

- When IP adopts a **harmonized PDG standard**, that harmonized version becomes the mandatory requirement in India.

Proposal to include recombinant factor C from Stakeholder

IPC receives proposal for inclusion of on rFC or rLAL in IP

Justification:

- Sustainable method to replace LAL from horse shoe crab (endagered/vulnerable), Sustainability in terms of horseshoe crab population diminishment and its availability in limited geographical region
- Reproducibility-no lot to lot variability in production of rFC
- Specificity-no Factor G hence no false positive

Challenges

- Lack of Sufficient Product-Specific Validation Data
- Performance equivalence/comparison only with LAL test is sufficient or with Rabbit pyrogen test also required?
- Matrix Interference in Vaccines, blood product and biologicals
- Limited Collaborative Data Across Industry
- Variability in Acceptance Across Pharmacopoeias
- Complexity of Submitting Post-Approval Changes
- Equipment & Infrastructure Constraints

Thank You

BUSINESS STANDARD,MUMBAI, 26 NOVEMBER 2025

18 nations and rising: India quietly builds global support for its Pharmacopoeia

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USE OF IP & IPRS IS SOCIAL AND LEGAL OBLIGATION FOR "IP" PRODUCTS

IP is available in both as Hard Copy and Online

***Refer www.ipc.gov.in* & www.onlineip.in**