Event

Animal Testing Replacement for Vaccines

A One Health View: Global Outlook and Future Stratergy

An Animal-Free Safety Assesment (AFSA) Collaboration Conference co-organised by

Humane World for Animals and IABS

Hotel Westin Grande Sukhumvit, Bangkok, Thailand, 2-4 December 2025

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.

Indian Pharmacopoeia perspectives on alternatives to animal methods in testing of vaccines for human and animal use

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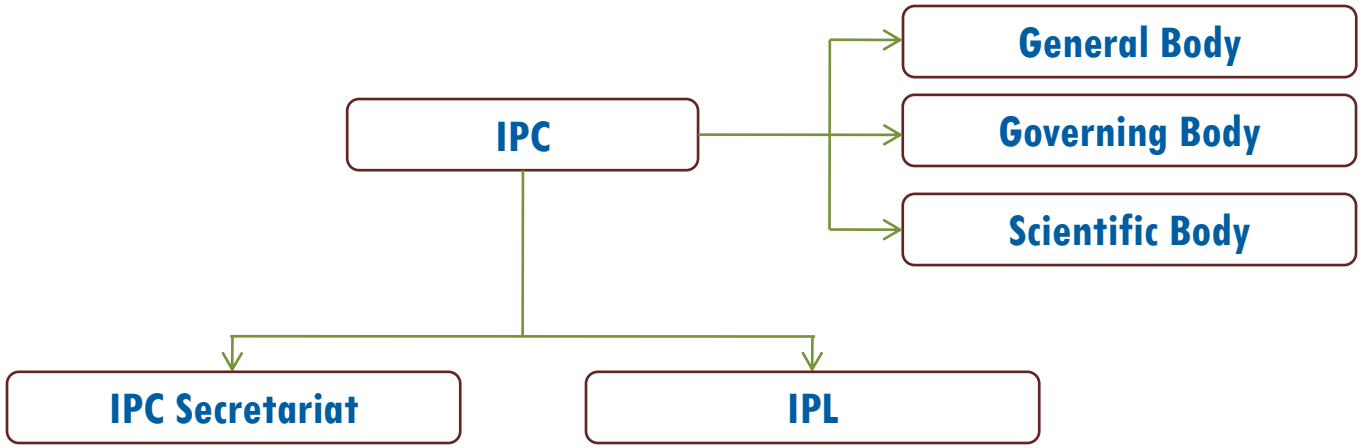
Indian Pharmacopoeia Commission (IPC)

- 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

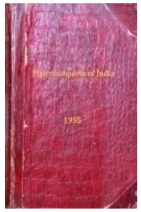
Indian Pharmacopoeia-

- A book of standards published by Indian Pharmacopoeia Commission (IPC). 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.

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

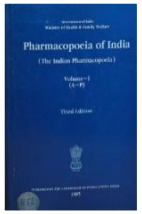
Journey of Indian Pharmacopoeia Editions

1955 — First Edition
1 Volume
986 Monographs
Title of monographs in Latin
Supplement in 1960

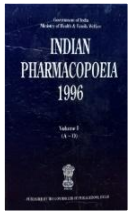


1966 — Second Edition
1 Volume
890 Monographs
Title of monographs changed from Latin to English
Supplement in 1975

1985 — Third Edition
1 Volume
886 Monographs
Anti-cancer Monographs Incorporated
Addenda in 1989 & 1991

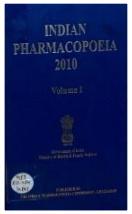


1996 — Fourth Edition
2 Volumes
1149 Monographs
Addenda in 2000, 2002, and 2005
Veterinary Supplement in 2000

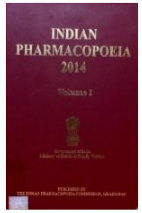


2007 — Fifth Edition
3 Volumes
Published by CIPL
1623 Monographs
Addenda in 2008

2010 — Sixth Edition
3 Volumes
Published by IPC
1968 Monographs
Biotech Monographs Incorporated
Addendum in 2012

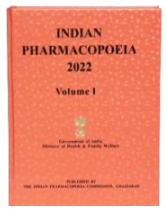


2014 — Seventh Edition
4 Volumes
Separate Veterinary Volume
2586 Monographs
Radiopharmaceutical Monographs Incorporated
Addenda in 2015 & 2016

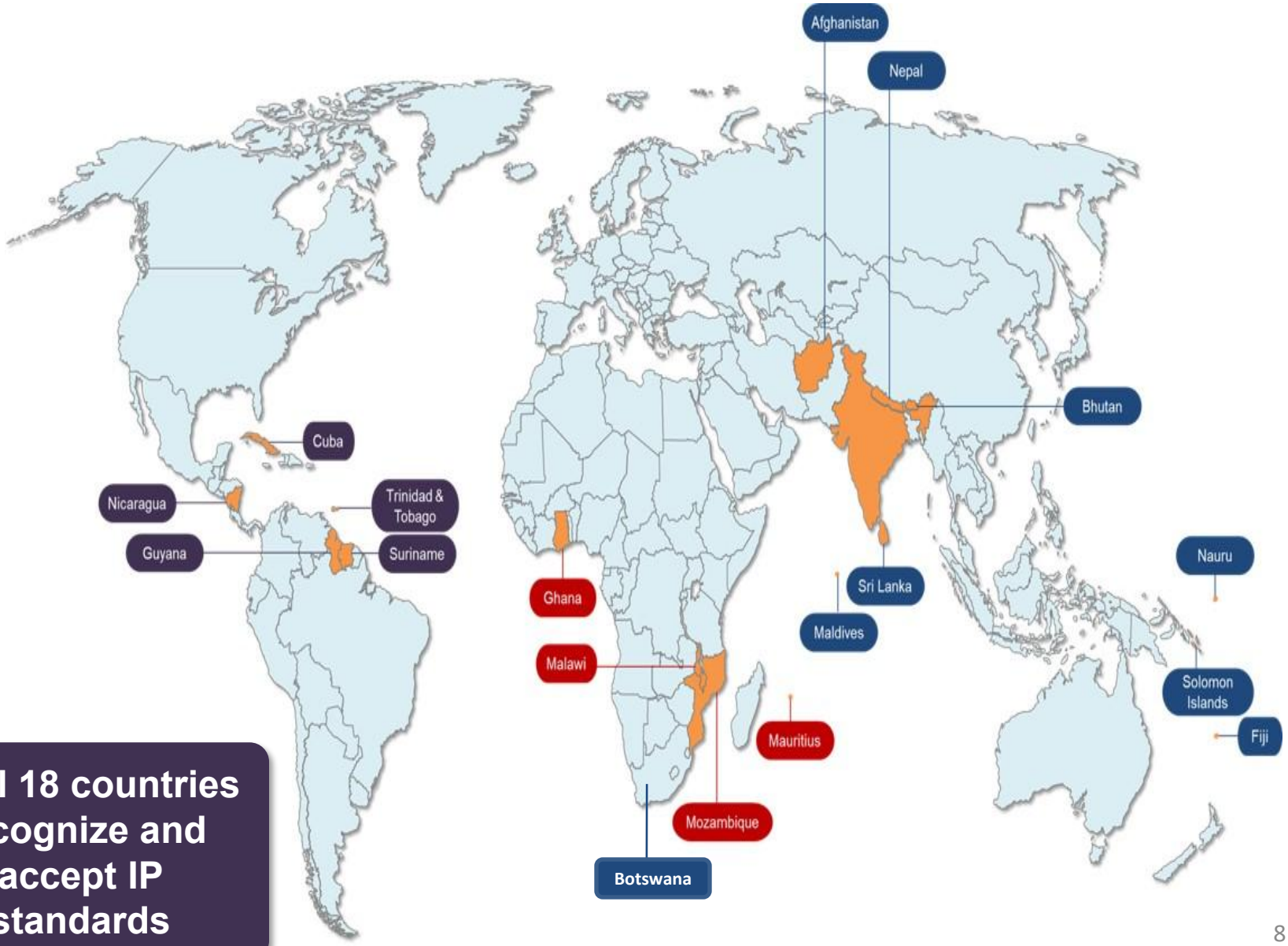


2018 — Eighth Edition
4 Volumes
3098 Monographs
Allergen Monograph Incorporated
Addenda in 2019 & 2021

2022 — Ninth Edition
4 Volumes
Separate Veterinary Volume
3190 Monographs
Including biological monographs for Mabs and Hexavalent vaccines Incorporated
Addenda in 2019 & 2021



Global Recognition of the IP



Total 18 countries recognize and accept IP standards

Indian Pharmacopoeia

Current edition: IP 2022 & its Addendum

- 3227 monographs and 227 General Chapters
- API & formulations, biologicals, Herbal & Phytopharmaceuticals, Vitamin & Minerals etc-Human & Animal use

Upcoming edition: IP 2026

- IP 2026: 3340 monographs and 232 General Chapters
- Blood components, mAbs etc are new

Veterinary products-Separate volume

Indian Pharmacopoeia Reference Substances (IPRS)

- IPRS are highly-characterized physical specimens used in testing as per pharmacopoeia requirements
- to help ensure the identity, strength, quality, and purity of drugs as given in the IP.
- IPC ranks at *3rd* globally in supply of RS (More than 1326 standards)
- More than 11 countries globally purchases IP standards

International Cooperation
Memorandum of Understanding (MoU)

- United States Pharmacopoeia (USP)
- British Pharmacopoeia (BP)
- Federal State Budgetary Institution “Scientific Centre for expert evaluation of medicinal products” of the Ministry of health of the Russian Federation (FSBI “SCEEMP”), Russian Federation

International Cooperation

- IPC became **member of the PDG** along with European Pharmacopoeia (EP), Japanese Pharmacopoeia (JP), and United States Pharmacopoeia (USP) during the PDG Annual Meeting held from 3rd-5th October 2023 at USP, Hyderabad

- **International Meeting of World Pharmacopoeias (IMWP)-** IPC hosted 15th Meeting February 2025

International Cooperation

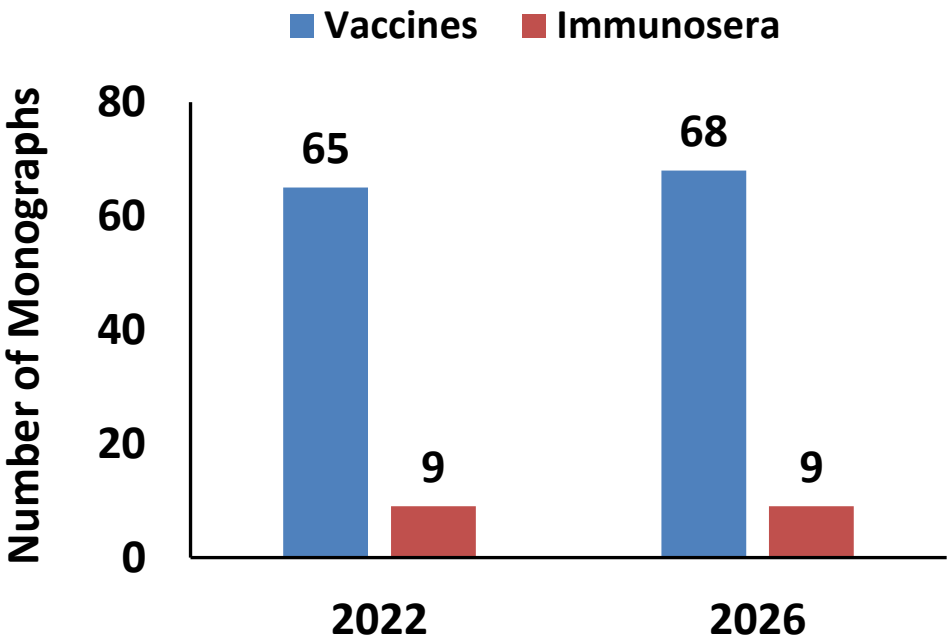
- IPC hosted 1st and 2nd Policy Makers Forums with regulators and pharmacopoeia scientist from 37 countries

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'

Vaccines and Immunosera for Human use



Total Number of monographs in IP 2022: 3227
IP 2026: 3340

Vaccines and Immunosera for Human use

Animal methods and its alternatives in IP

S.NO	Animal method in IP	Alternatives/non-animal testing
1.	Abnormal Toxicity	Waive off from final lot release in General Requirements; Included in addendum 2016 to IP 2014
2.	Potency Test (Introduction of serological Assay)	Diphtheria, Pertussis and Tetanus and its combination vaccines; Included in IP 2018
	(Provision of Multiple Dilution to single dilution)	Reduced to Single dilution method in Diphtheria and Tetanus (Adsorbed), ant its combination Vaccines; Included in IP 2018
	Potency Test	During developmental stage, once consistency established *in-vitro* potency can be adopted; Included in IP 2018
3.	Rabbit Pyrogen Test	Replaced By Bacterial Endotoxin Test (BET); Included in IP 2018
4.	*Specific Toxicity	Omission from final bulk release in Diphtheria and its combination vaccines; Included in IP 2022 List attached

Continued…

Vaccines and Immunosera for Human use

Animal methods and its alternatives in IP

S.NO	General Chapter/Guidelines
5.	Guideline on the Bacterial endotoxins tests; Included in IP Addendum 2024 to IP 2022 (IP 2022, 2.2.33) • Provision to use other validated methods not mentioned in Bacterial endotoxins 2.2.3
6.	*Detection of viral extraneous agents using High Throughput Sequencing (HTS) (IP 2026, 2.2.35)
7.	Monocyte Activation Test (IP 2018, 2.2.5)
8.	Substitution of *in-vivo* Method(s) by *in-vitro* Method(s) for the Quality Control of Vaccines; Included in IP Addendum 2024 to IP 2022 (IP 2022, 2.7.20)

Note: Text mentioned with (*) is in line with WHO "Guidelines on the replacement or removal of animal tests for the quality control of biological products" Annexure 2

Detection of viral extraneous agents using High Throughput Sequencing (HTS) (IP 2026, 2.2.35)

- NGS (also known as high-throughput sequencing) – Sensitive and demonstrated capabilities for broad virus detection, sensitive

List of General Chapters

- Test for Extraneous agents in Viral Vaccine for Human Use (2.7.3),
- Test for Neurovirulence for Live Viral Vaccines (2.7.5)
- Test for Neurovirulence (NVT) for oral poliomyelitis Vaccine (OPV) (2.7.6)

List of Monographs: 16 nos

Nucleic Acid Amplification Techniques (IP 2022, 2.8.1)

- 2.7.3. Test for Extraneous Agents in Viral Vaccines for Human Use
- 2.2.35. Detection of Viral Extraneous Agents Using High-Throughput Sequencing (HTS)
- 2.7.11. Avian Live Virus Vaccines - Tests for Extraneous Agents in Batches of Finished Products
- 2.7.19. Management of Extraneous Agents in Immunological Veterinary Medicinal Products
- 2.7.10. Avian Viral Vaccines - Tests for Extraneous Agents in Seed Lots
- Human Papilloma virus (rDNA) monograph

Vaccines and biologicals for Human use-

Specific Toxicity test in vaccines containing Diphtheria Vaccine adsorbed

IPC received request to delete specific toxicity from lot release or make it optional (inline with WHO TRS and other international pharmacopoeia)

↓

Retrospective data of consecutive batches was submitted by respective stakeholders

↓

Proposal was discussed in Expert Working Group and also stakeholders' opinion was sought

↓

Waiver off given with a note mentioned in monograph of Diphtheria vaccine adsorbed

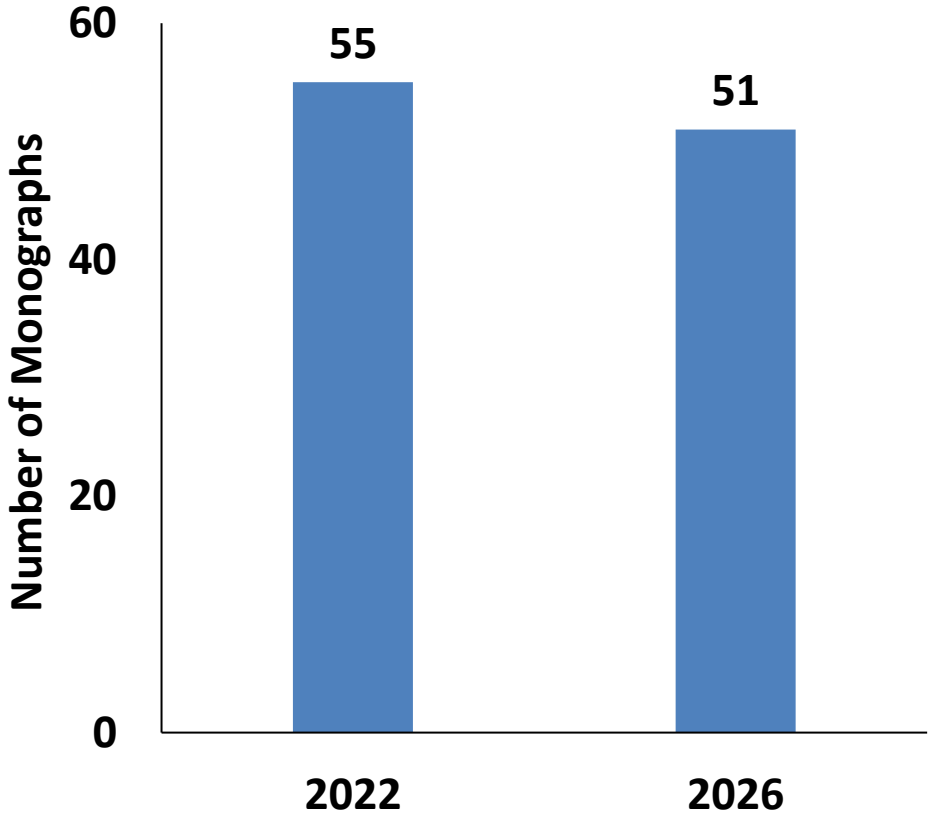
Provision to waive off Specific toxicity test from Diphtheria vaccine adsorbed has been given through following note-

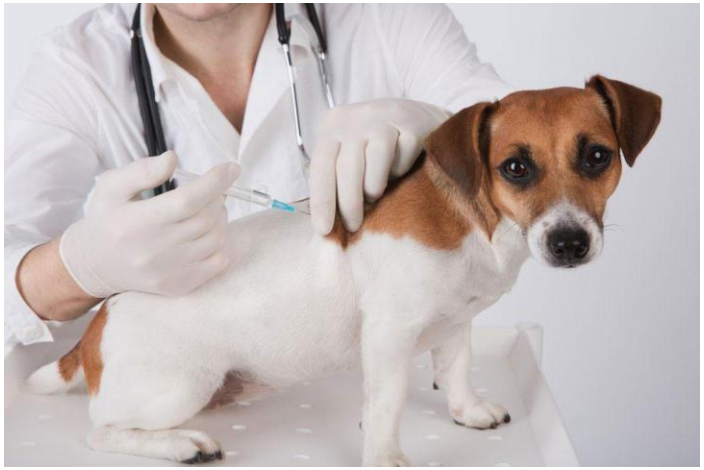
Note- *Specific toxicity test on the final bulk could be omitted for routine lot release once consistency of production has been established to the satisfaction of the National Regulatory Authority..*

Future Perspectives

- Deletion of histamine sensitization test from the final bulk testing of Pertussis acellular vaccine (adsorbed) and inclusion of CHO cell assay test method at antigen level.
- Inclusion of separate general chapter for CHO cell assay in line with other pharmacopoeia
- General Chapter/guideline for Pyrogenecity
- *In-vitro* method for Rabies Antisera

Vaccines and Biologicals for Veterinary use





Vaccines and biologicals for Veterinary use

Animal methods and its alternatives in IP

S. No.	Animal method in IP	Waive Off/Alternatives/non-animal testing
1.	Reversion to virulence	Reversion to virulence in live attenuated vaccines may be omitted; Included in IP 2026
2.	Target Animal Batch Safety Test (TABST)	Conditional waive-off form batch release; Included in IP 2022 (*Note*)
3.	Potency Test	In inactivated vaccines provision of use of validated *in vitro* method for batch release in place of challenge tests; Included in IP 2022 List of Monographs
		For live vaccines provision of Virus titre/Viable spore has been considered as potency test; Included in IP 2026
		In inactivated vaccines use of Small animals is given eg., Canine Coronavirus Vaccine, Inactivated; Included in IP 2022
4.	Identification	In veterinary vaccine monographs a provision for alternatively suitable validated immunochemical/ molecular biology methods has been given in some monographs like Avian Infectious Bronchitis Vaccine, Inactivated, Canine Corona virus vaccine, Inactivated, Canine Distemper vaccine, Live etc.

Vaccines and biologicals for Veterinary use

Target Animal Batch Safety Test (TABST)

IPC received request to waive off TABST

↓

Manufacturers were requested to submit relevant data for the said proposal

↓

Submission of Retrospective data of consecutive batches from domestic manufacturers

↓

Stakeholders Consultation

↓

Data discussed in Expert Working Group

↓

Waiver off given with a note mentioned in General Requirement

Note: *The batch safety test using target animal may be omitted if*

1] safety test has been performed with satisfactory results in master seed lot and

2] consistency of manufacturing process has been well established up to the satisfaction of NRA and

3] at least 10 consecutive production batches have been produced and comply with the safety test.

Significant changes to the manufacturing process may require resumption of routine safety testing to re-establish consistency.

Future Perspectives

- Complete waive off of TABST from veterinary vaccines monographs.

Conclusion

- IPC is committed in replacing animal methods and introducing alternatives, where ever possible based on scientific rationale and suitable data
- General notices in IP for alternative methods, stakeholders may adopt alternate method with the approval of regulatory authority
- Stakeholder may come forward for considering newer technologies during new product development & approval
- Newer technology providers :
  - may adopt cost-effective approach in developing new technologies
  - may focus on new products class, which are under process for regulatory approval
  - may focus on products class where interference are more like blood products, vaccines etc.

Thank You

BUSINESS STANDARD,MUMBAI, 26 NOVEMBER 2025

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

India quietly builds global support for its Pharmacopoeia

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

Target animal safety test (TABST)

The batch safety test using target animal may be omitted if 1] safety test has been performed with satisfactory results in master seed lot and 2] consistency of manufacturing process has been well established up to the satisfaction of NRA and 3] at least 10 consecutive production batches have been produced and comply with the safety test. Significant changes to the manufacturing process may require resumption of routine safety testing to re-establish consistency.

List of Monographs

1. Avian Spirochaetosis Vaccine (Inactivated),
2. Canine Coronavirus Vaccine (Inactivated),
3. Canine Leptospirosis Vaccine (Inactivated),
4. Canine Parvovirus Vaccine (Inactivated),
5. Duck Pasteurella Vaccine (Inactivated),
6. Egg Drop Syndrome Vaccine (Inactivated),
7. Infectious Chicken Anemia Vaccine (Inactivated),
8. Infectious Bursal Disease Vaccine (Inactivated),
9. Infectious Coryza Vaccine (Inactivated),
10. Salmonella Vaccine (Inactivated),
11. Anthrax Spore Vaccine (Live),
12. Avian Infectious Bronchitis Vaccine (Live),
13. Canine Parvovirus Vaccine (Live)

Specific Toxicity in Diphtheria Vaccine and its Combination, and conjugate vaccines containing Diphtheria toxoid as Carrier Protein

- Adsorbed Diphtheria, Tetanus and Hepatitis B (rDNA) Vaccine,
- Adsorbed Diphtheria, Tetanus, Pertussis (Acellular Component) and Haemophilus influenzae Type b Conjugate Vaccine,
- Adsorbed Diphtheria, Tetanus, Pertussis (Acellular Component) and Hepatitis B (rDNA) Vaccine,
- Adsorbed Diphtheria, Tetanus, Pertussis (Acellular Component), Inactivated Poliomyelitis Vaccine and Haemophilus influenzae Type b Conjugate Vaccine,
- Adsorbed Diphtheria, Tetanus, Pertussis (Acellular Component), Hepatitis B (rDNA), Poliomyelitis (Inactivated) andHaemophilus influenzae Type b Conjugate Vaccine
- Adsorbed Diphtheria, Tetanus, Pertussis (Acellular Component) and Inactivated Poliomyelitis Vaccine
- Adsorbed Diphtheria, Tetanus, Pertussis and Poliomyelitis (Inactivated) Vaccine
- Adsorbed Diphtheria, Tetanus, Pertussis, Poliomyelitis (Inactivated) and Haemophilus influenzaeType b Conjugate Vaccine
- Adsorbed Pertussis Vaccine (Acellular Component)
- Adsorbed Pertussis Vaccine (Acellular, Co-Purified)
- Diphtheria and Tetanus Vaccine (Adsorbed)
- Diphtheria and Tetanus Vaccine (Adsorbed) for Adults and Adolescents

Continued…..

- Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed)
- Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and Haemophilus influenzae Type b Conjugate Vaccine (Adsorbed)
- Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA), Poliomyelitis (Inactivated) and Haemophilus influenzae Type b Conjugate Vaccine (Adsorbed)
- Diphtheria, Tetanus, Pertussis (Whole Cell) and Hepatitis B (rDNA) Vaccine (Adsorbed)
- Diphtheria, Tetanus, Pertussis (Whole Cell) and Haemophilus influenzae Type b Conjugate Vaccine (Adsorbed)
- Diphtheria Vaccine (Adsorbed)
- Diphtheria Vaccine (Adsorbed) for Adults and Adolescents
- Diphtheria, Tetanus and acellular Pertussis vaccine (Adsorbed, reduced diphtheria and acellular pertussis antigen content): dTaP for adults and adolescents
- Meningococcal Group A, C, W135, Y and X Conjugate Vaccine
- Meningococcal Group A, C, W135 and Y Conjugate Vaccine
- Haemophilus Influenzae Type B Conjugate Vaccine
- Group A Meningococcal Conjugate Vaccine
- Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed)

List of Monographs

1. Bivalent Poliomyelitis Vaccine Type 1 And 3, Live (Oral)
2. Human Papillomavirus Vaccine (rDNA)
3. Inactivated Hepatitis A Vaccine (Adsorbed)
4. Influenza Vaccine (HUMAN, Live Attenuated)
5. Japanese Encephalitis Vaccine (HUMAN)
6. Japanese Encephalitis Live Vaccine (HUMAN)
7. Japanese Encephalitis Vaccine Inactivated (ADSORBED, HUMAN)
8. Measles Vaccine (Live)
9. Mumps Vaccine (Live)
10. Poliomyelitis Vaccine (INACTIVATED)
11. Rabies Vaccine, HUMAN
12. Rotavirus Vaccine (Live Attenuated, ORAL)
13. Rubella Vaccine (Live)
14. Tick-borne Encephalitis Vaccine (INACTIVATED)
15. Varicella Vaccine, Live
16. Yellow Fever Vaccine