

# BRIEF ON ASIA & AFRICA



Post Approval Change

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**DCVMN**  
**INTERNATIONAL**  
Developing Countries Vaccine  
Manufacturers Network International



# INDIA

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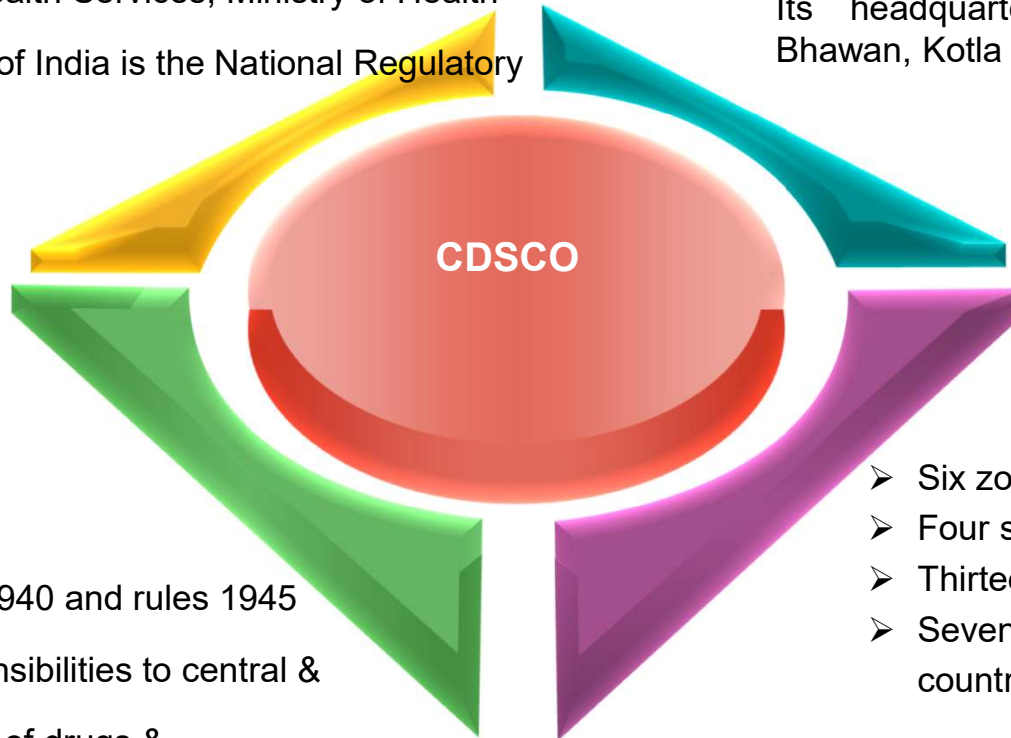


# The Central Drugs Standard Control Organisation (CDSCO)

## The Central Drugs Standard Control Organisation (CDSCO)

under Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India is the National Regulatory Authority (NRA) of India.

Its headquarter is located at FDA Bhawan, Kotla Road, New Delhi 110002.

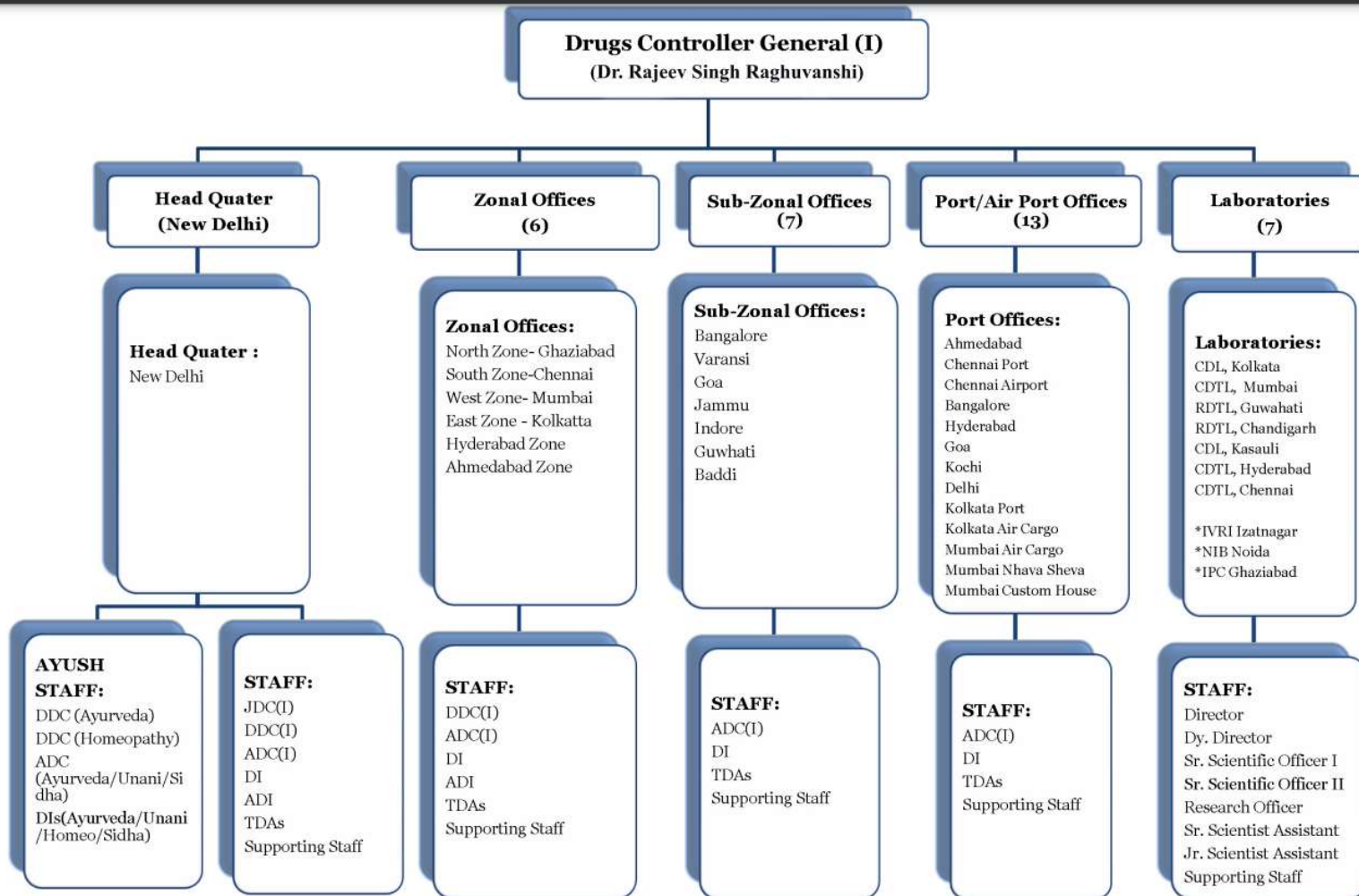


The Drugs & Cosmetics Act, 1940 and rules 1945 have entrusted various responsibilities to central & state regulators for regulation of drugs & cosmetics. **Now includes Medical devices**

- Six zonal offices
- Four sub zonal offices
- Thirteen Port offices
- Seven laboratories spread across the country

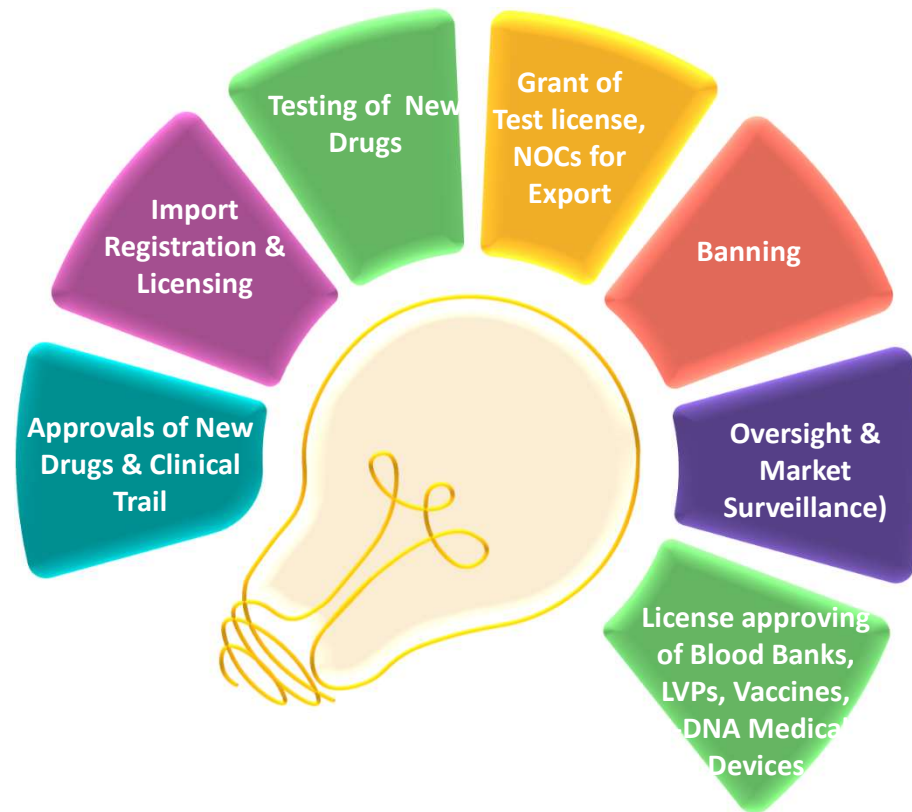
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# The Central Drugs Standard Control Organisation (CDSCO)



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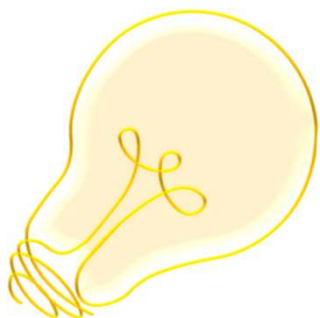


# Post Approval Change Guideline In India

**Post approval changes in Biological Products: Quality Safety and Efficacy Documents.**

Document No. - PAC/1108

Version – 1.1



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## PAC CLASSIFICATION IN INDIA

Classification as per CDSCO-PAC/1108-1.1	Types
Level I- Supplements*	Major Quality Changes
Level II- Notifiable Changes*	Moderate Quality Changes
Level III- Annual Notification	Minor Quality Changes

*\*Initially there was a provision of auto approval of PAC for level I Supplement and level II notifiable change, if not opined by the authority within the time period of 30 days and 15 days respectively.*

This has been omitted vide clarification and Amendment dated 5<sup>th</sup> Aug 2010.

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## PAC CLASSIFICATION IN INDIA

Classification as per CDSCO-PAC/1108-1.1	Common Supporting Document
Level I- Supplements (Major Quality Changes)	1. A covering letter. 2. Side-by-side comparison of the previously approved and the changed information.
Level II- Notifiable Changes (Moderate Quality Changes)	3. An electronic or hard copy of the Quality Overall Summary (QOS).

- 1. The cover letter should include a list of changes describing each in sufficient detail to allow for a quick assessment on appropriate reporting category.*
- 2. Side-by-side comparisons, where relevant and applicable.*
- 3. In the QOS only those sections affected by the proposed change(s) should be included, sections not affected by the change(s) should be deleted from the QOS).*

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## PAC CLASSIFICATION IN INDIA

Classification as per CDSCO-PAC/1108-1.1	Common Supporting Document
Level III- Annual Notification (Minor Quality Changes)	Any data that may have been generated by the Manufacturer in support of a Level III change should be submitted annually but should be available to DCG(I) within fifteen (15) calendar days, if requested.



# SRILANKA

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## PAC CLASSIFICATION IN SRILANKA

Country	Responsible NRA	Region	NMRA classification
Sri Lanka	NMRA	ASIA	MAV - Major Variation MIV <sub>1</sub> - Minor variations requiring approval MIV <sub>2</sub> - Minor variations requiring notification

The guideline was prepared based on the reference from two WHO Guidelines

1. WHO Guideline on Procedures and Data Requirements for Changes to Approved Biotherapeutic Products, 2017 2.
2. Annex 4 WHO TRS 993, Guidelines on Procedures and Data Requirements for Changes to Approved Vaccines, 2015

No separate guideline , however separate appendix guideline is available.

For biologicals and vaccine there are no separate post approval change guidelines. However, there is a separate Appendix II “*Examples of documentary requirement of variation applications for biologicals / biotech products*” which indicated the condition to be fulfilled and the supporting documents to be provided.

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## PAC CLASSIFICATION IN SRILANKA

Type of Variation/PAC	Procedure	Timeline for NMRA
MAV - Major Variation	If the application fulfils the requirements, NMRA shall issue an approval for the proposed change.	120 working days
MIV <sub>1</sub> - Minor variations requiring approval	If the application fulfils the requirements, NMRA shall issue an approval for the proposed change.	90 working days
MIV <sub>2</sub> - Minor variations requiring notification	To consider as approved if no response from NMRA within 30 working days	30 working days, if there is a concern

All Documents in support of an application for variation should be submitted along with administrative documents, among other, as the following,

- (i) A statement letter that declares there is no other change except for the proposed variation.
- (ii) A comparative table of the proposed changes including reference of changes.
- (iii) Justification of the proposed changes.
- (iv) Certificate of Registration and all prior approvals of Variation issued by the NMRA including the appendices.
- (v) Other required administrative documents.



# PHILIPPINES

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## PAC CLASSIFICATION IN PHILIPPINES

Type of Variation/PAC	Procedure	Timeline for FDA
MaV- Major Variation.	If the application fulfils the requirements (conditions and supporting documents) as per described under MaV, the Drug Regulatory Authority shall issue an approval for the proposed change.	Within a duration subject to country specific proposal, following receipt of a valid notification.
MiV-PA- Minor Variation (Prior Approval).	If the application fulfils the requirements (conditions and supporting documents) as per described under MiV-PA, the Drug Regulatory Authority shall issue an approval for the proposed change.	
MiV-N- Minor Variation (Notification).	Notification “Do & Tell” If the notification fulfils the requirements (conditions and supporting documents) as per described under MiV-N, the Drug Regulatory Authority shall acknowledge receipt of a valid notification.	

- The post approval change guideline is specifically for Pharmaceutical product and does not include biologics in its scope.
- The Guideline was prepared based on the reference from following WHO guidance which are not vaccine specific.
- “Guidance on Variations To A Prequalified Product Dossier, 2007”, “WHO Technical Report Series, No. 953, 2009”.
- For Human Influenza vaccine however, Strain clearance guidelines are available under major and minor category as Mav-SC, MiV-SC.



# MALAYSIA

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## PAC CLASSIFICATION IN MALAYSIA

Type of Variation/PAC	Maximum Review Period
Major variation ( <b>MaVB</b> )	90 Working Days
Minor variation requiring approval ( <b>MiVB-PA</b> )	60 Working Days
Minor variation requiring notification ( <b>MiVB-N</b> )	30 Working Days

- The Malaysian Variation Guideline For Biologics (MVGB) is based on the adaptation of WHO TRS 993 (2014) Annex 4: “Guidelines on Procedures and Data Requirement for Changes to Approved Vaccines”.
- However, the modifications have been made taking into considerations of current Malaysian Variation Guidelines (MVG) and also current local requirements and policies based on the latest Drug Registration Guidance Document (DRGD).
- Malaysia have separate Post approval guidance for biologics which also includes vaccine.





# TANZANIA

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## PAC CLASSIFICATION IN TANZANIA

Type of Variation/PAC	Procedure	Timeline
<b>Major variation (Vmaj)</b>	A letter of acceptance will be issued for all major variations when the variation is considered acceptable.	6 Months
<b>Minor variation (Vmin)</b>	Such variations can be implemented if no objection letter has been issued within four (4)months. Should questions arise during the specified period; the change can only be implemented on receipt of a letter of acceptance from TMDA.	4 Months
<b>Notifications (N)</b>	Such changes can be implemented immediately at the time of submission and they can be considered accepted if an objection is not issued within two (2) months of the date of acknowledgement of receipt of the application.	2 Months

- In Tanzania the post approval guideline has been prepared referencing *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh report*. Geneva, World Health Organization, 2015, Annex 4 (WHO Technical Report Series, No.993).
- There is a separate vaccine specific post approval change Guidelines on variations i.e.(TMDA/DMC/MRE/G/014), First Edition February, 2021.



# SOUTH AFRICA

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## PAC CLASSIFICATION IN SOUTH AFRICA

Type of Variation/PAC	Procedure	Timeline
Type II amendments (Major changes)	The Type II amendments must be reviewed and approved by SAHPRA prior to implementation.	≤ 120 working days
Type IB amendments (Moderate changes)	Implementable after 60 working days	7 Working days for acknowledgement. 60 Working days for evaluation. Deemed acceptable if not response in 60 days.
Type IA amendments (Minor changes)	May be implemented without prior approval	30 days SAHPRA should be notified of the changes within 12 months of implementation
Type IA <sub>IN</sub> amendments (minor changes, Immediate Notification)	Minor amendments of Type IA <sub>IN</sub> require immediate notification to SAHPRA	30 days

- In south Africa the post approval guideline has been prepared referencing World Health Organization, 2015, Annex 4 (WHO Technical Report Series, No.993).



# EGYPT

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## PAC CLASSIFICATION IN EGYPT

Type of Variation/PAC	List of Document for All Variation
Major Quality Changes	1. Covering letter with cleared & detailed scope on applicant head letter dated, signed, stamped. 2. Registration license (copy) 3. Variation Application form for each variation describing the variation submitted with cleared & detailed scope as in covering letter. 4. Approval on the variation from the Health authority in the country of origin (Legalized), or other relevant documents (CPP, .....). For imported products. 5. A declaration on applicant head letter that all data in the file is true, accurate and identical to the submitted soft copy. 6. Payment receipt.
Moderate Quality Changes	
Minor Quality Changes	

- In Egypt for post approval change “Guideline on administrative requirements for variation submission of biological products, Version No: 3.0 , Issue Date: 26/1/2022” is followed.
- The guideline primarily addresses the requirement of the administrative documents that are not covered by WHO guideline.
- Egypt follows the Guidelines on procedures and data requirements for changes to approved vaccines, Annex 4, TRS No 993

## PAC CLASSIFICATION IN EGYPT

### Egypt PAC guideline list the requirements for Some Variations which they indicate is not mentioned in WHO Guidelines

Requirements for Insert update either SmPC or PIL or IPI

Requirements for pack update:

- Design
- Colour
- No. of units/pack.

Requirements for Market Authorization Holder / License Holder Change:

- The variation Change In MAH / License Holder.
- The variation either Change in Name or Address.

Requirements for Applicant Change.

Requirements for Manufacturing Facility Change:  
If the variation either Change in Name or Address

Requirements for Product Name Change

Requirements for Annual Strain

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# SUMMARY

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Country	Responsible NRA	Region	PAC Classification
India	CDSCO	Asia	Level I- Supplements (Major Quality Changes). Level II- Notifiable Changes (Moderate Quality Changes). Level III- Annual Notification (Minor Quality Changes).
Sri Lanka	NMRA	Asia	MAV- Major Variation. MIV <sub>1</sub> - Minor variations requiring approval. MIV <sub>2</sub> - Minor variations requiring notification.
Philippines	FDA	Asia	MaV- Major Variation. MiV-N- Minor Variation (Notification). MiV-PA- Minor Variation (Prior Approval).
Malaysia	NPRA	Asia	MaVB- Major Variation. MiVB-N- Minor Variation (Notification). MiVB-PA- Minor Variation (Prior Approval).
South Africa	SAHPRA	Africa	Type II amendments (Major changes). Type IB amendments (Moderate changes). Type IA amendments (Minor changes). Type IA <sub>IN</sub> amendments (Minor changes, Immediate Notification).
Tanzania	TMDA	Africa	Major variation (Vmaj). Minor variation (Vmin). Notifications (N).

# SUMMARY

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graph LR; A{{SUMMARY}} --> B[In Malaysia, Sri Lanka, South Africa, Tanzania & Egypt Post Approval Change guidelines has been prepared referring WHO TRS 993, Annex4.]; A --> C[There are no WHO reference Indicated in Indian Post Approval Change Guidelines.]; A --> D[The Classification labels are different in different Countries.]; A --> E[India, South Africa, Sri Lanka, Malaysia, Tanzania, Egypt has separate biologicals/Vaccine specific PAC guidelines. Philippines PAC guidelines does not include biologics .];
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In Malaysia, Sri Lanka, South Africa, Tanzania & Egypt Post Approval Change guidelines has been prepared referring WHO TRS 993, Annex4.

There are no WHO reference Indicated in Indian Post Approval Change Guidelines.

The Classification labels are different in different Countries.

India, South Africa, Sri Lanka, Malaysia, Tanzania, Egypt has separate biologicals/Vaccine specific PAC guidelines. Philippines PAC guidelines does not include biologics .

