

# Vaccine International Standards (IS)

- WHO Guideline, Annex 2, TRS No. 932, including vaccine IS is under revision.
- Vaccine IS are included in the draft TRS, but the guidance scope is broader than vaccines.
- This provides an opportunity to reflect on key issues related to vaccine IS.
- When an IS when is available, it should be incorporated into the control strategy of a product.
- Note that It's the manufacture's responsibility to maintain the consistency of a product over its self-life, and life-cycle relative it's approved specification.
- "Like for like" consideration of the IS CQAs and those of proposed analytes are important.

# Example of Same Reference Standard Used in Both In Vivo and In Vitro Assays

## Should the same standard be used?

- **Not necessarily:** the draft WHO recommendations emphasize that:
- The same reference **can be used** if the measurand is the same (e.g. same antigen or functional activity)
- But **parallel qualification is essential**. If the in vivo and in vitro assays:
  - Measure **different biological endpoints** (e.g. protection vs antigen quantity),
  - Or have **different matrix sensitivities**, then **assay-specific calibration or separate unitages** must be used.
- Enables use of a **common material**, but **distinct IU or Arbitrary Unit** per method
- Promotes **bridging studies** rather than forced equivalence
- Supports gradual **transition from in vivo to in vitro**, while maintaining traceability

## **Regulatory Note:**

- WHO allows **multiple unitages per reference**

# Example: Transitions from in vivo to in vitro testing

<b>Feature</b>	<b>Rabies Vaccine</b>	<b>IPV Vaccine</b>
Same IS used?	Yes (7th IS, 16/204)	Yes (Sabin IS, 12/104)
In vivo assay?	NIH Mouse Protection	Rat Immunogenicity
In vitro assay?	ELISA, SRD (glycoprotein)	D-antigen ELISA
Unitage same?	No (different IUs)	No (IU vs D-antigen units)
Bridging performed?	WHO collaborative study	WHO collaborative study
Regulatory strategy?	Assay-specific IU	Dual-use with clear unit distinction