

Vaccine standardization in the context of PQ

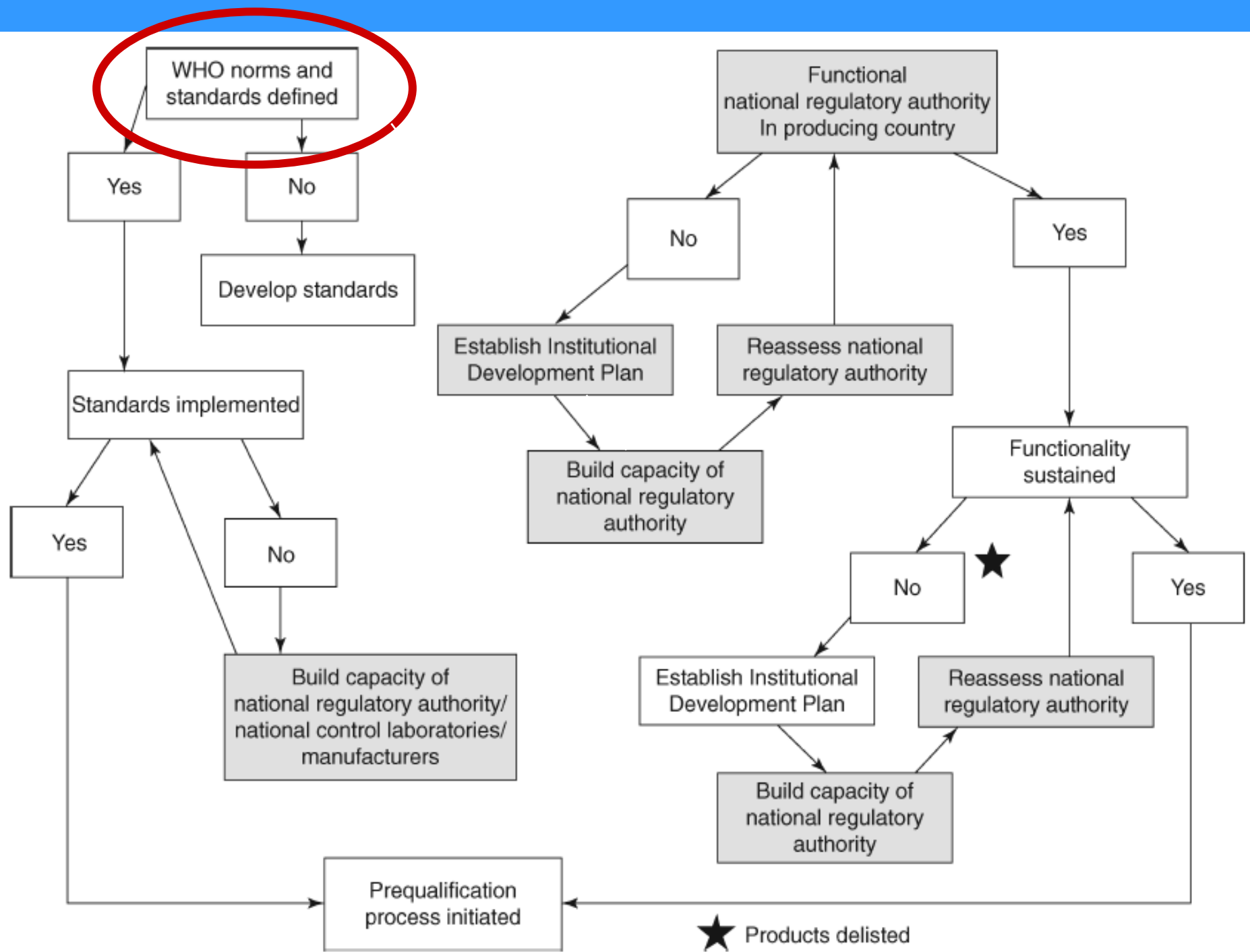
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**World Health
Organization**

Outline

- WHO standards for vaccines
- Vaccines of assured quality
- Written and measurement standards - 40 years analysis
- Basis for vaccine PQ
- Development of new and revision of existing standards - plan for 2011/2013
- Summary
- Way forward



WHO Biological Standardization

Global written standards

Global measurement standards



Evolving concept

<http://www.who.int/biologicals/en/>



370 WHO measurement Standards are available; define the IU

Global consensus

- 1) Standardization of assays
- 2) Development and refinement of QC tests
- 3) Scientific basis for setting specifications

67 WHO Written Standards

Biological Standardization as constitutional responsibility

- WHO is mandated by its Member States to "...develop, establish and promote **international standards for biological products**"
- Biological products for WHO cover vaccines, biological therapeutics, blood products and selected in vitro diagnostics
- Implemented by Expert Advisory Panel (EAP) and **Expert Committee on Biological Standardisation (ECBS)**
- Served by secretariat in the Quality Safety & Standards (QSS) Team

WHO Collaborating Centres for biological standardization

- NIBSC (all biologicals)
- CBER/FDA (all biologicals)
- PEI (blood products and related IVDs - expansion to vaccines under consideration)
- NIID, Japan (vaccines)
- TGA (vaccines)
- KFDA (Korea) - designated in 2011 (vaccines and biotherapeutics)
- Under consideration: BTGD (Canada); NICPBP (China); Thai NCL
- Strategic direction: synchronized approach for the network of CCs for Biological Standardization

WHO Written Standards for Vaccines

- Technical specifications that help define safe and efficacious vaccines
- Intended to be scientific and advisory in nature
- Basis for **vaccine prequalification**
- Guidance for NRAs and manufacturers on international regulatory expectations for the **production and quality control of vaccines, non-clinical and clinical evaluation of vaccines**
- Facilitating international harmonization of vaccine licensure
- Living documents revised in response to scientific advances

Scope: Recommendations to assure quality, safety and efficacy of pneumococcal conjugate vaccine (an example)

Development and endorsement of WHO written standards

- Drafting group meeting to initiate drafting (scope, structure, approach, and major scientific/technical issues)
- Informal consultation (regulators, academicians, industry experts)
- **Web publication of a draft: call for comments (*new procedure since 2009)**
- Distribution to EAP and Member States as "BS document" to obtain comments
- ECBS review - discussion, revision, and decision (-> report to SAGE & Exec Board)
- Internal clearance (DGO approval)
- **Web publication of electronic document (final document available)**
- Editing & proofreading
- Printing as Annex to WHO TRS

World Health Organization Goal

Ensure that "100%" of vaccines used in all national immunization programmes are of assured quality



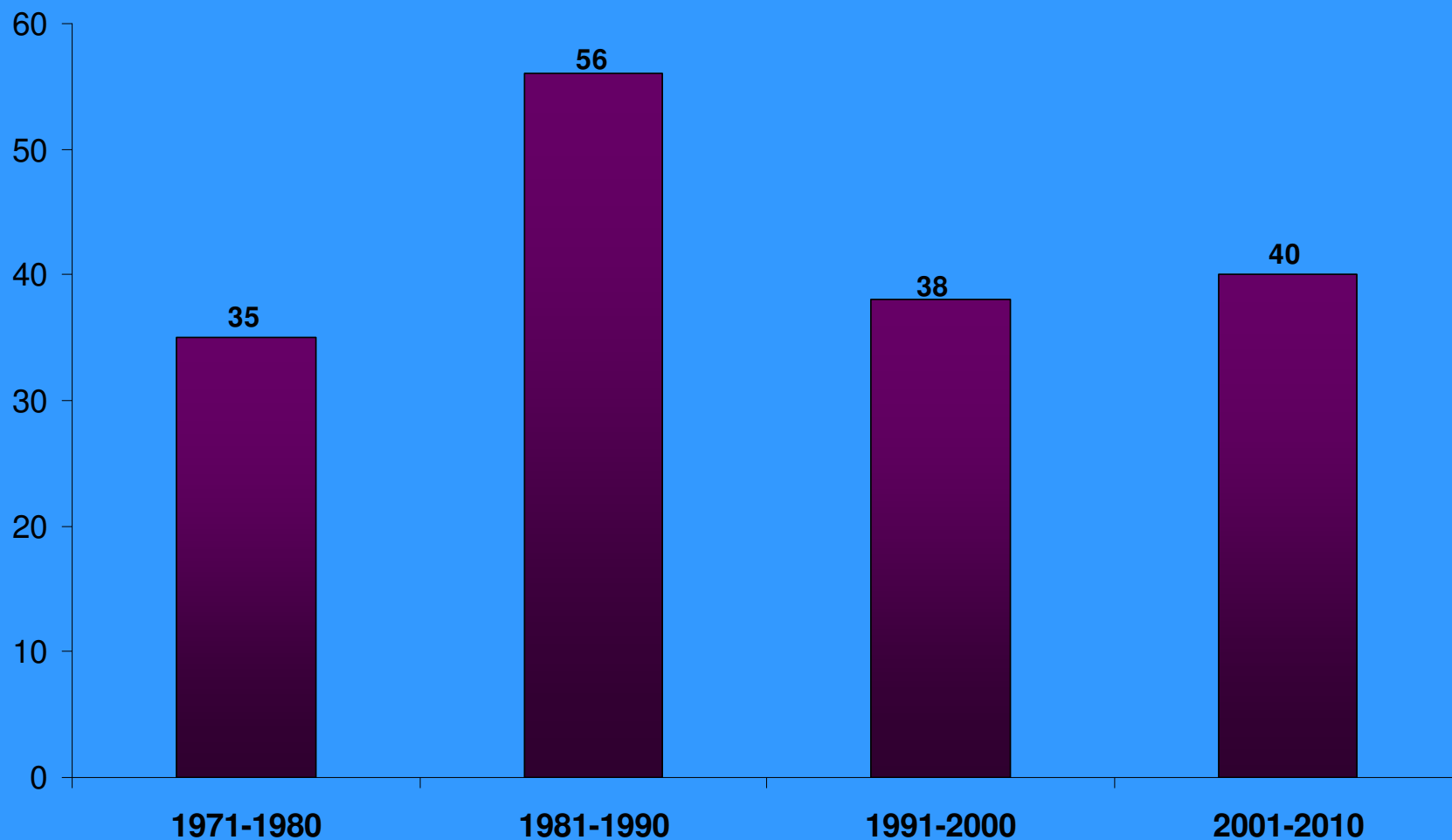
Definition

- ✓ National Regulatory Authority (NRA) independently controls the quality of vaccines in accordance with the six specified functions defined by WHO
- ✓ No unresolved confirmed reports of quality related problems

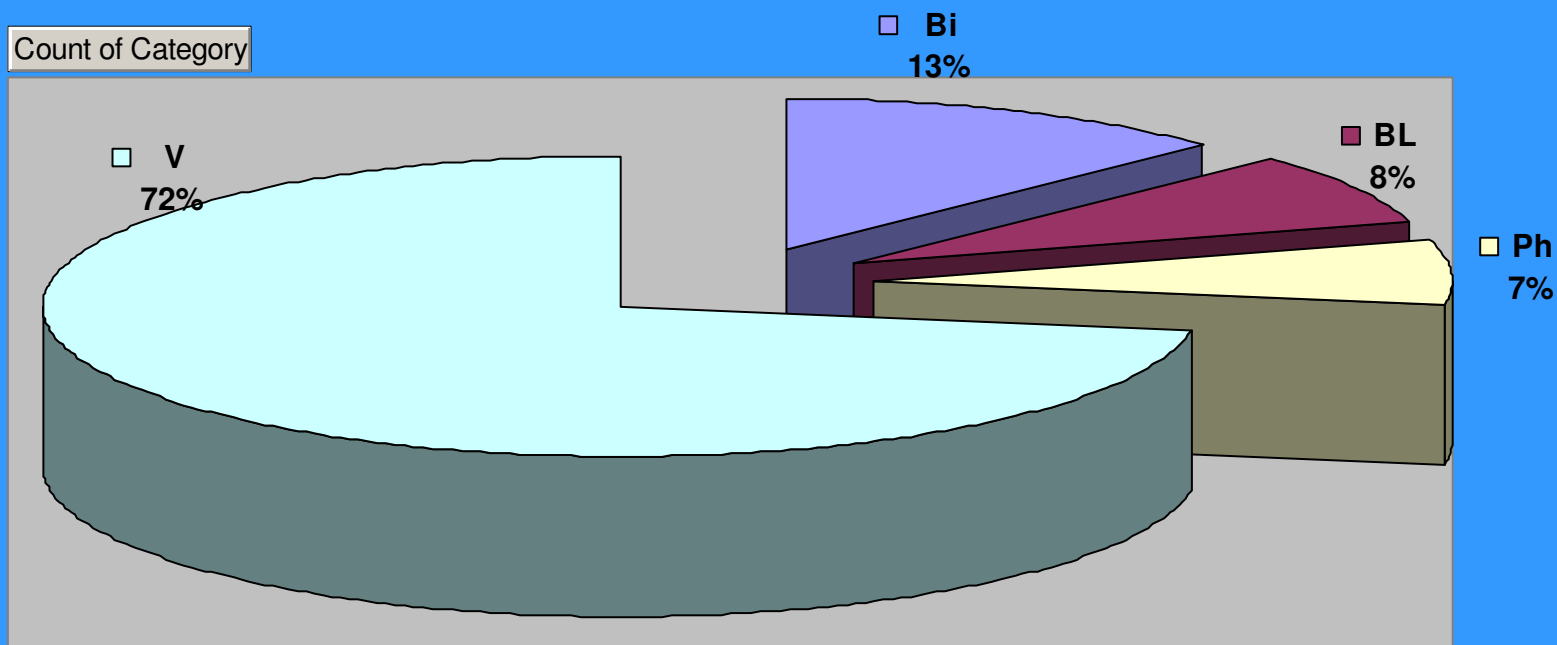
Guided by WHO Expert Committee on Biological Standardization ECBS): Recommendations to assure quality, safety and efficacy of vaccines (WHO Technical Report Series (TRS))

Written Standards
Established/Revised for Vaccines
& Biologicals

No. of Written Standards for Vaccines & Biologicals for 4 Decades (N=174)

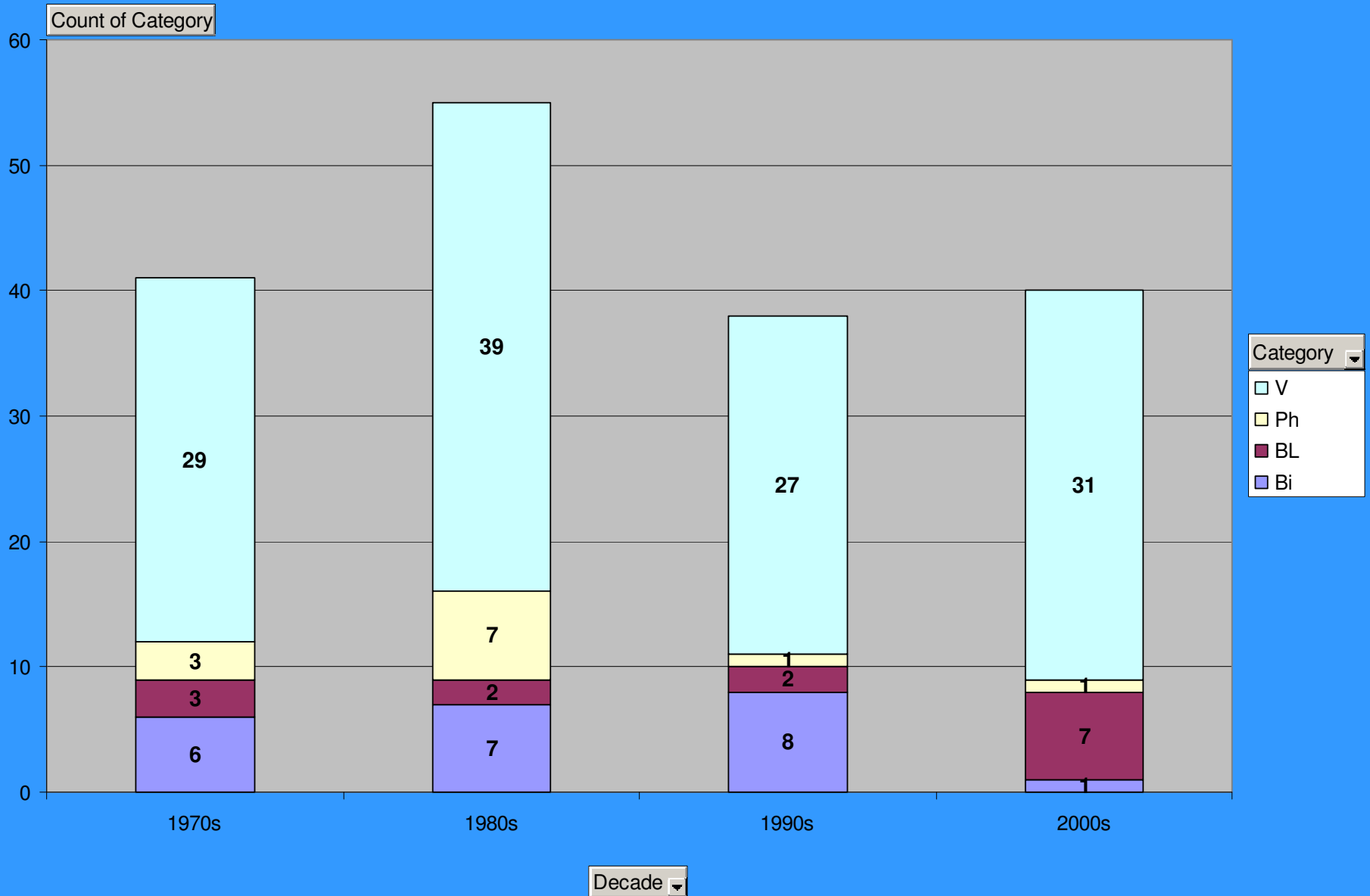


No. of Written Standards for Vaccines & Biologicals for 4 Decades (N=174): Analysis by Area

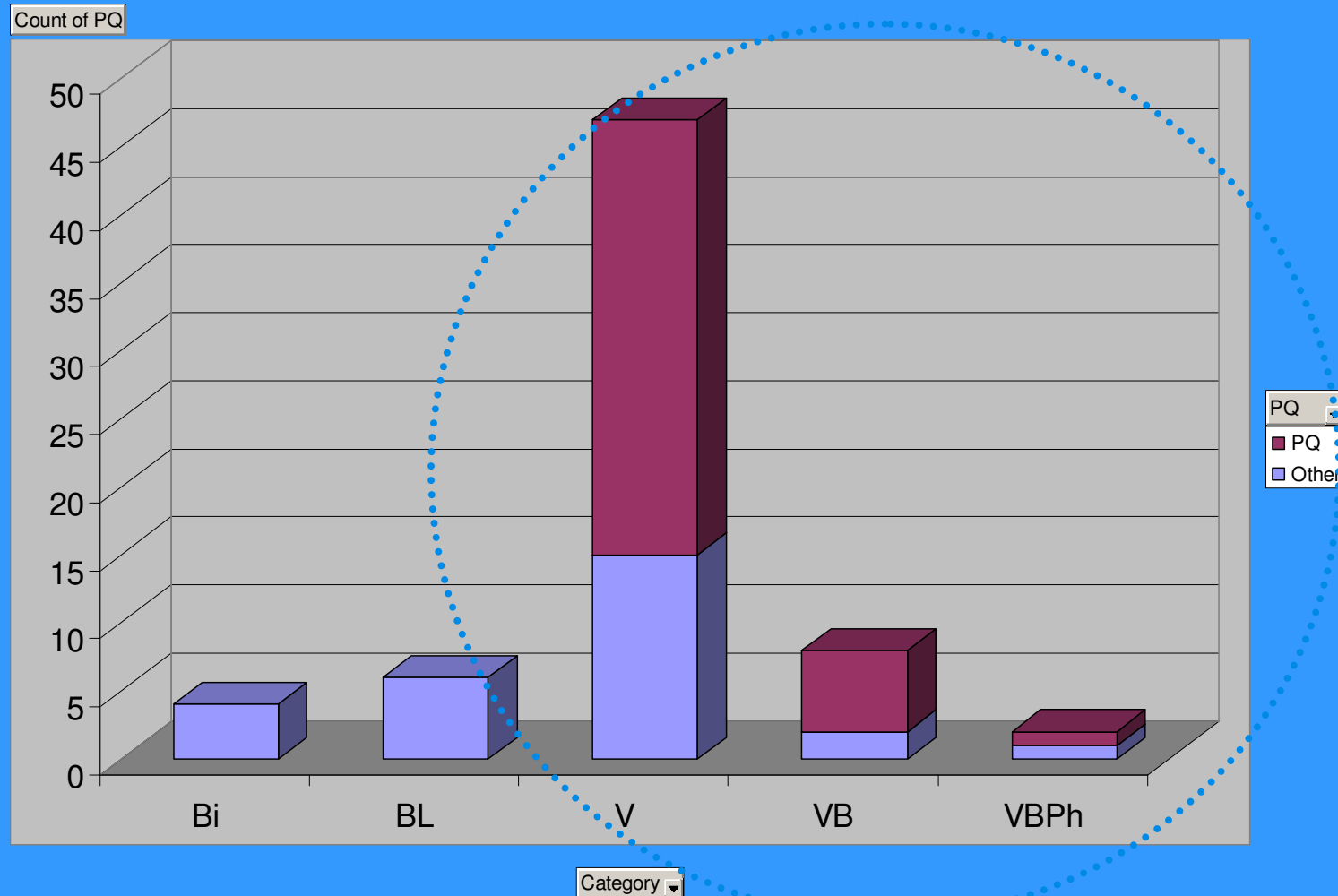


V, Vaccine; Bi, Biologicals; BL, Blood; Ph, Pharmaceuticals

No. of Written Standards for Vaccines & Biologicals for 4 Decades (N=174): Trend Analysis by Area



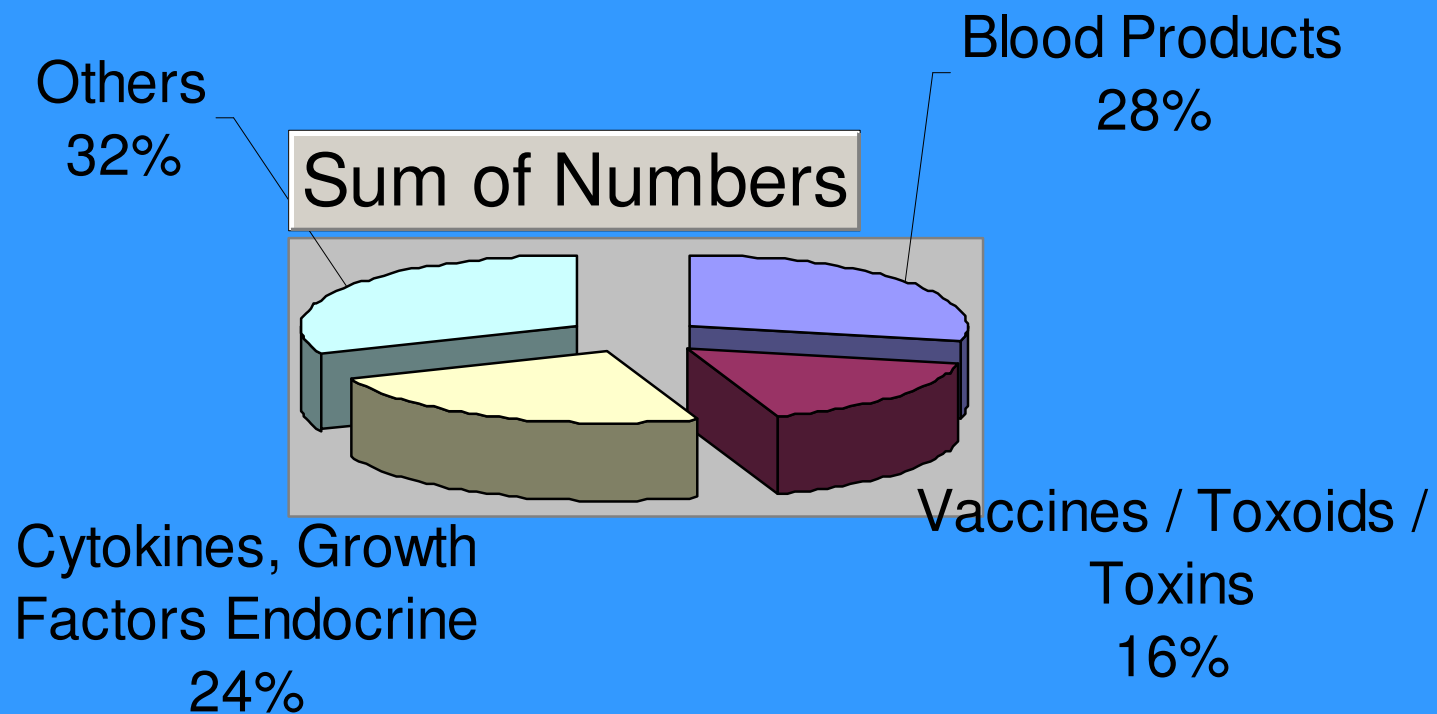
Living Written Standards for Vaccines & Biologicals (1948 – present, N=67): Basis for Vaccine PQ



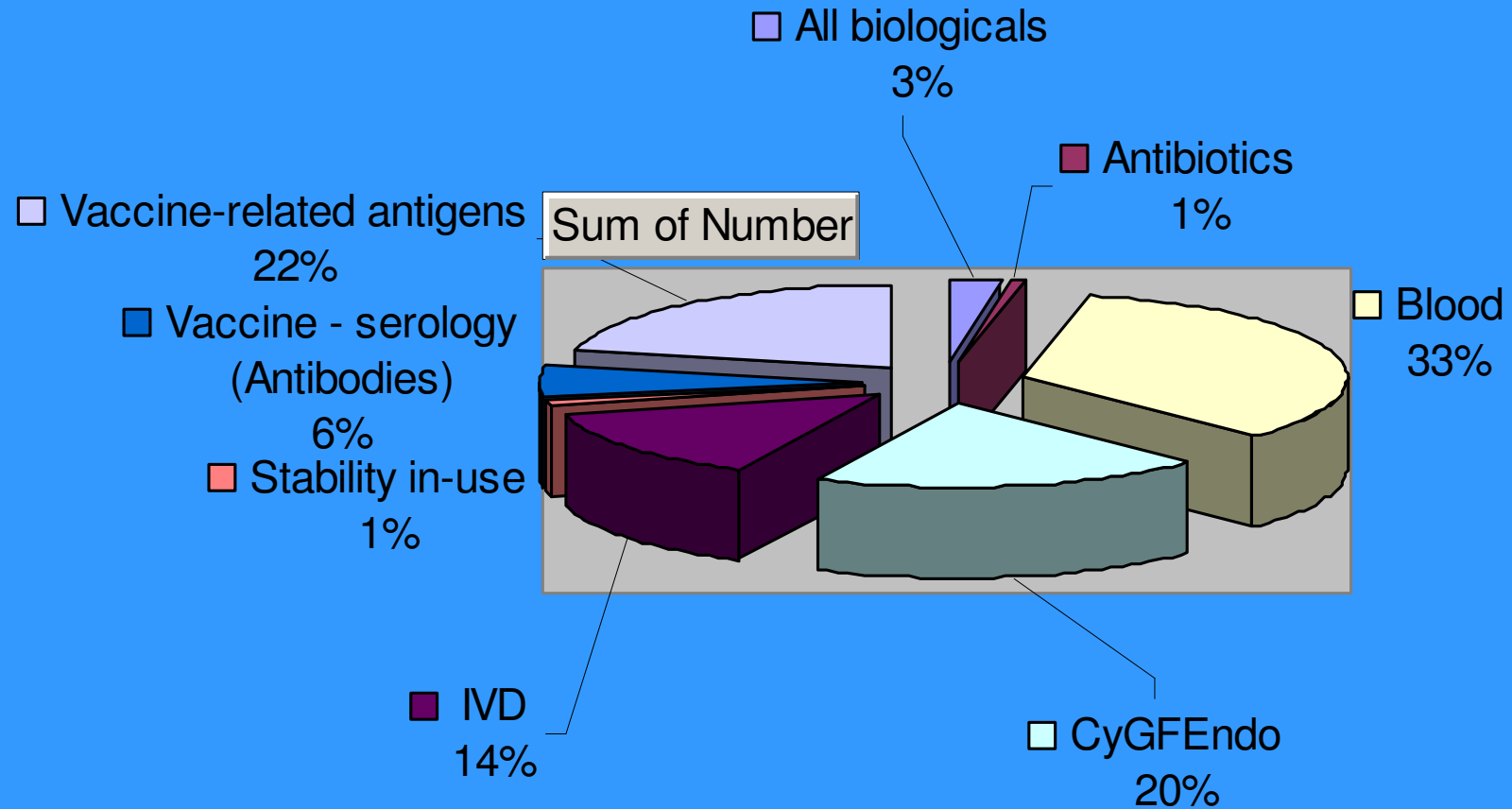
Bi, Biotherapeutics other than blood; **BL**, Blood Products; **V**, Vaccine;
VB, Vaccine+Biologicals; **VBPh**, Vaccine+Biologicals+Pharmaceuticals

WHO International
Biological Reference
Preparations (IBRPs):
An analysis of 10-year data


Living Measurement Standards for Vaccines & Biologicals (1948 – present, N=370)



WHO International Biological Reference Preparations (IBRPs) Established in 2001-2010: Analysis for Proportion by Area



Revision of written standards - current status and plan for 2011-2013 -

Recommendations/ Guidelines	ECBS
<ol style="list-style-type: none"> 1. Cell substrates (TRS 878) 2. Yellow Fever Vaccine (TRS 872) 3. Hepatitis B recombinant (TRS 786, 889) 4. Independent vaccine lot release (new) 	<p style="text-align: center;">2010</p> <div style="text-align: center;">  <p>Adopted</p> </div>
<ol style="list-style-type: none"> 5. Dengue (TRS 932) 6. BCG (TRS 745 and 771) 7. Acellular pertussis vaccine (TRS 878) 8. DTP vaccines (TRS 800) 9. Combined vaccines based on DTP - new 	<p style="text-align: center;">2011</p>
<ol style="list-style-type: none"> 10. OPV (TRS 904 and 910) 11. IPV (TRS 926) 12. Malaria vaccine - new 13. Risk assessment - new 	<p style="text-align: center;">2012/ 2013</p>

Summary

- Total no of living WHO Written Standards for vaccines and other biologicals is 67 as of 2010
- Development of Written Standards for vaccines has been major part of work, comprising 72% of total written standards in the previous 4 decades.
- 85% of them (57/67) have served as the basis for WHO prequalification of vaccines

- Total no of living WHO Measurement Standards for vaccines and biologicals is 370 as of 2010.
- An analysis of the latest 10-year data on the establishment of Vaccine-related antigen preparations comprise 22% (33 of N=152 2001-2010)

Way forward

- Issues of importance for defining strategic direction for coming 10 years and beyond:
 - Better way for measuring impact of WHO standards in the regulation of vaccines
 - More precise indicators
 - Link with NRA strengthening
 - Use of WHO standards for vaccine PQ
 - Scope of work
 - Vaccines, some biotherapeutics, biologicals in general
 - Pre-normative, normative and post-normative
 - Collaboration with other standard setting bodies
 - Funding of vaccine standardization

Many thanks

- To all collaborators who contributed to the development of standards
- To my colleagues Jinho Shin, Christoph Conrad and Sue Jenner for the analysis of 40 years data
- Colleagues from PQ team Nora Dellepiane and Sergio Nishioka