



**CONSIDE**

CONSORTIUM FOR THE STANDARDIZATION  
OF INFLUENZA SEROEPIDEMIOLOGY

# Pathway for development of an influenza antibody standard

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# How useful is an antibody standard?

- In several international collaborative studies on influenza serology, the use of an antibody standard has reduced between-laboratory variability by 50% - **but**
  - International antibody standards take months to prepare, evaluate, assign titre and to make available (7 months for H1N1pdm09; 19 months before WHO approval)
  - They have depended on availability of human positive sera/plasma; a laboratory to process the serum; willing volunteers to test the candidate standard; statistician for the analysis; WHO to assign International Standard status; a laboratory to distribute standard
  - This means that unless plans are made, an antibody standard may not be ready in time



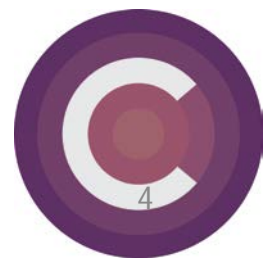
# Antibody Standard Hierarchy

- **International Standard –primary standard**
  - Authorised by WHO – usually assigned International Unitage, but International Antibody Standards have also been assigned HI and MN titres
  - Usually freeze dried by WHO laboratory for long term stability
  - Distributed in small quantities ie cannot be used in every assay
  - Calibrated by international collaborative study
  - Can be used to calibrate secondary standards
- **Secondary Standard**
  - Can be sourced, produced and calibrated locally
  - Frozen antibody is OK – shorter life
  - Available in larger quantities ie can be used in every assay



# Alternative Antibody Standard Hierarchy

- **International reference reagent**
  - No WHO status, no need to wait for WHO ECBS to authorise, but can be used as an International Standard – probably will be assigned an HI and MN titre
  - Could be freeze dried or frozen by any lab agreed by international community
  - Distributed in small quantities ie cannot be used in every assay
  - Calibrated by international collaborative study
  - Can be used to calibrate secondary standards
- **Secondary Standard**
  - Can be sourced, produced and calibrated locally
  - Frozen antibody is OK – shorter life
  - Available in larger quantities ie can be used in every assay



# Stages in antibody standard preparation - 1

## Recognition of need

- WHO/OIE/CONSISE to coordinate international response to an incident/outbreak and to identify need for antibody standard eg do we need one for H7N9?
- Without international need, it is unlikely that labs will commit to help

## Source the antibody (assuming it is human serum/plasma)

- Need a pool of a minimum 1 litre of +ve serum/plasma
- Could be post-infection, post-vaccination
- Needs informed consent from donors and approval from appropriate ethics committee
- This all takes time unless there are prior agreements/ethical consent in place



# Stages in antibody standard preparation - 2

## Processing antibody

- Need WHO-recognised lab for an International Standard, not so for reference reagent
- Antibody preparations to be tested for antibody to influenza virus and for safety from blood-borne agents
- Antibody preparations to be pooled/diluted to have medium titre
- Antibody pool to be filled in 1ml (0.5ml) quantities, labelled and either frozen or freeze dried – ideally a minimum of 2,000 vials
- Retest processed antibody pool
- Accompanying documents prepared for distribution



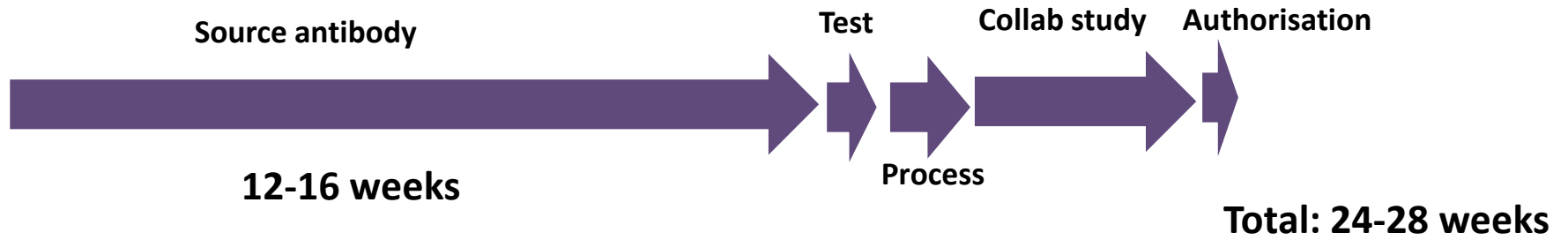
# Stages in antibody standard preparation - 3

## Calibration of antibody standard

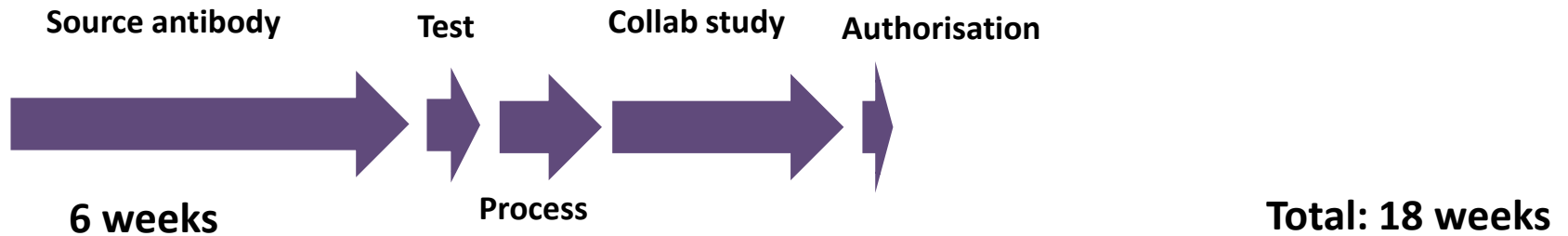
- Candidate standard distributed to approximately 15 labs, ideally with some test sera
  - Having agreements in place beforehand will speed up process
- Labs to quickly assay (HI and MN) standard (and test sera) on approx 3 occasions. Results submitted to coordinating lab.
- Statistician to analyse data; report shared with participants for comment; agreement reached on assigned unitage/titre
- Authorisation of standard (WHO or other)



# Human antibody



# Animal antibody





Thank you