The Global Action Plan for Influenza Vaccines

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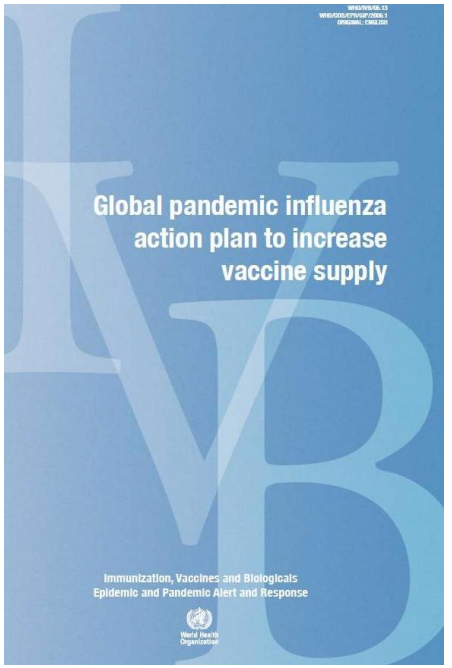
APACI 2nd Summit, 11 June 2015, Hanoi

2006: The Global Action Plan for Influenza Vaccines (GAP)

- Global shortage of vaccines in the event of a pandemic
- Inequitable access to the available vaccines
- 3 objectives:
  - 1. Increase in seasonal vaccine use
  - 2. **Increase in vaccine production capacity**
  - 3. Research and development for better vaccines



Objective 2: Technology transfer and seed funding

- 14 LMIC manufacturers in the programme
- IVAC, Vietnam joined in 2007

Objective I
Evidence to drive Policy

- Disease Burden
- Economic Burden
- Vaccine Efficacy
- Cost Effectiveness

⇨

- All regions
- All age groups
- All vaccines
- All scenarios

Examples of difficult choices to make in LMICs:
- TIV or LAIV?
- which age group to prioritize?
- QIV or TIV?

Support SAGE recommendations, national immunization policy

Objective I: National policy for seasonal influenza vaccination

Table 1: National policy for seasonal influenza vaccination

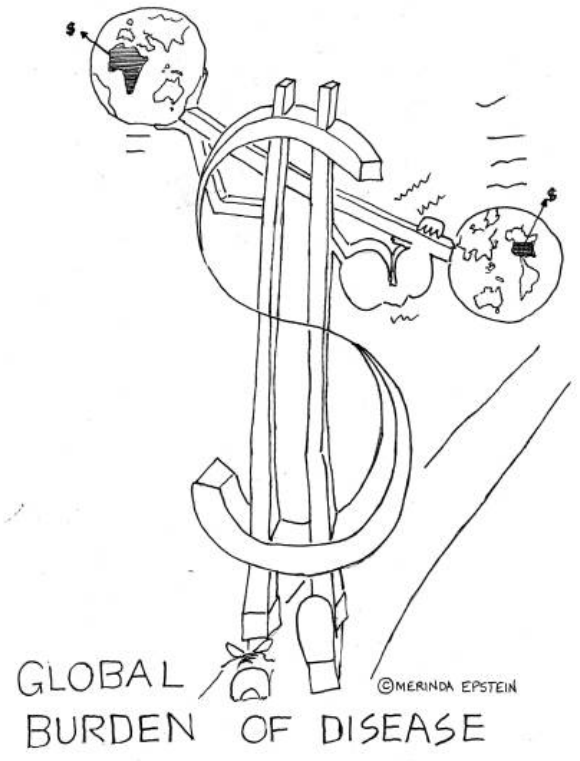
Countries (%) with	Europe, N America (n=27)	Asia Pacific (n=38)	Central, South Americas (n=39)	Africa (n=48)	Middle East (n=13)
National seasonal influenza vaccination policy	76%[1]	26%	90%	8%	62%
Vaccine formulation recommended					
- NH		18%	56%	2%	23%
- SH		11%	31%	2%	0%
- Both		8%	0%	0%	0%
- None		63%	13%	96%	77%
Target groups in policy					
- Elderly	100%[2]	26%	87%	8%	31%
- Children	22%	16%	79%	4%	23%
- Persons with chronic illnesses	100%	16%	79%	4%	23%
- Pregnant women	37%	16%	41%	0%	23%
- Healthcare professionals	85%	26%	74%	4%	23%
- Hajj travellers		8%[3]			
Availability of influenza vaccine[4]					
- public sector only		0%	10%	0%	0%
- private sector only		37%	13%	25%	0%
- both sectors		21%	59%	4%	23%
Vaccination free in public sector		13%	56%	2%	15%
Countries able to meet WHA 56.19 resolution (coverage>75% in elderly)[5]	4%	13%	33%	0%	15%

Source: Hirve S. WHO/GIP (2015), in press: Seasonal Influenza Vaccine Use in Low and Middle Income Countries in the Tropics and Subtropics

Objective I: Maternal Influenza Immunization

TASKFORCE TO EVALUATE INFLUENZA DATA TO INFORM VACCINE IMPACT AND ECONOMIC MODELLING (March 2015)

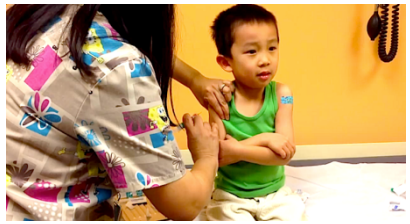
- *"influenza disease burden data may not be sufficient to inform decision-making in many countries regarding routine immunization of pregnant women with influenza vaccine".*
- *Without baseline disease burden estimates, …, the public health utility of incorporating influenza vaccine into national immunization programs remains unknown".*



Source: http://www.who.int/immunization/sage/meetings/2015/april/1_Interim_Report_WHO_Initiative_Vaccine_Research_24March_2015_execSAGE.pdf?ua=1

Focus perhaps more to children?

- Chair conclusions of a recent meeting on seasonal influenza vaccination in the European Union[1)]:
  - evidence for paradigmatic shift of influenza control, addressing potential of influenza vaccination of children (indirect effects) and herd protection.
  - More epidemiological evidence needed to confirm findings of modelling studies which demonstrate VE and CE of childhood influenza vaccination



- Recent CE in Thailand suggests seasonal influenza vaccination of children good short-term value for money[2)]:
  - estimate health benefits and cost-effectiveness of flu vaccination among Thai children aged two to 17 years: largest reduction to influenza and associated mortality obtained by vaccinating 2-17 year olds with LAIV;
  - predicting to prevent about 3,000 deaths annually in Thailand, mostly as a result of reducing influenza transmission to people over 60 years of age.

1) Flashreport high level hearing on implementation EU Council Recommendation on seasonal influenza vaccination, Luxembourg 29-30 April 2015

2) Meeyai A, et al. Seasonal influenza vaccination for children in Thailand: a cost-effectiveness analysis. PLoS Med 2015 May;12(5):e1001820.

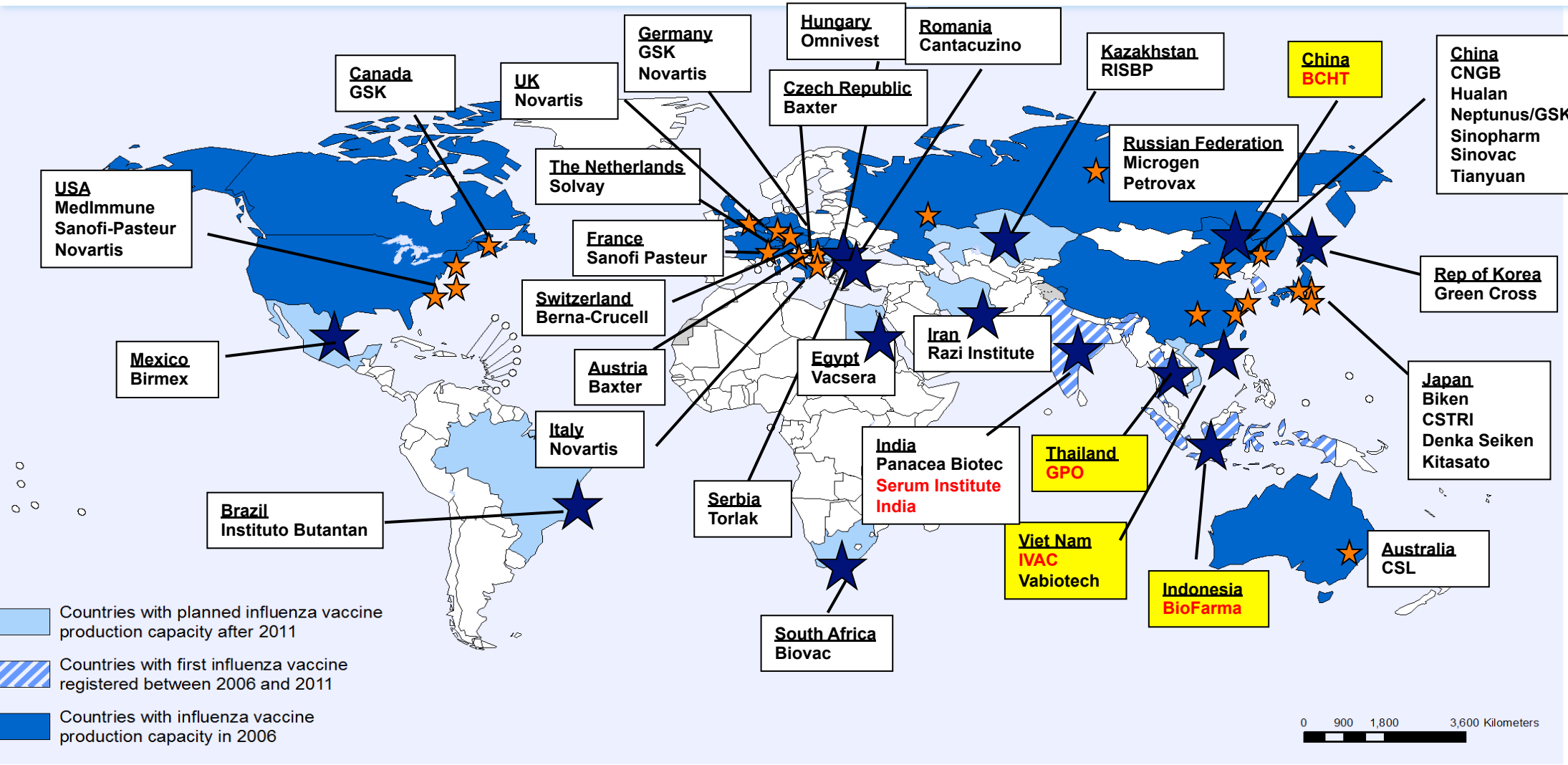
Objective II: Increase Production Capacity
Recent Changes in the Vaccine Landscape

- Consolidation:
  - Novartis vaccines unit sold to GSK
    - Influenza franchise acquired by CSL
- Abandoned:
  - Baxter tissue-culture influenza vaccine
  - Crucell egg-based influenza vaccine

- New players and technologies
  - Protein Science's baculovirus-based vaccine approved – in theory large expansion capacity
  - Adjuvanted seasonal vaccine approved for infants (Canada)
  - USA preference for LAIV for infants reversed

Source: Kieny MP.t presented at 8th WHO International Partners Meeting, Sao Paulo, Brazil, March 17-18, 2015

Objective II: Influenza Vaccine Manufacturers (actual and potential)



One producer (AdImmune) in Chinese Taipei

★ = Manufacturers in WHO's capacity building program

India – Serum Institute of India

- Achievements
  - pH1N1 pLAIV WHO prequalified 2012
    - Sub-license of Russian LAIV technology through WHO
  - seasonal LAIV approved in 2014 for ages 2 and older; WHO prequalification pending
    - Phase II, III clinical studies in Bangladesh and Senegal with PATH finalized
    - Current annual production capacity is 10 million doses per year

- Ongoing
  - development of cell-based seasonal LAIV
  - preclinical work on LAIV H7N9

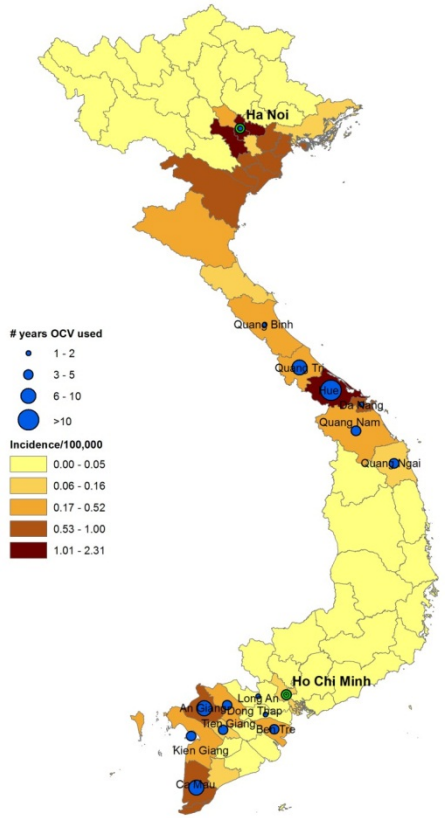
South- East Asia & China

- Indonesia – Bio Farma
  - State owned, supplier of PQ'd vaccines, fill-finish with bulk from BIKEN (Japan), seasonal **TIV** vaccine licensed in 2009, Haji pilgrims main market.
- Thailand – GPO
  - State owned; two tracks: **TIV:** seasonal fill-finish with bulk from Kaketsuken (Japan), Phase 1/2 study local TIV pending,**LAIV:** pH1N1 through WHO (licensed 2011). Phase 1 and 2 studies with H5N2 completed, licensure pending.
- China – BCHT
  - Private; several vaccines on market (Rabies, Hepatitis A), large scale facility completed, awaiting CFDA approval for **LAIV** Phase 1 and Phase 2 clinical studies
  - China has many other **TIV** vaccine manufacturers.
- Viet Nam – IVAC

Local vaccine manufacturing in Vietnam?

Example: cholera vaccine

Date	Events
1980s	NIHE develops in Hanoi a killed whole cell *V. cholerae* O1 vaccine (OCV) without the costly cholera toxin B subunit, following tech transfer from Sweden
1992-1993	Open field trial in Hue: 2 doses OCV safe, immunogenic; 66% protection in individuals over 1 year of age
after 1992	V *cholerae* O139 added making it bivalent; shown to be safe and immunogenic
1997	Bivalent OCV tested in field trial in Nha Trang in 300.000 residents; no cholera occurred in 2 subsequent follow up years, precluding VE estimates
1997	Bivalent OCV licensed as ORC-Vax, made by Vabiotech and introduced in national routine immunization programme
1998	Mass vaccination program in individuals over 2 years of age in half the communities of Hue. No cholera detected for 2 years, despite intensive surveillance
2000	Remaining communities in Hue vaccinated
2003	Outbreak in Hue; case control study shows 50% long term protection after 3-5 years
2009	ORC-Vax reformulated to comply with cGMP; licensed as mORC-Vax



average annual cholera incidence and oral cholera vaccine use, 1998–2012

Source: Anh DD et al.(2014) Oral Cholera Vaccine Development and Use in Vietnam. PLoS Med 11(9): e1001712

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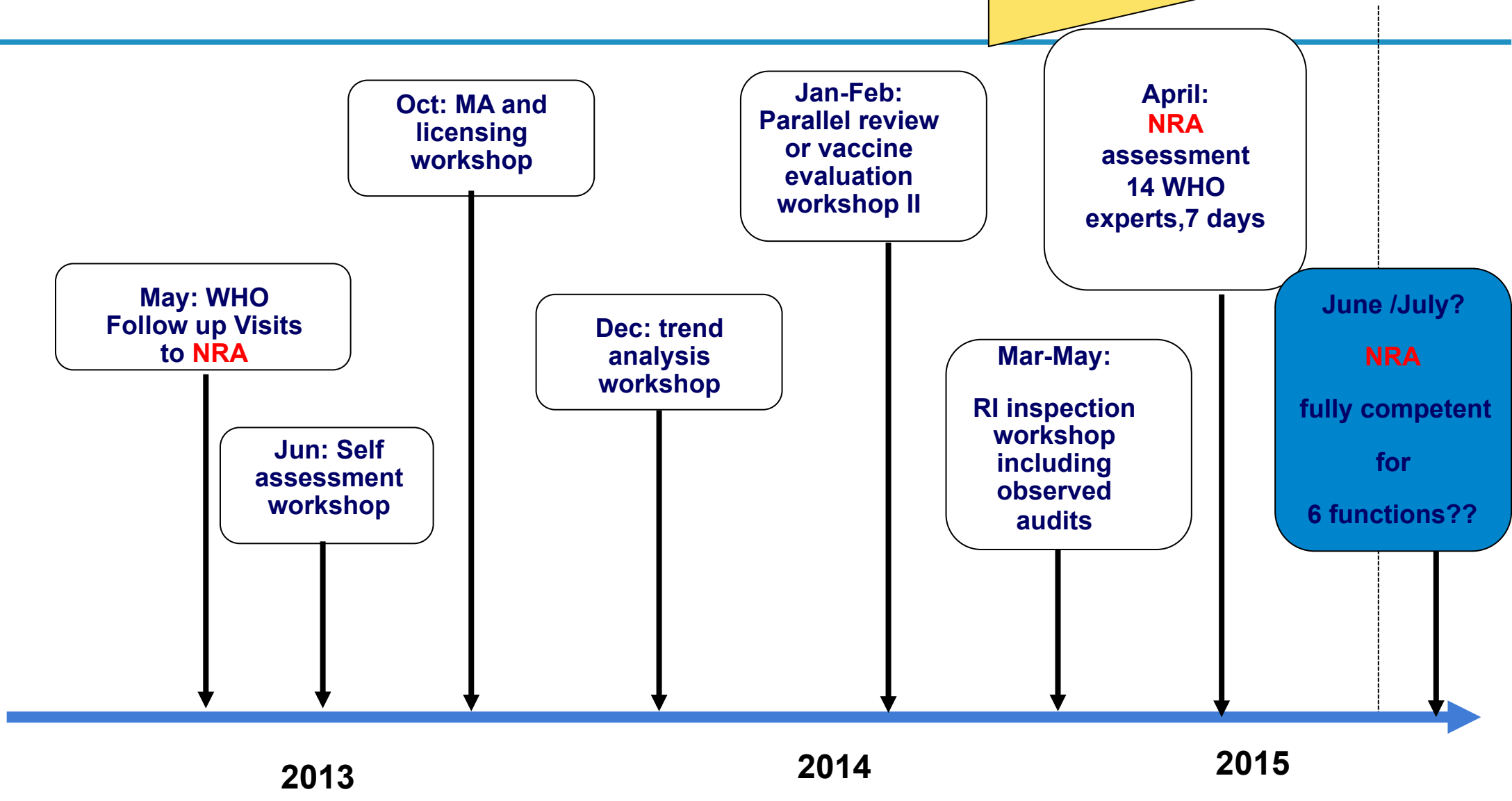
Influenza Vaccine at IVAC

- 2007 – 2014
  - Manufacturing plant and chicken farm
  - H1N1 and H5N1: Phase 1 completed
  - Seasonal vaccine: animal studies completed
  - Preparing Phase 2/3 for H5N1 and seasonal vaccines

- 2015-2016
  - Clinical trials (with PATH and BARDA) planned: Phase 1 seasonal and Phase 2/3 H5N1
  - NRA fully competent and continued support from MOH




Viet Nam's regulatory strengthening roadmap



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In Summary

- Prospects for influenza vaccine manufacturing in Viet Nam:
  - excellent progress:
    - in clinical development and clinical trials;
      - basic production infrastructure and the human capacity exists
    - in quality
      - regulatory environment close to become fully competent
    - policy coherence at Government level
      - industrial, health, vaccine procurement, immunization
  - to reach sustainability, need to develop and adopt an evidence-based seasonal influenza immunization policy

Concluding Remarks on GAP Objectives

- Implementation of evidence-based policies to increase seasonal influenza uptake slower than anticipated
- Current global pandemic capacity significantly improved, but still insufficient to meet demand in event of pandemic, in particular when 2 doses would be needed
- A "truly" universal vaccine highly desirable but unlikely to be licensed within next 10 years; an incremental improvement seems feasible.

CLOSING THE GAPs”

THIRD WHO CONSULTATION ON THE GLOBAL ACTION PLAN ON INFLUENZA VACCINES

November 2016

Geneva, Switzerland

http://www.who.int/influenza_vaccines_plan/en