Toward a revised global typhoid immunization policy

ASTMH
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Joachim Hombach
Initiative for Vaccine Research (IVR), WHO

Current typhoid vaccination policy

WHO Position Paper 2008*

ommendations for parenteral Vi polysaccharide and oral Ty21a vacci

grammatic use for endemic disease & outbreak control

h-risk groups and populations, including school-age and/or presch
children

al data required for vaccination strategies

ub-populations at risk (to support risk-based strategy)

ge-specific incidence rates

ensitivity of prevailing strains to relevant antimicrobials

ost-effectiveness analyses

chool enrolment rates etc.

WHO Position Paper on typhoid vaccines (2008)
tp://www.who.int/wer/2008/wer8306.pdf

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Current utilization of typhoid vaccine:

Typhoid vaccination programmes or recommended use by country (excluding vaccination of travellers), WHO South-East Asia and Western Pacific Regions, 2009–2013[a]*

ountry or area	National policy (Year issued)	Geographic and risk targets for vaccination (excluding travellers)	Type of
t Asia Region			
	No	State of Delhi; 2–5 year old children	ViPS
	Yes (2012)	Sub-national; school aged children, food handlers	ViPS
	Yes (~1970)	National; food handlers, high-risk groups	ViPS
acific Region [b]			
	Yes (2008)	National; military personnel, laboratory workers routinely working with S. Typhi	Ty21a ar
russalam	No	Food handlers	ViPS
	No	Subnational; selected high-risk groups [c]	ViPS
ublic of	Not available	National; high-risk groups	ViPS
	Not available	Subnational; food handlers	ViPS
	Yes (1997)	Subnational (selected high-risk provinces); 3–10 year old children [e]	ViPS

presented reflect typhoid vaccination any time during the review period in countries or areas for whom data were available. The following countries and areas reported
in either public or private sector: Bhutan, Cook Islands, Japan, Kiribati, Nauru, Nuie, Palau, Papua New Guinea, Samoa, Solomon Islands, Timor Leste, Tokelau and Tuv
vaccination of food handlers in Singapore (since the 1970s) was rescinded in 2010, therefore Singapore is not included in the table.
n national immunization programme. Provinces choose their own strategies including, school-based vaccination of children in high-risk areas, vaccination of food hand
sponse vaccination, and vaccination for a wide age range in high-risk areas of high-risk provinces.

*(*Date et al., MMWR, Oct 3, 2014)*

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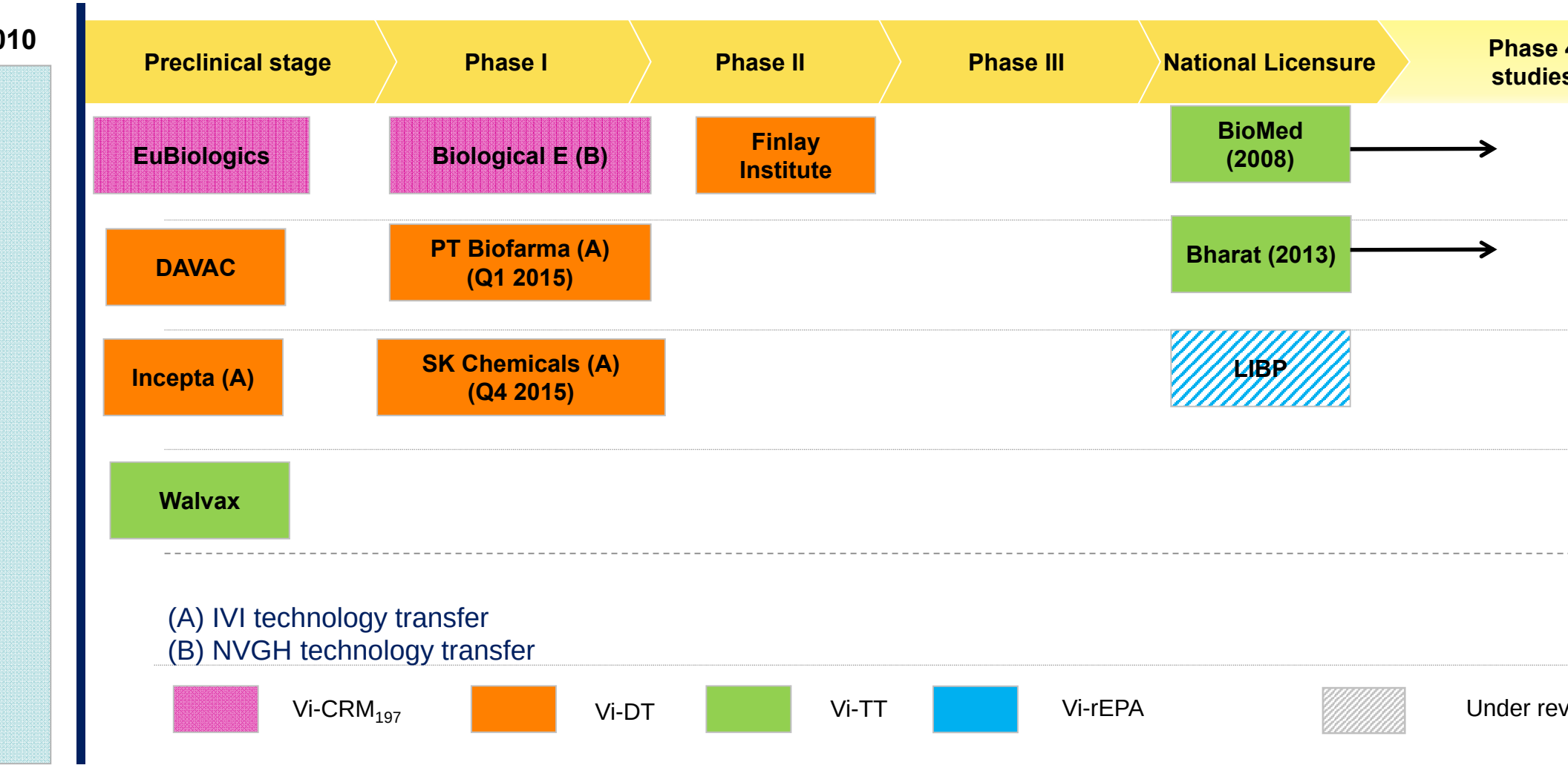
Typhoid conjugate vaccines - expectations

hat are the expected benefits of TCVs over the existing typh ccines?

- Improved level and duration of clinical protection
- Should boost Vi-primed (natural or plain Vi vaccine)
- Broader age range (i.e., immunogenic in children <2 years)
- Simplified delivery strategies
- Co-financing (funding support where applicable) and possibly better cost-effectiveness
- Improved vaccine acceptance and uptake

we have the necessary data to review WHO's global policy phoid?

Typhoid conjugate vaccine pipeline*



formation available as at Aug 2014

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What could be addressed with an update of the current global policy?

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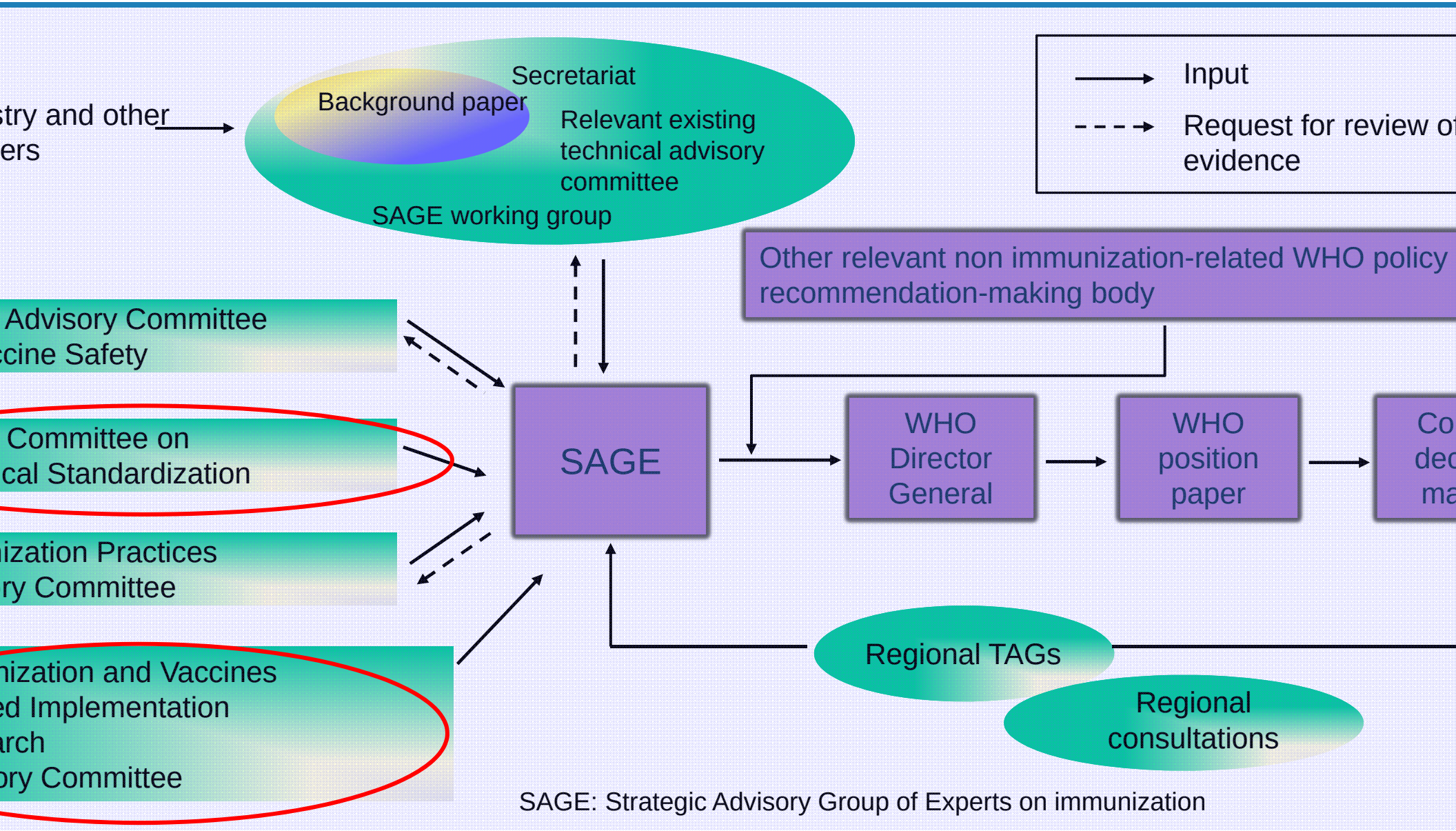
Pathways for WHO Recommendations on Vaccine Use

(http://www.who.int/immunization/policy/sage/en/)



SAGE: Strategic Advisory Group of Experts on immunization

Key considerations for evidence to support update of the current global policy (I)

E reviews will include **new or relevant data** on:

itude of the public h problem

- Disease burden estimates, epidemiological trends, factor analysis
- Cost of illness and cost effectiveness
- Antibiotic resistance
- Diagnostic challenges

ention and control sures

- Use of current vaccines and barriers to uptake (in particular issues with potential implications for TCV
- Integration with other interventions

Key considerations for evidence to support update of the current global policy (II)

oid conjugate nes - characteristics performance

- Composition, safety, immunological parameters
- Dose-scheduling
- Eventual booster requirements
- Vaccine efficacy, effectiveness and impact on clinic disease (incl. mathematical modelling data)

rammatic issues for ne use

- Target population (risk-based strategy)
- Delivery and integration strategies
- Logistics (e.g. packaging, cold chain volume, VVM)

-licensure assessment of TCV based on immunogen and/or clinical efficacy

Guidelines on the quality, safety and efficacy of typhoid conjugate vaccines. 2013
ww.who.int/biologicals/areas/vaccines/TYPHOID_BS2215_doc_v1.14_WEB_VERSION.pdf?ua=1

formed by immunogenicity, safety and efficacy data on NIH Vi-rEPA vac
ot a marketed product)

onsidered:

- No efficacy or effectiveness data for any TCV in < 2y
- Not possible to do comparative studies with ViPS in < 2y

ey parameters for clinical evaluation

- **≥ 2y: license on immunogenicity; no efficacy data needed**
- **≤ 2y: sponsor & NRA to consider value and feasibility of efficacy data OR assessment of immunogenicity with post-approval effectiveness studies**

Vaccine performance data needs for future SAGE policy review* (1)

d on WHO Expert Consultation to review adequacy of the clinical data to rt public health recommendations for use (2-3 July 2014)

w.who.int/immunization/research/meetings_workshops/typhoidvaccines_july14/en/

ditional clinical data should be generated for SAGE policy review

more robust immunogenicity data; all age groups

- memory, duration of protection and need for boosters
- full immunogenicity profile as described I WHO TRS guidelines

possibility to bridge immunogenicity data to children in 9-23 m age group fo provisional recommendations

Some clinical efficacy data highly desirable; particularly in children <2 y for recommendations across all age groups.

Vaccine performance data needs for future SAGE review* (2

able vaccination regimens tested in ViCV clinical trial trials to date in the <2 y
group (based on age groups for which primary end points reported)

Vi-rEPA	3 doses at 2, 4, 6 m (co-admin with EPI vaccines) + boos at 12 m
rat Vi-TT	single dose in 6 m-2 y age group study ongoing for co-admin with 9 m Measles licensed for single dose in >=6 m, children and adults
GH/BioE Vi-CRM	single dose at 9 m 3 doses at 6, 10 and 14 wks (co-admin with EPI vaccines

(*http://www.who.int/immunization/research/meetings_workshops/typhoidvaccines_july14

Reviewing other policy-related data

views by WHO's Immunization and Vaccines-related Implementation
search Advisory Committee (IVIR-AC) (Sept 2014)

- disease burden (IVI)
  - incl. adjustments for access to safe water, blood culture sensitivity, CFR
- mathematical modelling of impact of vaccination (IVI, NVGH and Yale modelling grou
- economic burden (IVI)
  - cost effectiveness, cost of illness

R-AC broadly supportive of methodological approaches

- recommendations issued on further sensitivity analyses
- absence of data on a number of key parameters (e.g. age-specific data, CFR, access to c may warrant investments to generate data prospectively to guide future analyses

http://www.who.int/immunization/research/committees/ivir_ac/en/

ected SAGE & WHO pathway to revise the typhoid immuniza policy – Global level

evelop schedule for SAGE review based on ailability of the clinical data and access to ccine;

tablish SAGE Working Group
- reviews evidence and specific questions related to TCV use (GRADE approach)
- prepares a report of the evidence to be submitted to SAGE

AGE final recommendations → updated policy sued in WHO position paper

WHO vaccine prequalification is independent of E

itional critical areas for adopting/implementing a revised pol
Regional & national levels

velopment of local policies or guidance for implementation

- Regional Immunization Technical Advisory Groups (ITAGs)
- NITAGs or other relevant advisory bodies

ccine licensure and supply issues

- WHO prequalified vaccine for UN supply where applicable
- Dependent on potential Gavi funding window, successful applications for fu
  support by Gavi-eligible countries

ccine delivery strategies, coverage monitoring and impact evalua

- Surveillance and epidemiological risk factor assessment

Strategic Demand Forecast Assumptions: Typhoid conjugate vaccine[1]

Element	Assumptions	Confid
ountry scope	89 endemic countries (71 Gavi-eligible countries + 18 non-Gavi eligible lower-middle-income countries (LMICs)	n/a
rget population	**High Burden Countries:** • Routine: Surviving Infants and 6-year olds • Campaigns: 1-<15-year olds • Urban slums + Rural areas without access to clean water [2] **Medium Burden Countries:** • Routine: 6-year olds • Campaigns: 6-<15-year olds • Urban slums [2]	Low
Schedule	**High Burden Countries:** Routine: 2 doses; Campaign: 1 dose **Medium Burden Countries:** Routine: 1 dose; Campaign: 1 dose	Low
Product(s)	Current: no pre-qualified vaccine available Future: 5-dose liquid vial (Anticipate earliest Gavi-supported introduction 2020)	Current Product: Future Product:
Vastage factor	Routine: 1.33 Campaign: 1.11	Medium
financing policy	• Gavi fully funds campaigns and co-finances routine • LMIC demand fully country financed • After graduation, Gavi support ends and countries fully finance this vaccine	High
Other	• No supply or financial constraints applied in the base unconstrained scenario • Buffer: Routine – 25% change in demand between years; Campaign – 0% change in demand between years • The SDF assumes that products purchased with Gavi support are WHO pre-qualified. Countries that prefer to self-procure vaccines using Gavi support are required to assure that international standards of quality are met.	n/a

nconstrained
n slum data and WHO/UNICEF Joint Monitoring Programme (JMP) for Water Supply and Sanitation.

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