Guidance on Data Sources for Applications for Typhoid Conjugate Vaccine (TCV)

The purpose of this document is to provide an organizing tool for countries to collate and analyze typhoid-related epidemiological and other data for inclusion in applications submitted to Gavi for support to introduce typhoid conjugate vaccine (TCV). The text describes the steps a country can take to collect evidence of both past and current typhoid disease as well as assessing other sources of evidence which indicate likely future risk. **Tables 1 & 2 should be included as part of a submitted application to Gavi for new vaccine support specific to TCV.**

Overview

Typhoid cases occur both sporadically and in epidemics. In addition, epidemiological data have demonstrated both temporal and geographic heterogeneity in typhoid incidence. Thus the amount of typhoid in a given area may vary considerably over time, and only a small part of a country may experience cases at any given time even though a larger area may be at risk due to sanitary conditions favourable to the spread of typhoid. At-risk areas that do not have typhoid disease one year can have it in following years. A country considering whether and how to use typhoid conjugate vaccine should take into account both evidence of past typhoid occurrence which demonstrates a definite risk and other sources of evidence which indicate a likely risk of typhoid, such as modelling data or risk factor assessments to inform potential use and strategy of TCV. Evidence of past typhoid disease which demonstrates a continued risk of typhoid disease strongly supports the need to introduce TCV, but the absence of such evidence of past typhoid disease does not preclude the introduction of TCV, if other evidence indicates a risk of typhoid disease.

In light of the 2018 WHO recommendations[1] that countries can introduce TCV on a universal, risk-based, or phased approach, a country considering introducing typhoid conjugate vaccine should assess the risk of typhoid for subnational level administrative areas, i.e., each province or state if feasible. A country may choose to introduce TCV nationally, only in certain areas, or in a phased manner in which some areas introduce TCV before others.

Countries may conclude that different areas have different risks of typhoid disease. These differences may drive varied decisions about introducing typhoid vaccine in different areas. Such conclusions and the basis for them should be clearly stated in the application for Gavi support.

Countries are requested to complete Tables 1 and 2 below to inform their assessment of local typhoid disease burden and include them as part of the submitted materials for the application for Gavi support. If additional support is needed to analyze the results of the tables, please consult the Gavi SCM who can link countries to additional technical resources, including Gavi Alliance partners to help analyze the output.

Step 1: Assess Evidence of Past or Current Typhoid Disease

For the assessment of evidence of definite risk of typhoid disease, a country should attempt to review all sources of credible evidence of past typhoid disease from the previous five years if available, including:

[1] http://apps.who.int/iris/bitstream/handle/10665/272272/WER9313.pdf?ua=1 *(accessed August 18, 2018)*

- Records of **laboratory-confirmed typhoid cases (positive blood cultures)** at laboratory facilities that perform blood cultures in that country, including any antimicrobial resistance testing results
- Records of **in-country laboratory-confirmed typhoid outbreaks**, including blood culture confirmed typhoid cases and non-traumatic terminal[2] ileal perforations
- Records of **laboratory-confirmed typhoid cases confirmed through molecular testing**, such as polymerase chain reaction, using a known or validated protocol, such as in a research study

Sources for this information can include:

- In-country surveillance data[3] and/or research study data of laboratory-confirmed typhoid cases (not including cases confirmed with only a positive Widal test)
- In-country surveillance data on laboratory-confirmed typhoid outbreaks, which may be identified through blood culture testing or non-traumatic terminal ileal perforations
- Surveys of in-country laboratory facilities that perform blood cultures
- Surveys of tertiary care hospitals where patients with ileal perforations would be admitted

It should be noted that surveillance data on suspected typhoid (or enteric fever) cases or cases classified as typhoid solely on the basis of positive Widal tests are not considered credible evidence of past typhoid disease.

Table 1: Country Assessment of Surveillance Data Sources on Typhoid Disease Burden

DATA SOURCE	Yes/No	NOTES/QUESTIONS TO CONSIDER (IF APPLICABLE)

In-country surveillance of laboratory-confirmed typhoid within the past 5 years		• For data on individual laboratory-confirmed cases (blood culture or molecular testing):
		  • If from surveillance, specify whether active or passive[4]
		  • The age groups of cases
		  • The month, year, and geographic area that cases occurred in
		  ▪ For each geographic area, population covered in location(s) identified / % of the total country population
		  • The number of cases confirmed by each method, specifically blood culture and molecular testing.
		  • Annual incidence of laboratory-confirmed typhoid disease
		  • Antimicrobial resistance testing results by year
		  • If available, where *Salmonella* Typhi falls in the rank order of causes of community-acquired bloodstream infections at a site or in national data

Research study data demonstrating laboratory-confirmed typhoid from a normally sterile site (e.g., blood) within the past 5 years		
Surveys of in-country laboratory facilities that perform blood cultures		

[2] If the ileal site (e.g., terminal) is unknown for all cases, you may give the total number of ileal perforation cases, and the proportion of cases documented to have perforations in the terminal ileum

[3] WHO Typhoid surveillance standards can be found here: http://www.who.int/immunization/monitoring_surveillance/burden/vpd/standards/en/

[4] Passive case detection means that health facility staff detect and report cases from among patients presenting to the specific facility/facilities, while active surveillance means that designated surveillance staff are directly involved in detecting cases. For example, surveillance staff may do a regular review of facility registers and have regular contact with clinicians regarding potentially missed cases. Compared to passive methods, active surveillance is more resource-intensive and expensive; it is often used for VPDs in the elimination or eradication phase, to characterize VPD epidemiology or vaccine impact in discrete populations or sentinel sites, or in specific situations such as in outbreak response.

DATA SOURCE	Yes/No	NOTES/QUESTIONS TO CONSIDER (IF APPLICABLE)

In-country laboratory-confirmed typhoid outbreaks, which may be identified through clusters of non-traumatic terminal ileal perforations		• For laboratory-confirmed typhoid outbreak data:
		  • The month and year of the start of each laboratory-confirmed typhoid outbreak
		  • Number of total cases (suspect and confirmed) in each laboratory-confirmed typhoid outbreak
		  • Antimicrobial resistance testing results, particularly by year of those results
		  • How each laboratory-confirmed typhoid outbreak was identified, for example, through increased occurrence of blood-culture confirmed typhoid cases, increased occurrence of antimicrobial resistant typhoid disease, or increased occurrence of non-traumatic ileal perforations

Evidence of high rate(s) of non-traumatic terminal ileal perforations (e.g., presented as a proportion of all acute abdominal emergencies requiring surgery)		Please specify: • Rate(s) of non-traumatic terminal ileal perforations and why considered high (e.g., comparison with literature or increasing rates in the same site(s)). • Proportion of ileal perforation cases with lab confirmation of *Salmonella* Typhi.

Step 2: Assess Evidence Which Indicates a Likely Risk of Typhoid Disease

For the assessment of evidence of likely risk of typhoid disease, a country should attempt to review all sources of credible information predictive of future risks, including:

- Modelled burden or prediction of typhoid disease based on country-specific data and data from global models and comparable neighbouring countries
- Surveillance data from neighbouring or similar countries on laboratory-confirmed typhoid cases and outbreaks
- Laboratory-confirmed *Salmonella* Typhi from environmental sampling
- Data on risk factors for typhoid disease, such as lack of access to improved water and adequate sanitation

Sources for this information include:

- Published and unpublished typhoid modelling studies
- Neighbouring country surveillance data on laboratory-confirmed typhoid cases and outbreaks (not including cases confirmed with only a positive Widal test) and clusters of non-traumatic ileal perforations
- Water and sanitation assessments
- Assessments of other risk factors for typhoid disease
- Surveys of any groups conducting environmental surveillance for *Salmonella* Typhi in a country

Table 2: Country Assessment of Alternative Data Sources on Typhoid Disease Burden

DATA SOURCE	Yes/No	NOTES/QUESTIONS TO CONSIDER (IF APPLICABLE)
Published and unpublished modeled burden of typhoid fever based on country-specific data or from global models and neighboring countries (e.g. not based on in-country data)		Some modeling examples to consider: • Antillón M, Warren JL, Crawford FW, Weinberger DM, Kürüm E, Pak GD, Marks F, Pitzer VE.The burden of typhoid fever in low- and middle-income countries: A meta-regression approach. PLoS Negl Trop Dis. 2017 Feb 27;11(2):e0005376. doi: 10.1371/journal.pntd.0005376. eCollection 2017 Feb. • IHME GBD data visualization tool: http://www.healthdata.org/gbd/data-visualizations) Please specify: • The group that completed the modelling • The date the modelling was performed • The age group(s) and areas covered by the modelling • The projected burden of typhoid disease or risk of typhoid disease for an area
Neighbouring country government surveillance data on laboratory-confirmed typhoid cases and outbreaks and clusters of non-traumatic ileal perforations		Please specify: • The country/countries the data are from and geographic proximity or risk factor profile considered similar to your country • The age groups of cases • The month, year, and geographic area(s) that cases occurred in • The number of cases confirmed by each method, for example blood culture, molecular testing, etc. • Annual incidence of laboratory-confirmed typhoid disease • Antimicrobial resistance testing results, particularly by year of those results
Laboratory-confirmed *Salmonella* Typhi from environmental sampling		Please specify: • The group that performed the assessment • Date(s) and geographic area of the assessment • The findings of the assessment • Any link with clinical typhoid cases if applicable
Risk factors for typhoid fever, e.g., lack of access to improved water and adequate sanitation		Please specify: • Description of the risk factor(s) being assessed • The group that performed the assessment • Date(s) and geographic area of the assessment • The findings of the assessment