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TECHNICAL CONSULTATION ON TRACHOMA SURVEILLANCE

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Technical Consultation on Trachoma Surveillance

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This report contains the collective views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization.

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Contents

List of acronyms

TF	Trachomatous inflammation-follicular
TT	Trachomatous trichiasis
WHO	World Health Organization

1. Introduction

1. 1 Based on disease prevalence, several national trachoma programmes have now discontinued one or more components of the intervention strategy against trachoma[1] and are ready to initiate trachoma surveillance. **The role for surveillance in this context is to provide some level of certainty that elimination prevalence targets have been sustainably achieved, following the first assessment that demonstrates their attainment, by revealing disease re-emergence if (and only if) re-emergence is occurring.**

1.2 The trachoma surveillance guidance previously provided by the World Health Organization (WHO), presented in the 2008 report on the "Meeting on Post-Endemic Surveillance for Blinding Trachoma"[1], is excerpted in Annex A. Unfortunately, as noted at an informal meeting on trachoma surveillance held in conjunction with the 13th International Symposium on Human Chlamydial Infections in June 2014, that guidance is perceived both to be difficult to implement in a standardized way, and to lack an evidence base that might promote confidence in its sensitivity and specificity for detecting disease re-emergence. The brief for the present consultation, held in September 2014, was **to revise, where indicated, the WHO guidance on the nature and frequency of surveillance data that programmes should collect and compile in order to successfully declare elimination of blinding trachoma as a public health problem.** Participants are listed in Annex B.

1.3 To achieve this, the consultation reviewed previous efforts to conduct trachoma surveillance and existing knowledge about the natural history and epidemiology of trachoma, and identified priority questions for which further data gathering or analysis of existing datasets might be important to inform surveillance guidance. Interim trachoma surveillance standard operating procedures were developed, and are presented as Annex C of this report. **Those standard operating procedures need ratification by WHO's Strategic and Technical Advisory Group on Neglected Tropical Diseases before they can be considered formal guidance to trachoma elimination programs**.

1.4 Before and during the actual discussions, the consultation was labelled the "Technical Consultation on Post-Mass-Drug-Administration Surveillance for Trachoma". However, it was acknowledged during the consultation that surveillance may on occasions be needed in areas where mass drug administration has not taken place. The more generic term, "**trachoma surveillance**", is therefore used instead of "post-mass-drug-administration surveillance" in this report (including its title), and in the interim standard operating procedures[2].

1.5 For the purposes of the consultation, trachoma surveillance was defined as **monitoring and evaluation activities that assess the outcome of a trachoma elimination programme, conducted**

[1] The intervention strategy for trachoma is encapsulated by the acronym "SAFE", which represents **S**urgery for in-turned eyelashes ("trachomatous trichiasis"), **A**ntibiotics to clear conjunctival *Chlamydia trachomatis* infection, and **F**acial cleanliness and **E**nvironmental improvement to reduce transmission of conjunctival *C. trachomatis*.

[2] The term "post-endemic surveillance" used for the 2008 WHO meeting (see paragraph 1.2) is also imperfect because elimination of blinding trachoma as a public health problem from a particular population does not mean that trachoma is no longer an endemic disease in that population.

after elimination prevalence targets appear to have been achieved, in a defined trachoma endemic area.

1.6 Trachoma surveillance activities include (a) those that occur up to the time that preparation of a dossier for validation of elimination (of trachoma as a public health problem) is justified ("**pre-validation trachoma surveillance**"), and (b) those that occur after the time that preparation of a dossier is justified ("**post-validation trachoma surveillance**"). This consultation focused on drafting guidance (as interim standard operating procedures) for pre-validation trachoma surveillance.

1.7 The optimal approaches for pre-validation trachoma surveillance depend in part on the methodology employed for undertaking impact assessments, because when such assessments show that elimination prevalence targets have been achieved, they provide the starting point for surveillance. WHO has not previously produced any formal guidance on impact assessments. Informally, programmes have been advised to conduct impact assessments in the same way as baseline surveys, i.e., cluster random-sample surveys of 20-30 clusters, powered to estimate an expected prevalence of the sign "trachomatous inflammation-follicular" (TF) in children [2]. Work to examine the geo-statistical considerations of sampling in trachoma impact assessments is now being commissioned by WHO. In the meantime, interim standard operating procedures for trachoma impact assessments are presented here as Annex D to this report. (A modification to the current programmatic decision-making algorithm in response to impact assessment data has been included, in order to remove uncertainty for districts in which the TF prevalence in 1-9 year-olds is 5-9.9% by codifying the previous (variable) practice of undertaking one further year of implementation of elimination activities before repeating an impact assessment.)

1.8 The 1998 World Health Assembly Resolution 51.11 on "Global Elimination of Blinding Trachoma" [3] did not include definitions for the elimination of blinding trachoma [4], which were eventually established in 2003 [5]and have since been slightly modified [6]. In principle, there is no impediment to further modifying elimination targets or changing related guidance to programmes, but generally this should be done only where the evidence base mandates change.

1.9 The consultation reviewed both published and unpublished data that might help answer questions relevant to trachoma surveillance. Unpublished data were discussed with the understanding that this would be done "off the record", and participants signed non-disclosure agreements in relation to those parts of the conversation. In this report, therefore, sample references are provided to support some but not all of the decisions made.

1.10 **Neither the recommendations made at this consultation, nor the interim trachoma surveillance standard operating procedures, nor any standard operating procedures ratified by WHO's Strategic and Technical Advisory Group on Neglected Tropical Diseases and offered as formal guidance to trachoma elimination programs should be considered to limit programmes from undertaking trachoma surveillance activities that are more comprehensive. Rather, they should be considered the minimum set of activities that are recommended, made available as interim standard operating procedures, or offered as ratified standard operating procedures, respectively**.

1.11 Neither the recommendations made at this consultation, nor the interim trachoma surveillance standard operating procedures, nor any standard operating procedures ratified by WHO's Strategic

and Technical Advisory Group on Neglected Tropical Diseases and offered as formal guidance to trachoma elimination programs should be considered to be final and unchanging. **Guidance should be expected to evolve as the evidence base that can be used to inform that guidance develops**. Programmes that have already used a set of ratified standard operating procedures to declare elimination of trachoma as a public health problem and have had that declaration validated will not be compelled to re-apply for validation in the event that standard operating procedures are subsequently updated.

2. What makes people go blind from trachoma?

2.1 The consultation reviewed published and unpublished evidence on trachoma's natural history, rates of progression, drivers of disease, and risk factors for blindness (*Table 1*).

Table 1. What is known (and not known) about the natural history of trachoma (CO="corneal opacity", CT=*Chlamydia trachomatis*, TF="trachomatous inflammation-follicular", TI="trachomatous inflammation-intense", TS= "trachomatous scarring", TT="trachomatous trichiasis")

	Uninfected to TF/TI	TF/TI to TS	TS to TT	TT to CO
What is already known	CT causes **inflammatory responses** influenced by host determinants; progression to TF (and TS, and TT) is driven at least in part by these inflammatory responses **Other pathogens** may produce clinical phenotypes that meet the definition of TF or TI, and/or exacerbate disease [7-9] **Follicles persist** in populations with higher baseline prevalence of active trachoma and ongoing low levels of CT infection	Repeated episodes of TF/TI are required to generate TS Risk of TS is related to **inflammatory scores** rather than follicular scores [10] Prevalence and incidence of TS increase with **age** [11,12] TS is associated with **female gender** in many populations [12,13] The incidence of TS in children is higher among those experiencing **constant severe active trachoma** [13,14] According to one model [15], the threshold **number of infections required for the development of TS and TT may be up to 88 and 130, respectively**	Prevalence and incidence of TT increase with **age** [11,16] **Inflammation** and **host responses** contribute to progression from scarring to TT Patients with worsening TT often have **papillary conjunctival inflammation** [17,18] TT increases risk of non-CT **bacterial infection**, which is associated with **increased inflammation**, **scarring**, and CO [19,20] Risk of non-CT **bacterial infection** is proportional to **severity of scarring and trichiasis** [19,21] Increased risk of conjunctival non-CT bacterial infection among **females** [20]	Prevalence of CO increases with **age** [11] **Severity of entropion** is associated with severity of CO [19,22,23] **TS** is associated with loss of conjunctival Goblet cells and lacrimal outflow obstruction, resulting in dry eye and a tear film that is abnormal in both volume and constitution, impairing normal corneal defenses. Nasolacrimal duct obstruction due to scar can, conversely, lead to persistent tearing and secondary conjunctivitis. **Traumatization of the cornea** from TT can provide a route of entry for non-CT bacteria, precipitating bacterial keratitis, leading to CO
What we do not know	The explanation for continuing persistence of follicles in formerly-trachoma-endemic populations with apparent absence of transmission of conjunctival CT infection	Role of other pathogens in generation of TS Relationship between steady-state prevalence of CT (or TF, or TI), and incidence of TS (or TT), in different populations Relationship between reductions in prevalence of CT (or TF, or TI) following trachoma elimination interventions in a population, and changes in incidence of TS (or TT, or CO) Intensity of CT infections or episodes of inflammation required to generate TS (or TT)	Relationship between steady-state prevalence of TS, and incidence of TT, in different populations To what extent, if any, trachoma elimination interventions reduce the incidence of TT in people with TS	Rate of progression from TT to CO To what extent, if any, trachoma elimination interventions reduce the incidence of CO in people with TT

3. What constitutes elimination of trachomatous trichiasis (TT) as a public health problem?

3.1 Current guidance suggests that a TT prevalence ≥1% in people aged 15 years and above is a public health problem [5]. In 2003, the elimination target for TT was set as an 80% reduction in this prevalence, translating to an elimination threshold of <2 cases per 1000 people aged 15 years and above, or (assuming that people aged 15 years and above constitute approximately half of the population) <1 case per 1000 total population [5]. Although it is vital to include a morbidity indicator as a programme target, the consultation considered whether reducing the prevalence of TT to < 1 per 1000 total population is appropriate and achievable. A number of issues were discussed (see below, paragraphs 3.2 to 3.5):

3.2 As programmes mature and treat the TT backlog, the demand for TT surgery may decrease. As a result, in some countries, achieving the elimination goal of <1 TT case per 1000 total population may require programme personnel to go door-to-door to find cases, offer surgery, and record refusal. This may be impractical, and will be kept under review. **(No change to current guidance.)**

3.3 In developed countries, the prevalences of vision-threatening states from other blinding conditions that are equivalent to TT (e.g., uncorrected refractive error of sufficient magnitude to cause moderate to severe visual impairment, or vision-threatening diabetic retinopathy) are higher than 1 per 1000 total population. Reducing the prevalence of TT to <1 per 1000 total population in trachoma-endemic countries, where there are almost always greater challenges to the health care infrastructure and competing healthcare priorities, may be very difficult, but there are currently insufficient data to establish whether or not the target is optimal from a public health perspective. **(No change to current guidance.)**

3.4 Eyelid and eyelash abnormalities other than posterior lamellar scarring from trachoma (e.g., epiblepharon, distichiasis) can cause eyelashes to touch the eye, and there is an underlying level of non-trachomatous trichiasis everywhere, potentially causing misdiagnosis of such conditions as TT in trachoma-endemic areas. The prevalence of non-trachomatous trichiasis is not known for either non-trachoma endemic areas or trachoma-endemic areas. The distinctions between TT and non-trachomatous trichiasis are important in the clinical care of individual patients (if the aberrant eyelashes in involutional trichiasis, epiblepharon or distichiasis are not vision-threatening), and important from an epidemiological/public health perspective with respect to (a) planning the need for TT surgery services and (b) their impact on apparent achievement of TT elimination targets. Therefore, **in impact assessments and trachoma surveillance, when TT is observed, graders should attempt to evert the eyelid to assess for and record the presence or absence of conjunctival scar. The presence of scar, or the inability to evert the lid because of lid tightness, should be taken to indicate that the trichiasis is TT**.

3.5 Studies on data entry errors were reviewed. In prevalence surveys for TT, recorders need to enter data on a question with two or three possible responses ("Is there TT in this eye?"; possible responses: no, yes, unable to examine eye). In published studies, the most closely comparable scenario to this is one in which respondents were asked to electronically record answers to a question with two possible responses; the observed error rate was approximately 0.6% (6 per 1000) [24]. In data from six countries that have participated in the Global Trachoma Mapping Project (in

which a record suggesting the observation of TT in a child triggers direct contact from the data manager to the field team for verification of the finding), the range of estimated false positive TT rates arising purely from recording error was 0.0-0.5 per 1000 right eyes, and 0.0-0.9 per 1000 left eyes, varying by country. Overall, amongst 219,401 children examined in these six countries, the false positive TT error rate arising from recording error alone was 0.16 per 1000 right eyes, 0.36 per 1000 left eyes, and 0.45 per 1000 individuals. **Electronic data collection systems should automatically alert recorders to the recording of the presence of TT in survey data for an individual of any age, by giving a distinctive warning, requiring the recorder to check and confirm the finding.**

3.6 The principal benefit of the TT elimination target being framed as the prevalence of TT "unknown to the health system" is that in areas where effective programmes have been active for several years, individuals with TT who are "unknown to the health system" can be assumed to have non-recurrent incident disease not previously detected by the programme, while cases "known to the health system" have generally been previously offered TT surgery. Many programs face high rates of surgical refusal. Excluding "known cases" removes the refusals (and those already scheduled to have surgery, and recurrent cases) from the numerator of the prevalence equation. While there is currently no standard methodology for distinguishing trichiasis cases "known to the health system" from those "unknown to the health system", the Global Trachoma Mapping Project is currently supporting a number of trachoma impact assessments in which a draft methodology is being tested. **Experience with this methodology should be formally reviewed as soon as possible.**

3.7 Current guidance recommends that programmes report their TT recurrence rate "as part of their health information system, with a target of achieving 10% or less recurrence at one year after surgery" [6]. The potential to achieve this target depends in part on the severity of cases, and programmes may have difficulty achieving ≤10% recurrence. Still, aiming for the target, routinely monitoring the outcome and transparent reporting are all desirable. **(No change to current guidance.)**

3.8 Pre-validation trachoma surveillance for TT is intended to provide some level of certainty that the TT elimination target has been sustainably achieved, following the first assessment that demonstrates its attainment. **The best way to provide maximum confidence that prevalence of TT remains below the elimination target at the end of pre-validation trachoma surveillance is to undertake a prevalence survey for TT.**

3.9 **Dossiers submitted for validation of elimination of trachoma as a public health problem will need to include information about districts which had formal implementation of trachoma elimination activities, as well as information about districts which were considered to be non-endemic.** Information about the latter does not have to include data derived from a prevalence survey, but should include information to justify why the district was considered to be non-endemic.

4. What constitutes elimination of trachomatous inflammation-follicular (TF) as a public health problem?

4.1 Current guidance suggests that a district-level prevalence of TF in 1-9 year-old children of 10% or more is a public health problem justifying implementation of the antibiotic, facial cleanliness and environmental improvement components of the trachoma elimination strategy [5], including mass drug administration of antibiotics, and that mass drug administration to the whole population of the district should be continued until an impact assessment indicates that the prevalence of TF in 1-9 year-olds is below 10% [6]. There are no randomized controlled trial data to suggest that a prevalence of TF in 1-9 year-olds is a critical threshold as far as transmission of conjunctival *C. trachomatis*, or risk of generating conjunctival scar are concerned. However, there is general consensus that the 10% TF threshold is likely to be a conservative one, in the sense that if all populations in which this prevalence is exceeded could be included in effective trachoma elimination programmes, blindness from trachoma would be likely to be eliminated as a public health problem. **A TF prevalence of 10% in 1-9 year-olds remains the threshold above which full implementation of the antibiotic, facial cleanliness and environmental improvement components of the trachoma elimination strategy is recommended. Further data on the biological significance of this threshold would be welcome.**

4.2 Issues in estimating TF prevalence in 1-9 year-olds were discussed, including the difficulty in adequately ensuring international standardization of the large numbers of graders needed to conduct prevalence surveys at programme scale, the increasing programmatic significance of false positive TF diagnoses as the true TF prevalence falls towards the TF elimination target of 5% in 1-9 year-olds, the phenomenon of TF being found in populations in which the prevalence of conjunctival *C. trachomatis* infection has been reduced to very low levels, and operational considerations related to the most appropriate age range to sample. **In order to provide evidence with which to consider changes to intervention stopping rules, further research was felt to be important** (paragraphs 4.3 to 4.7)**:**

4.3 **The research community is asked to examine age-specific prevalence of TF in different age bands within impact assessment datasets generated using internationally standardized graders.** If this allowed programmes conducting impact assessments and surveillance to examine only pre-school-age children, for example, more epidemiologically valid data might be produced (because such children are more often found at home at the time of a survey team's visit). There may also be incentives to harmonize the age band included with that used in surveys for other diseases. (The "transmission assessment survey" for lymphatic filariasis enrolls school-entrance-age children: 6-7 years.)

4.4 **The research community is asked to examine the potential utility of additional or alternative clinical signs to TF in programmatic decision making.** Intense conjunctival inflammation clearly plays an important role in disease progression and could be considered here, though the difficulties in training graders to reliably recognize the presence or absence of low prevalence clinical signs, and to prove that they are able to do so, are acknowledged.

4.5 **The research community is asked to examine the relevance of the change in the prevalence (as opposed to prevalence at only one time point) of TF (and/or additional or alternative clinical signs) in programmatic decision making.**

4.6 **The research community is asked to examine the potential utility of prevalence (and change in prevalence) of markers of conjunctival *C. trachomatis* infection in programmatic decision making.** The prevalence of TF shows good correlation with the prevalence of conjunctival *C. trachomatis* at baseline, but falls much more slowly than does the prevalence of conjunctival *C. trachomatis* following interventions [25-27]. In populations in which the prevalence of TF in 1-9 year-olds is <5% (therefore ready for surveillance), infection levels are expected to be extremely low. While there may be a role for estimating infection prevalence during surveillance, more data are needed before markers of infection could be considered for inclusion in trachoma surveillance standard operating procedures.

- Data on the district-level prevalence of clinical signs and infection (and antibody positivity) in post-intervention trachoma-endemic districts are now being collected through a project led by the Task Force for Global Health.
- Limited data suggest that the rate at which infection prevalence declines (from baseline to impact assessments) may help to predict the likelihood of re-emergence. Further work to investigate this would be helpful.

4.7 **The research community is asked to examine the potential utility of prevalence of antibodies to species-specific *C. trachomatis* antigens in programmatic decision making.** Serology allows estimates of prevalence of exposure to infection (as opposed to the point prevalence of current infection), and when combined with age [28], could be a useful measure of transmission intensity over time. Serology has the additional advantage of being suited to integration with other population-based surveys in which dried blood spots are collected. More data are needed, however, before serology could be considered for inclusion in trachoma surveillance standard operating procedures. Several phases of investigation are likely to be required:

- Data on the prevalence of clinical signs and antibody positivity (and conjunctival *C. trachomatis* infection) in post-intervention trachoma-endemic districts are now being collected through a project led by the Task Force for Global Health.
- Comparison of age-seroprevalence curves in districts with high, medium and low prevalence of TF and conjunctival *C. trachomatis* infection, before, during and after intervention, would be informative.
- Modelling of seroprevalence data will be helpful to determine appropriate sampling approaches in post-intervention districts and investigate possible thresholds for programmatic decision making.

4.8 Pre-validation trachoma surveillance for TF is intended to provide some level of certainty that the TF elimination target has been sustainably achieved, following the first assessment that demonstrates its attainment. **The best way to provide maximum confidence that prevalence of TF remains below the elimination target at the end of pre-validation trachoma surveillance is to undertake a prevalence survey for TF.**

4.9 **Dossiers submitted for validation of elimination of trachoma as a public health problem will need to include information about districts which had formal implementation of trachoma**

elimination activities, as well as information about districts which were considered to be non-endemic. Information about the latter does not have to include data derived from a prevalence survey, but should include information to justify why the district was considered to be non-endemic.

5. Are TT and TF (and/or related markers of inflammation and/or infection) the only critical indicators for trachoma elimination?

5.1 Current guidance suggests that indicators of success in implementation of the facial cleanliness and environmental improvement components of the trachoma elimination strategy will vary from country to country and should be defined at the national level [6]. There are no new data that mandate change. **(No change to current guidance.)**

5.2 The prevalence of visual impairment due to trachoma is not currently included in the definition of elimination of trachoma as a public health problem. While tools are available to allow the measurement of visual acuity and determination of causes of blindness in reasonably large samples of people (see, e.g., the Nakuru Eye Disease Cohort Study [29]), district-level estimates of the prevalence of trachoma-related blindness are likely to have wide confidence intervals, and determining the most likely cause of blindness or visual impairment in an individual requires fairly advanced ophthalmic knowledge and experience, and would therefore be difficult to undertake in multiple district-level surveys at national scale. **(No change to current guidance.)**

6. At what administrative level should surveillance be undertaken?

6.1 Current guidance (Table 2) suggests that:

a. baseline mapping be conducted at district[3] [2] or (where trachoma is widespread and highly endemic) larger-than-district level [6];
b. implementation be conducted at district level [2];
c. impact surveys be conducted at district level [6];
d. elimination of TT be defined as a prevalence estimated at district level [6];
e. elimination of TF be defined as a prevalence estimated at sub-district or village level[4] [6]; and
f. surveillance be conducted at district level [1] (*Table 2*).

The consultation considered whether it is cost-effective and practical to implement at district level, evaluate outcome at district *and* sub-district or village level, and then conduct surveillance at district level. Effectiveness, cost and practicality issues are presented in paragraphs 6.2, 6.3 and 6.4 respectively.

Table 2. Currently-recommended evaluation and implementation units

Phase	Baseline	Implement	Impact assessment #1 ("outcome")	Impact assessment #2 ("outcome")	Surveillance
When indicated	Not previously mapped; trachoma suspected	Trachoma endemic	After 3-5 years of programme implementation	Impact assessment #1 shows TF<10%	When country has met elimination criteria
Name of unit	Evaluation unit	Implementation unit	Evaluation unit	Evaluation unit	Evaluation unit
Administrative level	District or super-district	District	District	Sub-district or village (for TF)	District
Method of evaluation	Cluster random sample survey, 20-30 clusters	Not applicable	Cluster random sample survey, 20-30 clusters	Cluster random sample survey, 20-30 clusters	Convenience sample of children and adults in 2-4 purposively selected communities

[3] For trachoma elimination purposes, districts have been defined as the normal administrative unit for health care management, which for purposes of clarification consists of a population unit between 100,000-250,000 persons.

[4] For trachoma elimination purposes, sub-districts have been defined as a geographic or other grouping of at least three villages that permits finer stratification of a district into sub units that might be expected to have greater or lesser prevalence of trachoma, based, for example, on knowledge of higher versus lower rates of trachoma at the start of the program, or geographical information such as clustering of villages around "hotspots" (villages proven to have high rates of trachoma), or that had presence or absence of water resources or other infrastructure that might indicate differing rates of trachoma. Villages have been defined as population units of 8,000-10,000 persons.

6.2 The effectiveness of the guidance outlined in paragraph 6.1 is likely to depend on (a) the relationship between the prevalence of TF and the risk of future trachoma-related blindness; (b) the programme's ability to reduce that risk with intervention; and (c) the sensitivity of surveys for detecting post-intervention foci of conjunctival *C. trachomatis* infection ("hot spots") that might result in re-emergence of TF to significant levels in adjacent populations. Useful data pertaining to (a) and (b) are scarce. Although conducting impact assessments at sub-district level increases spatial resolution for TF (and therefore the expected sensitivity for detecting post-intervention hot-spots), experience to date suggests that sub-districts that have relatively high prevalences of TF at impact assessment do not result in re-emergence of TF to significant levels in adjacent sub-districts.

6.3 Available data show a large range in costs for population-based trachoma surveys. For the Global Trachoma Mapping Project, the mean cost of baseline mapping has ranged from approximately $2,500 to nearly $16,000 per district [30]. In earlier surveys, published costs ranged from $1,511 to $25,409 per district [31]. Conducting surveys at sub-district level at the impact assessment #2 stage multiplies survey costs by a factor between 2 and 50 (depending on the number of sub-districts per district) compared to impact assessment #1.

6.4 From a practical perspective, using sub-districts as the evaluation unit for estimating TF prevalence at the impact assessment #2 stage:

- requires the mobilization, training and standardization of personnel on a scale that is often not feasible;
- prevents integration with district-level surveys undertaken for other diseases (preventing potential cost-savings); and
- is unpopular with programmes, because discontinuing antibiotic mass drug administration in some sub-districts but not others often causes residents of villages that no longer receive antibiotics to express displeasure that neighbouring villages still receive them.

6.5 For all of these reasons, **impact assessments should be conducted at district level. Conducting impact assessments at sub-district level is no longer recommended.**

7. How and when should surveillance be conducted?

7.1 Current guidance for surveillance (Annex A) recommends examination of individuals in 2 to 4 purposively selected communities per district at each surveillance time point [1]. The consultation expressed concerns that the resulting data could be influenced considerably by both bias and chance effect, via factors involved in selection of the communities, small sample sizes, and the difficulty in predicting the (hopefully) rare event of re-emergence, in addition to the usual difficulties involved in trachoma data that have been presented above. It was therefore agreed that an epidemiologically rigorous cluster random sample survey would provide a better basis for programmes to make inferences at district level. **Pre-validation surveillance should be based on repeat cluster random sample surveys. The use of sentinel sites is no longer recommended.**

7.2 Current guidance for surveillance (Annex A) recommends that surveillance be undertaken as an annual activity. It would be very expensive to undertake annual cluster random sample surveys, and this is unlikely to be necessary. In a very highly trachoma-endemic population in which antibiotic mass drug administration was experimentally stopped when (a) prevalence of conjunctival *C. trachomatis* was very low but (b) prevalence of TF remained very high, significant re-emergence of conjunctival *C. trachomatis* infection occurred in some villages by two years after cessation [32]. Correlation between village-level prevalence of conjunctival *C. trachomatis* infection at baseline and the rate of return of infection was poor; whether this lack of correlation would also hold true using district-level prevalences is not known. Given that these villages discontinued mass drug administration well before meeting the recommended TF prevalence threshold for stopping, and had unusually high prevalences of TF and *C. trachomatis* infection at baseline, this study could be considered a demonstration of the worst-case scenario; but even here, the increase in TF prevalence in the first year after discontinuation was small. **The pre-validation surveillance survey should be conducted two years after the impact assessment has shown that elimination targets have been reached.**

7.3 **The pre-validation surveillance survey should estimate both the prevalence of TF and the prevalence of TT.**

7.4 **Funders are requested to plan to (a) support trachoma surveillance activities, and (b) re-initiate elimination interventions, if surveillance data demonstrate re-emergence of disease.**

7.5 **Data from previous, current and future trachoma surveillance efforts should be requested by WHO for international compilation and ongoing analysis**, to allow the development of improved algorithms that would help to establish (a) the relative risk of re-emergence of disease after elimination targets have been reached; (b) whether or not there is a need for all post-intervention districts to undertake a pre-validation surveillance survey; (c) whether the surveillance strategy should be adjusted for individual districts on the basis of district-level risk factors for re-emergence; (d) the minimum number of clusters that should be sampled in a pre-validation surveillance survey.

7.6 Post-validation trachoma surveillance has not yet been considered.

8. Next steps

8.1 Present the interim standard operating procedures (as part of a comprehensive Neglected Tropical Disease document) to WHO's Strategic and Technical Advisory Group on Neglected Tropical Diseases for review and possible ratification. If revision is requested before ratification, consultation participants will be asked to reconvene by email or teleconference.

8.2 Present the interim standard operating procedures at the trachoma surveillance session of the October/November 2014 Coalition for Operational Research in Neglected Tropical Diseases meeting, to plan identified research activities.

8.3 Translate the interim standard operating procedures (and any subsequent updates) into French, Spanish and Portuguese.

8.4 Publish ratified standard operating procedures on the WHO website.

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Annex A. Previous guidance on trachoma surveillance

Excerpt from: Report on the Meeting on Post-Endemic Surveillance for Blinding Trachoma

World Health Organization, Geneva, 4-5 November 2008

Regarding TF:

Trachoma surveillance for TF prevalence should be conducted in 2 selected communities (with 1,000-2,000 habitants each) per endemic district per year biased to the least developed and suspected most endemic. The selected sites should rotate annually. If the selected districts have more than 200,000 habitants, the sentinel sites to evaluate in those districts shall be 4.

The evaluation must involve all school entrance-aged children where attendance is >90% and there is no gender bias. In the other cases the investigation should be conducted on a minimum of 50 children in the community (5-6±2 years of age), but if it is feasible all children in the community should be examined.

If the response to the examination is a TF<5% no actions are required.

If the response to the examination is a TF >5%, all children aged 1-9 year olds should be examined and all the positive cases should be treated and their families and neighbours should be investigated and treated. In these cases the examination should be also extended to nearby villages. Facial cleanliness and environmental change must be verified and implemented.

If TF >5% in all 1-9 year olds, AFE coverage should be assessed and the entire community should be treated. All school entrance aged children in all the surrounding sub-district communities should be examined and in TF results to be >5%, AFE strategy should be re-implemented for 3 years and the situation evaluated at the end of this period.

Regarding TT:

Trachoma surveillance for TT prevalence should be conducted as a TT screening in all people aged >40 years in the same 2 selected sentinel communities per endemic district per year. On the other hand, National Health System should be able to collect, analyses and furnishes every year number of TT cases evaluated and/or operated in the Country. In other words, also refused and recurrence cases must be reported per year. For this reason, all people referring to a hospital must be screened for trichiasis and in any cases volunteers in villages should be trained to detect trichiasis, also after the achievement of the certification. The ideal way to detect all cases should be organizing house-to house evaluation, but where this is not possible it must be useful to take advantage of other ophthalmic campaigns. The refused cases should be investigated as a further follow-up on surgical quality, which in any cases must be scheduled in the criteria for certification. In fact, each country must demonstrate the ability to discriminate approached/un-approached cases and to manage the incident cases.

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Annex C. Interim trachoma surveillance standard operating procedures

Trachoma elimination programme standard operating procedures

Trachoma surveillance

Version number: 1.01

Date of last amendment: 12 October 2014

Status: interim standard operating procedures, not yet ratified by WHO's Strategic and Technical Advisory Group on Neglected Tropical Diseases

Date of next planned review: 01 April 2015 **(Please note that this version is invalid after this date.)**

Responsible individual: Medical Officer, Trachoma, WHO Headquarters

10. Pre-validation trachoma surveillance should be conducted as a cluster random sample survey undertaken, in general, in each district in which trachoma elimination interventions have been required, two years after a district-level impact assessment shows that elimination targets for trachomatous trichiasis (TT) and trachomatous inflammation-follicular (TF) have been reached.
20. The pre-validation trachoma surveillance survey should estimate the prevalence of TT "unknown to the health system" in the whole population, and the prevalence of TF in 1-9 year-old children.
30. In trachoma surveillance surveys, when TT is observed, graders should attempt to evert the eyelid to assess for and record the presence or absence of conjunctival scar. The presence of scar, or the inability to evert the lid because of lid tightness, should be taken to indicate that the trichiasis is TT.
40. In trachoma surveillance surveys, electronic data collection systems (if used) should automatically alert recorders to the recording of the presence of TT in survey data for an individual of any age, by giving a distinctive warning, requiring the recorder to check and confirm the finding.
50. In trachoma surveillance surveys, mechanisms for robust supervision of field teams, with confirmation of at least a proportion of positive findings, must be in place.
60. Prevalence thresholds for programmatic decision-making after pre-validation trachoma surveillance survey are the same as those used for impact assessments, except that the finding of prevalences of TT and TF below the elimination targets does not indicate that the pre-validation trachoma surveillance period should recommence.
70. Programmes and funders should give strong consideration to (a) incorporating operational research elements in trachoma surveillance activities, and (b) contributing data to an international data repository for ongoing analysis, in order to help refine the evidence base for these and other standard operating procedures.
80. Post-validation trachoma surveillance has not yet been considered in this document.
90. TT surgical services should be provided until there are no longer any incident TT cases.

Annex D. Interim trachoma impact assessment standard operating procedures

Trachoma elimination programme standard operating procedures

Trachoma impact assessments

Version number: 1.01

Date of last amendment: 12 October 2014

Status: interim standard operating procedures, not yet ratified by WHO's Strategic and Technical Advisory Group on Neglected Tropical Diseases

Date of next planned review: 01 February 2015 **(Please note that this version is invalid after this date.)**

Responsible individual: Medical Officer, Trachoma, WHO Headquarters

10. Conduct a trachoma impact assessment as a cluster random sample survey in each district in which trachoma elimination interventions have been required, after at least five years of implementing interventions where the baseline prevalence of trachomatous inflammation-follicular (TF) in 1-9 year-olds was ≥30%, or after at least three years of implementing interventions where the baseline prevalence of TF in 1-9 year-olds was 10-29.9%.
20. If the ministry of health feels that it is unlikely that the elimination prevalence target for TT will have been met after the minimum periods specified in paragraph 10, they should consider delaying the impact assessment to allow time for further delivery of enhanced TT surgical services.
30. A trachoma impact assessment should estimate the prevalence of TT "unknown to the health system" in the whole population, and the prevalence of TF in 1-9 year-old children.
40. In a trachoma impact assessment, when TT is observed, graders should attempt to evert the eyelid to assess for and record the presence or absence of conjunctival scar. The presence of scar, or the inability to evert the lid because of lid tightness, should be taken to indicate that the trichiasis is TT.
50. In a trachoma impact assessment, electronic data collection systems (if used) should automatically alert recorders to the recording of the presence of TT in survey data for an individual of any age, by giving a distinctive warning, requiring the recorder to check and confirm the finding.
60. In a trachoma impact assessment, mechanisms for robust supervision of field teams, with confirmation of at least a proportion of positive findings, must be in place.
70. In a trachoma impact assessment, if the estimated TF prevalence in 1-9 year-olds is
    a. <5%, stop antibiotic mass drug administration, and commence pre-validation trachoma surveillance.
    b. 5-9.9%, implement one further year of the A, F and E components of the SAFE strategy (including district-wide mass drug administration of antibiotics), then repeat the impact assessment.

c. 10-29.9%, implement three further years of the A, F and E components of the SAFE strategy (including district-wide mass drug administration of antibiotics), then repeat the impact assessment.
d. ≥30%, implement five further years of the A, F and E components of the SAFE strategy (including district-wide mass drug administration of antibiotics), then repeat the impact assessment.

80. Programmes and funders are strongly encouraged to (a) incorporate operational research elements in trachoma impact assessments, and (b) contribute data to an international data repository for ongoing analysis, in order to help refine the evidence base for these and other standard operating procedures.