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Algorithms for the local response to cases of STEC infection V3.1

For use with the public health operational guidance 'Shiga-toxin producing *Escherichia coli* (STEC) V3.0'

January 2023

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Since 2013, many local NHS laboratories have introduced real-time polymerase chain reaction (PCR) testing as a gastrointestinal (GI) screening panel for faecal samples where infectious disease is suspected. These GI PCR panels include primers that detect Shiga toxin (*stx*) genes (*stx1* and *stx2*) that are possessed by all STEC. The introduction of *stx* PCR tests by a diagnostic laboratory is likely to lead to an increase in the number of STEC infections detected (O157 and non-O157) and consequently an increased number of notifications to local health protection teams (HPTs). Evidence of the public health impact of different non-O157 STEC is still emerging and a universal approach to the public health management of all *stx* positive results is not appropriate.

Local *stx* PCR positive but culture negative samples should be sent to the Gastrointestinal Bacteria Reference Unit (GBRU) for further investigation and for various non-O157 STEC serogroups to be identified. Referral of local culture negative samples is especially important for children, and those with bloody diarrhoea and haemolytic uraemic syndrome (HUS).

The ultimate aim of the public health response is to prevent disease and transmission associated with STEC infections. This is relatively rapid and straightforward for STEC O157 infections, because following an *stx* PCR positive result, local laboratories can proceed to test for and isolate O157 strains with reports of presumptive *E. coli* O157 infections usually available within 3 days of specimen collection, enabling the public health response to be commenced quickly.

Because *E. coli* O157 is not grown from the majority of *stx* PCR positive faecal specimens, and local laboratories cannot routinely isolate non-O157 STEC, there is a delay in full microbiological characterisation. Serotype and *stx* subtypes are usually reported by GBRU about 2 to 3 weeks after the HPT is first informed of the case.

Serotype is more readily available for STEC O26 (for which PCR testing has been implemented to provide a result 1 to 2 working days after the initial *stx* PCR profile). Like STEC O157, STEC O26 is more frequently associated with severe clinical outcomes, hospitalisation, and outbreaks in comparison to other STEC serotypes, and its isolation should prompt full public health actions.

The main aim of the public health response to non-O157 STEC is to prioritise the response to those cases most likely to be infected with viable STEC belonging to higher risk STEC strains,

including STEC O26 and HUSEC strains. By doing so, this guidance seeks to provide a proportionate response that protects the public's health while taking into consideration the workload implications for HPTs or local authorities, without imposing unnecessary restrictions on individuals.

While full characterisation of an STEC isolate is pending, local PCR and culture results, followed by GBRU in-house PCR results may be available. The following algorithms have therefore been divided into 3 stages based on this process to provide HPTs with guidance on how to respond to cases as each new piece of information becomes available.

The 3 algorithms are based on laboratory results as they become available, as follows:

- Stage 1 - Diagnostic laboratory results (PCR and culture), age of the case, and clinical history (HUS or bloody diarrhoea)
- Stage 2 – GBRU in-house PCR results (*stx* and *E. coli* attachment and effacing (*eae*) gene, plus STEC O26 identification)
- Stage 3 – GBRU serogroup or serotype including *stx* subtypes

The algorithms should be used for the investigation of single cases and is colour coded for public health management as follows:

- red border – full or majority of public health actions recommended
- amber border – limited public health actions recommended
- green border – warn and inform public health actions only, or no public health actions
- blue background – questions for decision-making process
- white – information only

Notes provide guidance and follow each stage in the algorithm.

Note that full context and accessible text versions of these algorithms are available in Appendix C of the [main report](#).

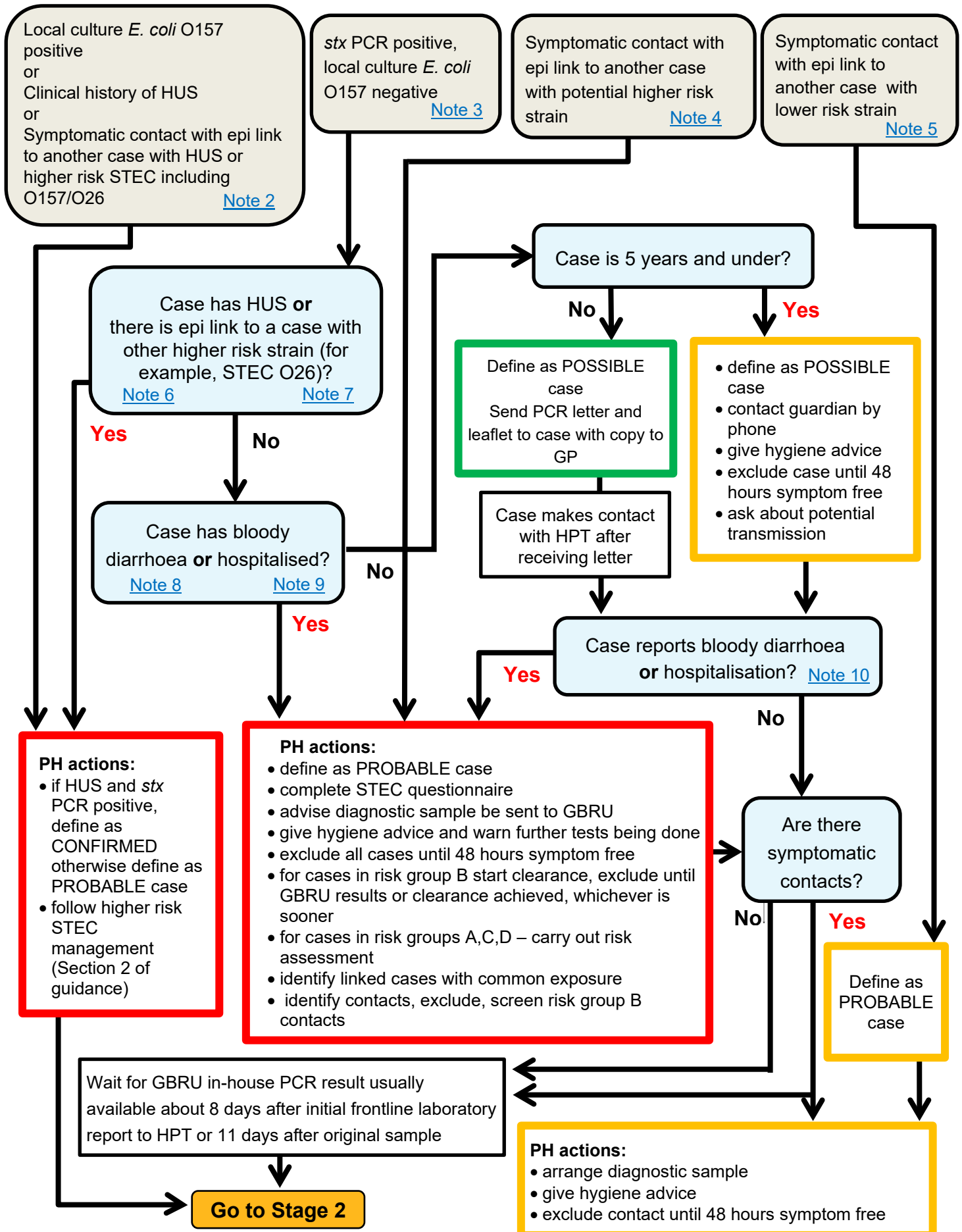
These algorithms should be used in conjunction with the following sections of the main report:

- Section 2. Public health management of STEC O157 and non-O157
- Section 3. Outbreaks and clusters

Stage 1

STEC algorithm

[Note 1](#)



Stage 1

Note 1

There are several ways potential STEC infections are reported to the HPT:

- local culture *E. coli* O157 positive
- notification of HUS
- symptomatic contact with an epidemiological link to another case with HUS, or culture confirmed O157 STEC, or culture confirmed non-O157 STEC belonging to a higher risk strain (*stx2a/2c/2d* and *eae/aggR* positive or STEC O26)
- local *stx* PCR positive, but local culture negative for *E. coli* O157
- symptomatic contact with an epidemiological link to another case with culture-confirmed potential higher risk strain (*stx2* and *eae*)
- symptomatic contact with an epidemiological link to another case infected with culture confirmed lower risk STEC strain (non *stx2a/2c/2d*)

For notifications of infective bloody diarrhoea, unless there is a known epidemiological link to a case with potential or confirmed higher risk STEC infection, public health action can usually wait until the local diagnostic laboratory culture results are known. If local laboratories are using PCR, initiation of public health action should follow locally agreed arrangements.

Note 2

Local culture *E. coli* O157 positive OR history of HUS

- define case as PROBABLE
- full public health actions as per higher risk STEC management for case and contacts are recommended

Rationale

Most cases of diarrhoea associated HUS are caused by STEC belonging to HUSEC strains.

Symptomatic contact with an epidemiological link to another case with HUS, or culture confirmed STEC of a higher risk strain, including O157, O26, and/or strains with a higher risk virulence profile (*stx2a/2c/2d* and *eae/aggR*)

- define case as PROBABLE
- full public health actions as per higher risk STEC management for case and contacts are recommended

Rationale

There is evidence of potential transmission of higher risk strain between the case and this symptomatic contact.

Note 3

Local *stx* PCR positive, local culture *E. coli* O157 negative

This is the usual result received by HPT and is the usual starting point of the response. Result may be received by phone call or SGSS import to HPZONE.

- clinical and demographic information should be reviewed
- if positive PCR results are received while local culture results are pending, it may be appropriate to commence public health actions, then to follow the relevant arm of the algorithm once culture results are available

Rationale

Stx PCR tests are highly sensitive and specific, but do not distinguish between viable and non-viable organisms or even free *stx*-bacteriophages in the faeces.

Note 4

Symptomatic contact with an epidemiological link to another case with a potential higher risk strain (*stx2* and *eae* regardless of *stx1*)

- follow the actions for cases with history of bloody diarrhoea (see Note 8, below)

Rationale

The case associated with this symptomatic contact may not subsequently be confirmed by GBRU to be a higher risk strain. Advice to implement pragmatic precautions (exclusion while symptomatic and providing hygiene advice) and complete the STEC questionnaire (information about potential transmission and contacts) aims to balance the risk of transmission against imposing restrictions on the case that may not be necessary.

Note 5

Symptomatic contact with an epidemiological link to another case with lower risk strain (non *stx2a/2c/2d*)

Define case as PROBABLE:

- arrange diagnostic sample, give hygiene advice, provide PCR letter or leaflet if not already done and exclude until minimum of 48 hours symptom free
- public health actions determined by diagnostic result

Rationale

There is an epi link to another case with a lower risk strain. The likelihood of serious illness or outbreaks is low. Manage like other non STEC gastrointestinal infections.

Note 6

Local *stx* PCR positive, local culture *E. coli* O157 negative with history of HUS or epidemiological link to case infected with a higher risk strain (HUSEC/STEC O26)

- *Stx* PCR positive and HUS: define case as CONFIRMED, or
- epidemiological link: define case as PROBABLE
- full public health actions as per higher risk STEC management for case and contacts are recommended

Rationale

Current case is *stx* PCR positive and is a contact of another case infected with a higher risk strain. There is evidence of possible transmission, or case of diarrhoea associated HUS, most of which are caused by a higher risk strain of STEC.

Note 7

Local *stx* PCR positive, local culture *E. coli* O157 negative no history of HUS and no epidemiological link to case infected with a higher risk strain

- review history for features of severe disease – bloody diarrhoea or admission for acute diarrhoeal illness. Depending on local arrangements, this information may be on laboratory request form or provided by reporting clinician/microbiologist
- in the absence of this information, the HPT should consider contacting the clinician who arranged for the test to confirm the history

Note 8

Local *stx* PCR positive, local culture *E. coli* O157 negative with history of bloody diarrhoea

History of bloody diarrhoea or admission with acute diarrhoeal illness has been reported on the laboratory result report or by the clinician or microbiologist:

- define case as PROBABLE
- complete STEC questionnaire
- provide hygiene advice (written if possible) and warn case that further tests are being done on the sample
- exclude all cases until 48 hours symptom free
- if case is in risk group B consider commencing clearance once 48 hrs symptom free and exclude until GBRU in-house PCR is known or clearance achieved, whichever is sooner (see Table 6)
- if case is in risk group A, C, D do not automatically exclude case: carry out risk assessment (see Table 6)
- identify any linked cases resulting from a common exposure
- if there are symptomatic contacts arrange single diagnostic sample, give hygiene advice and exclude them until 48 hours symptom free

- exclude and screen risk group B contacts
- wait for GBRU in-house PCR result, available around 11 days after sample collected before starting public health actions for asymptomatic contacts in risk groups A to D (see Table 7)

Rationale

Although the case has bloody diarrhoea, most isolates are not subsequently confirmed by GBRU to be viable STEC belonging to higher risk strains. However, bloody diarrhoea is more frequently associated with infection with higher risk strains. Advice to implement pragmatic precautions (exclusion while symptomatic and providing hygiene advice) and complete the STEC questionnaire (information about potential transmission and contacts) aims to balance the risk of transmission against imposing restrictions on the case that may not be necessary.

Note 9

Local *stx* PCR positive, local culture *E. coli* O157 negative no evidence of severe illness

Where there is no evidence of severe illness:

- define case as POSSIBLE
- if the case is aged 5 years and under it is recommended to make contact by phone with parent or guardian to confirm history and carry out a rapid risk assessment (see Appendix 2 of [the main report](#))
- provide written information to case (or parent or guardian) and copy to the GP (see Appendices 2 and 4)
- no other public health actions recommended at this stage
- wait for GBRU in-house PCR and culture results

Rationale

Young children are particularly susceptible to acquiring and transmitting STEC infections and that they are also at greater risk of developing severe infection such as HUS.

Note 10

Local *stx* PCR positive, local culture *E. coli* O157 negative patient reports bloody diarrhoea

If case makes contact with HPT and reports bloody diarrhoea or admission with acute diarrhoeal illness:

- manage as a potential higher risk strain as per Note 8, above

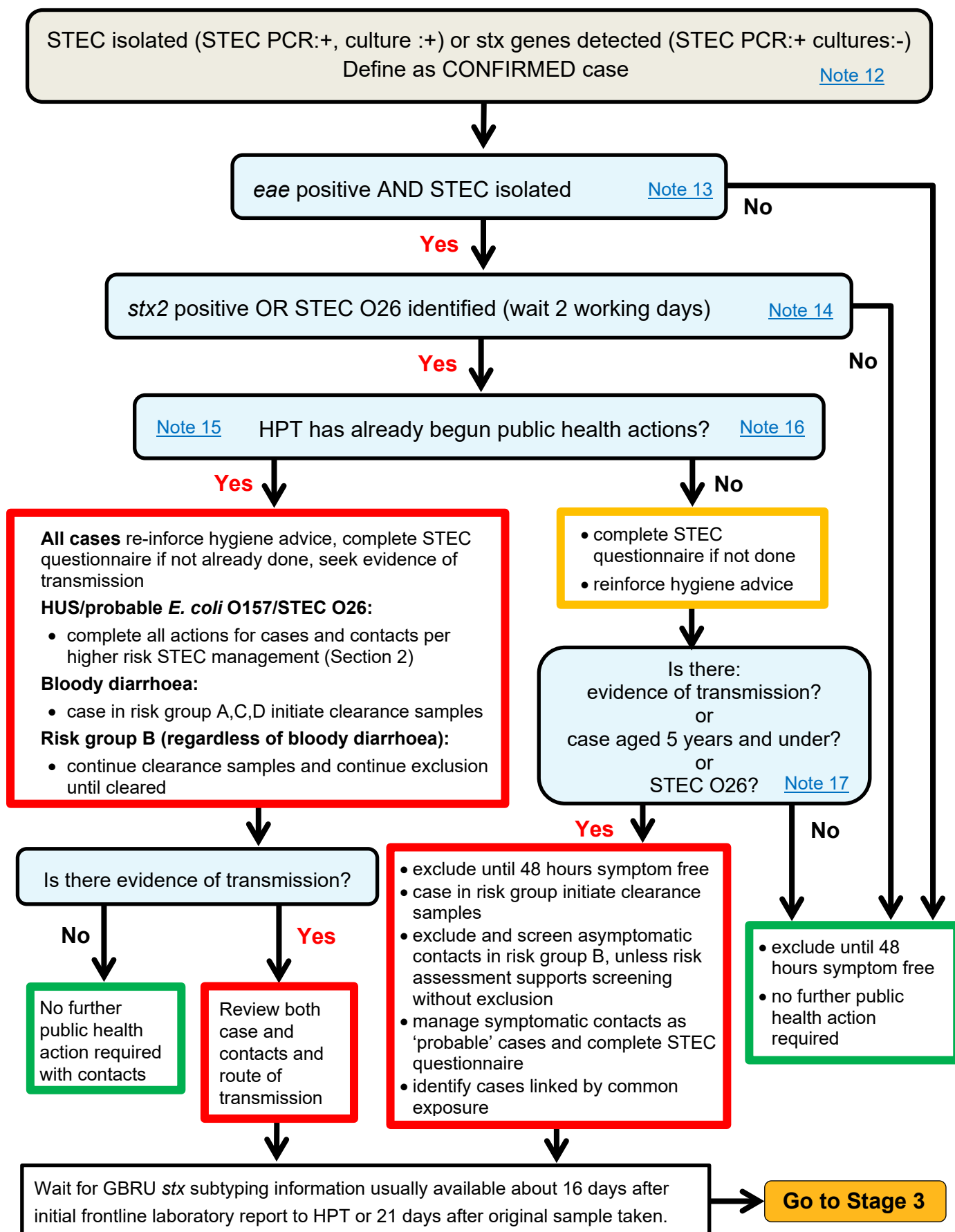
If case reports that contacts have been symptomatic:

- arrange single diagnostic sample per contact, give hygiene advice and exclude contact until 48 hours symptom free

Stage 2

GBRU in-house PCR result

[Note 11](#)



Stage 2

Note 11

Detection of *stx* and *eae* genes in a specimen does not indicate the viability of the organism. It is the combination of both *stx* and *eae* gene profile and culture result from GBRU which is most useful in directing public health actions. In stage 2, the possession of *stx2* and *eae* is used to identify infections caused by potential higher risk strains. Additional measures are recommended where STEC O26 is identified, as it is associated with severe disease (with *stx1* or *stx2*) and can be identified by GBRU at this stage.

Note 12

GBRU in-house PCR results

At this stage the GBRU in-house PCR results are reported on GDW2 and include the *stx* and *eae* results (see Appendix 1 of [the main report](#)):

- STEC isolated (STEC PCR:+ culture:+) – this indicates that STEC is present and viable, and an isolate is available for WGS
- *stx* genes detected (STEC PCR:+ culture:-) – this indicates that STEC is present, but the organism is not viable, or the numbers are too low to isolate
- STEC NOT isolated (STEC PCR:- culture:-) – this indicates that STEC is not present

Notes on PCR results

About 30 to 40% of *stx* PCR positive results are not confirmed by GBRU; this is because:

- DNA degrades quickly in faecal samples, the inherent turn-around time between local lab testing and GBRU testing can affect detection
- local diagnostic laboratories perform direct DNA extraction from the sample, whereas GBRU does an overnight broth enrichment step. If the bacteria are viable and multiply, the enrichment step increases the amount of DNA present; if the bacteria are dead, enrichment dilutes the DNA
- pathogens are not evenly distributed throughout a faecal sample

Be aware that the PCR result is from DNA extracted from a faecal sample. The combination of positive *stx1/stx2/eae* genes may be derived from more than one strain of STEC and non-STEC pathogens in that sample

Note 13

eae positive AND STEC isolated (culture positive)

- for all combinations of *stx1* and/or *stx2* with positive *eae* results, change case definition to CONFIRMED

- for all *eae* negative cases, there are no public health actions (until STAGE 3 results are known) beyond ensuring the case is excluded until 48 hours symptom free, beyond ensuring case is excluded until 48 hours symptom free
- if STEC is not isolated, there are no public health actions routinely recommended (until STAGE 3 results are known) beyond ensuring case is excluded until 48 hours symptom free

Note 14

Stx2 positive or STEC O26 identified

At the reference lab, a new PCR test has been added as an additional step to identify serogroup O26:H11 after STEC is isolated by culture. HPTs are advised to wait 2 working days after culture and *stx* results, especially for *stx1* and *eae*-positive cases. If O26 is not positive at that point, public health actions already commenced can be stopped.

- culture-positive STEC with *stx2* and *eae* is a potential higher risk strain
- all STEC O26 cases should be followed up, regardless of *stx/eae* gene profile
- in summary, if the result is positive for both *stx2* and *eae*, and organism is viable or STEC O26 is identified (regardless of *stx/eae* profile), go to the next question in the algorithm
- if *stx2* is negative and STEC O26 is not identified after 2 working days, there are no public health actions routinely recommended until STAGE 3 beyond ensuring the case is excluded until 48 hours symptom-free

Note 15

Case is already known to HPT and public health actions have been commenced

For cases with a history of HUS or probable *E. coli* O157, full public health actions are likely to have begun, and may have been completed, prior to the GBRU PCR result. If there is a history of bloody diarrhoea, some public health actions are likely to have begun, particularly if the case is in a risk group.

All cases:

- change case definition to CONFIRMED
- re-assess evidence of transmission (given that, potentially, a further incubation period has passed since initial contact with the case)

HUS/probable *E. coli* O157/O26:

- all actions as per higher risk STEC management should have been completed or are in progress, including providing advice and the possible exclusion and screening of contacts (see Table 7)

Cases with bloody diarrhoea:

- Review public health actions, including providing advice and the possible exclusion and screening of:
 - asymptomatic contacts in risk groups A, C, D ([Note 8](#)) (see Table 7)
 - symptomatic contacts (see Table 7)

Children under 6 years of age (risk group B) regardless of symptoms:

- if already excluded, continue until clearance has been achieved
- if not already excluded, carry out risk assessment to determine need for exclusion until clearance has been achieved (see Table 6). However, if there is evidence of transmission exclude until cleared

Rationale

The STEC is viable and a potential higher risk strain. It may not have produced serious symptoms in this case, but if the case is shedding, there is still the potential for transmission, particularly if the case is a young child. Some strains appear to cause more severe disease in secondary cases.

Note 16

Public health actions not started

If the HPT was not previously aware of the case, but identified it from GDW2 or if, from initial clinical history, the case had been assessed to be lower risk:

- case is defined as CONFIRMED
- complete the STEC questionnaire if not already done
- re-enforce hygiene advice that may have been provided to the case in the letter or leaflet
- assess for evidence of transmission:
 - if there is no evidence of transmission, exclude case until 48 hours symptom free, but there are no further public health actions for the case or their contacts
 - if there is evidence of transmission, then follow up is recommended

Rationale

This case is infected with a potential higher risk strain (serotype and *stx2* subtype not yet known). An assessment of potential transmissibility is advised, even though the strain has not caused severe illness in this case.

Note 17

Assess if:

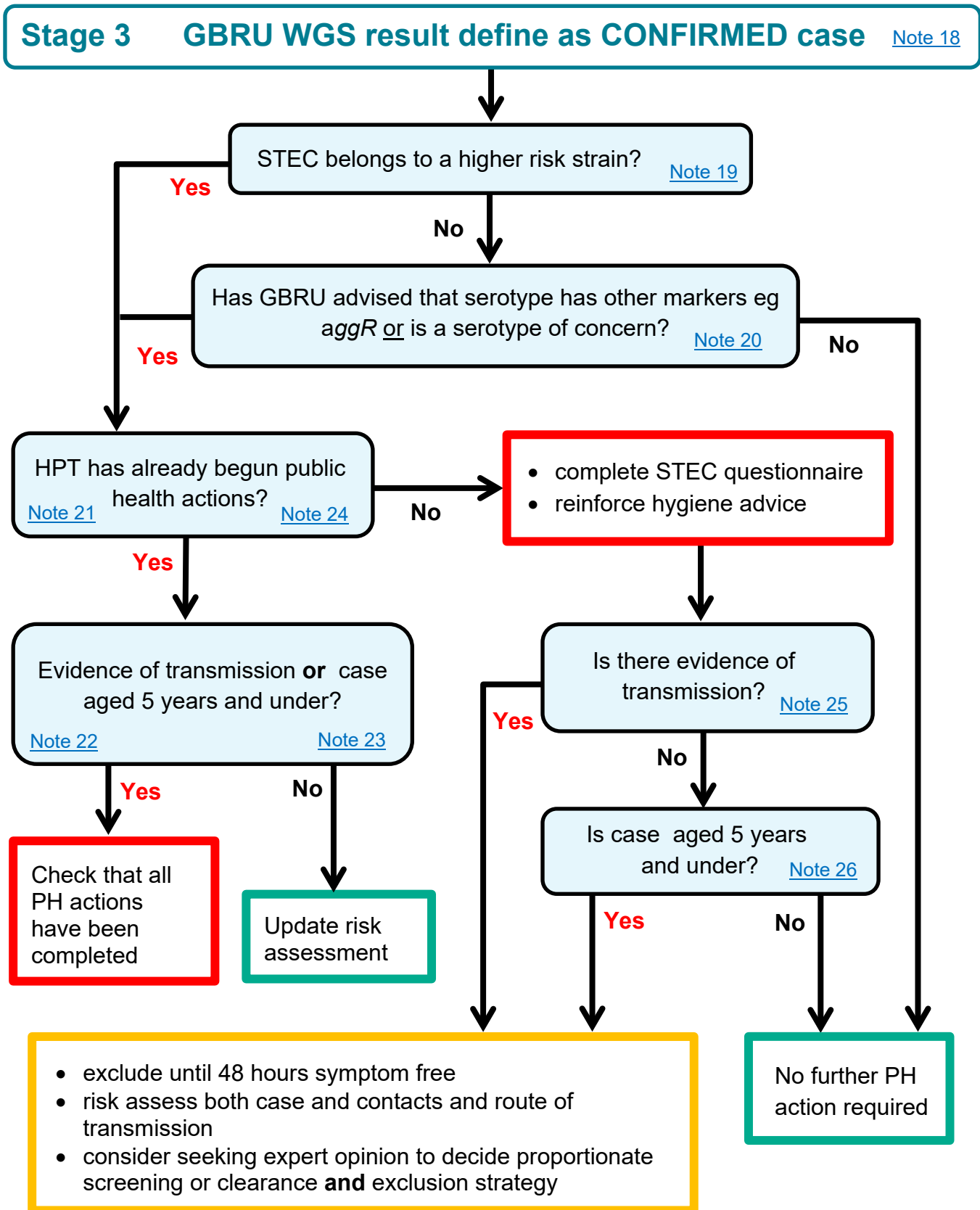
- evidence of transmission? or
- age 5 years or under? or
- STEC O26 identified?

If any of the above apply:

- if case is in risk group B, carry out risk assessment to determine need for exclusion until clearance has been achieved (see Table 6). However, if there is evidence of transmission, exclude until cleared
- if case is in risk group A, C, D, carry out risk assessment to determine need for exclusion until clearance has been achieved (see Table 6)
- asymptomatic contacts in risk group B: exclusion and clearance recommended. Risk assessment to determine need for exclusion may be considered (see Table 7). If there is difficulty in obtaining a screening sample or evidence of transmission, exclude until screened
- asymptomatic contacts in risk group A, C, D: screening not recommended (see Table 7)
- symptomatic contacts:
 - manage as a PROBABLE case
 - arrange single diagnostic specimen and exclude until 48 hours symptom free
 - if symptomatic contact is in risk group A-D continue to exclude until the diagnostic or screening result is known (see Table 7)

Rationale

Children aged 5 years and under can shed STEC for prolonged periods, and onwards transmission is not uncommon. If a case has symptomatic contacts, assume that transmission may have occurred.



Stage 3

Note 18

GBRU WGS results

- define case as CONFIRMED (if case not previously reported)

Rationale

The *stx* subtypes *stx2a/stx2c/stx2d* are strongly associated with risk of severe disease including HUS, particularly if positive for *eae* or *aggR* gene (as reported in GDW2).

Note 19

Serotype has the *stx* subtype *stx2a/2c/2d* (higher risk strain)

- it is recommended that all isolates with *stx2a/2c/2d* regardless of *eae* should be followed up for public health action
- GBRU provides the *aggR* result on GDW2
- all STEC O26 cases should be followed up, even with a non HUSEC profile

Note 20

Serotype has a lower risk strain profile

It is probable that, in future, other pathogenic strains will emerge and GBRU will alert HPTs if additional actions are recommended.

Rationale

Bacteria are constantly evolving there have been documented instances when an *E. coli* strain of low pathogenicity has acquired *stx* genes, or where new evidence has implicated a serotype or genotype in severe disease (for example, increased severe disease associated with STEC O26:H11, and a Europe-wide outbreak of HUS and other severe disease associated with EAEC O104:H4).

Note 21

Serotype has the *stx* subtype *stx2a/2c/2d* (higher risk strain) and the HPT has commenced public health actions

If the strain has the *stx* subtype *stx2a/2c/2d* (higher risk strain) and the STEC questionnaire has already been completed:

For cases with HUS / bloody diarrhoea / probable STEC O157/ STEC O26, public health actions will probably have been completed:

- check that all public health actions have been completed

For cases in risk groups, it is possible that there may be some outstanding public health actions, particularly if the initial GBRU result in Stage 2 was *stx2* but negative for *eae*:

- review public health actions already completed, and complete STEC questionnaire if not already done
- review risk assessment: consider the time period since original sample was submitted or disease onset date

For all other cases, there are no further public health actions.

Note 22

Case in risk group B or there is evidence of transmission

If there is evidence of transmission or the case is in risk group B:

- review all public health actions to ensure that they have been completed
- if no evidence of transmission, close case

Note 23

Case not in risk group B and no evidence of transmission

- if there is no evidence of transmission and the case is not in risk group there are no further public health actions
- if the case is in risk group A, C or D, follow guidance in Table 6

Note 24

Serotype has the *stx* subtype *stx2a/2c/2d* (higher risk strain) and the HPT has not begun public health response

For all cases:

- complete the STEC questionnaire
- reinforce hygiene advice verbally and in writing

If there is evidence of transmission:

- exclude case and symptomatic contacts until 48 hours symptom free
- complete risk assessment for case and symptomatic contacts and potential route of transmission
- consider obtaining expert opinion from GBRU, taking into account the risk presented by the serotype, the time period since original sample was submitted or disease onset date, and

risk assessment information for both case and symptomatic contacts to determine if further public health actions are recommended

Note 25

There is evidence of transmission

- exclude case and symptomatic contacts until 48 hours symptom free
- complete risk assessment for case and symptomatic contacts and potential route of transmission
- consider obtaining expert opinion from GBRU, taking into account the risk presented by the serotype, the time period since original sample was submitted/disease onset date, and risk assessment information for both case and symptomatic contacts to determine if further public health actions are recommended

Note 26

Risk group B and no evidence of transmission

- exclude case until 48 hours symptom free
- complete risk assessment for case and contacts and route of transmission
- consider obtaining expert opinion from GBRU, taking into account the risk presented by the serotype, the time period since original sample was submitted or disease onset date, and risk assessment information for both case and symptomatic contacts to determine if further public health actions are recommended

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