Interim Public Health Operational Guidance for Shiga toxin producing *Escherichia coli* (STEC)

Including STEC (O157 and non-O157) infections
Interim Public Health Operational Guidance for STEC

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SUSTAINABLE DEVELOPMENT GOALS
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<th>Public Health Operational Guidelines for Shiga toxin producing <em>Escherichia coli</em> (STEC)</th>
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<td>Recommended by</td>
<td>PHE Gastrointestinal Infections Leads Network</td>
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<td>Endorsed by</td>
<td>PHE Centres Health Protection Network</td>
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<tr>
<td>Approved by</td>
<td>PHE (national body tbc – awaiting approval)</td>
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**CONTACT INFORMATION**

<table>
<thead>
<tr>
<th>Name</th>
<th>Trish Mannes, Public Health England</th>
</tr>
</thead>
<tbody>
<tr>
<td>Email</td>
<td><a href="mailto:Trish.Mannes@phe.gov.uk">Trish.Mannes@phe.gov.uk</a></td>
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</tbody>
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Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>APHA</td>
<td>Animal and Plant Health Agency</td>
</tr>
<tr>
<td>Children aged 5 years old and under</td>
<td>All children up their 6th birthday</td>
</tr>
<tr>
<td>DEFRA</td>
<td>Department for Environment, Food and Rural Affairs</td>
</tr>
<tr>
<td>Diagnostic laboratory</td>
<td>Local hospital or regional laboratory services</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>E. coli</td>
<td>Escherichia coli</td>
</tr>
<tr>
<td>eae</td>
<td>E. coli attachment and effacing (eae) gene</td>
</tr>
<tr>
<td>EAEC</td>
<td>Entero aggregative E. coli</td>
</tr>
<tr>
<td>EH</td>
<td>Environmental Health</td>
</tr>
<tr>
<td>EHO</td>
<td>Environmental Health Officer</td>
</tr>
<tr>
<td>EIA</td>
<td>Enzyme-linked immunoabsorbent assay</td>
</tr>
<tr>
<td>FES</td>
<td>Field Epidemiology Service</td>
</tr>
<tr>
<td>FSA</td>
<td>Food Standards Agency</td>
</tr>
<tr>
<td>FWE</td>
<td>Food, Water and Environmental laboratories</td>
</tr>
<tr>
<td>GBRU</td>
<td>Gastrointestinal Bacteria Reference Unit</td>
</tr>
<tr>
<td>GDW</td>
<td>Gastro Data Warehouse</td>
</tr>
<tr>
<td>GI</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>HPT</td>
<td>Health Protection Team</td>
</tr>
<tr>
<td>HSE</td>
<td>Health and Safety Executive</td>
</tr>
<tr>
<td>HUS</td>
<td>Haemolytic Uraemic Syndrome</td>
</tr>
<tr>
<td>HUSEC</td>
<td>STEC strains that have been frequently reported to cause HUS</td>
</tr>
<tr>
<td>IMT</td>
<td>Incident management team</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Service</td>
</tr>
<tr>
<td>NIS</td>
<td>Public Health England National Infection Service</td>
</tr>
<tr>
<td>NSF</td>
<td>Non-sorbital-fermenting</td>
</tr>
<tr>
<td>OCT</td>
<td>Outbreak control team</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
</tr>
<tr>
<td>PHE</td>
<td>Public Health England</td>
</tr>
<tr>
<td>Reference laboratory</td>
<td>Specialist services as provided by the GBRU</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>RMP</td>
<td>Registered medical practitioner</td>
</tr>
<tr>
<td>STEC</td>
<td>Shiga toxin-producing <em>Escherichia coli</em></td>
</tr>
<tr>
<td>Stx</td>
<td>Shiga toxin</td>
</tr>
<tr>
<td>TMA</td>
<td>Thrombotic microangiopathy</td>
</tr>
<tr>
<td>VTEC</td>
<td>Vero cytotoxin-producing <em>Escherichia coli</em></td>
</tr>
<tr>
<td>WGS</td>
<td>Whole genome sequencing</td>
</tr>
</tbody>
</table>
Definitions used in this guidance

Following the introduction of PCR testing in diagnostic laboratories in recent years, the identification of STEC non-O157 infections has become more frequent. International studies and recent studies from the UK have found that for every one STEC O157 isolated, there are approximately 4-7 non-O157 STEC strains isolated, each possessing a combination of virulence factors (stx1, stx2 and eae) that may give rise to illnesses ranging from mild symptoms to HUS. (For further details, please see ‘Non-O157 STEC Evidence Base June 2018’ and background information Appendix B).

**AggR**

The aggR gene produces a virulence factor, the AggR activator. This factor is normally found in certain pathogenic *E coli* infections referred to as entero aggregative *E. coli* (EAEC). This virulence factor facilitates attachment of the bacteria to the gut, thereby establishing colonisation and infection of the host. When present with stx2a or stx2c or stx2d, there is a strong association with the risk of HUS as observed in a recent outbreak in Germany caused by a hybrid strain belonging to STEC O104:H4. AggR is not routinely reported on GDW and currently the only STEC strain that has been recognised internationally to possess it and to cause serious human illness is the hybrid Enteroadherent hemorrhagic *E. coli* (EAHEC) O104:H4.

**Eae**

The *E. coli* attachment and effacing (eae) gene produces the virulence factor intimin. This virulence factor appears to enhance the delivery of the shiga toxin into the enterocytes via the attachment of the bacteria to the gut, as for AggR above. When present with stx2a or stx2c or stx2d, there is a strong association with the risk of haemorrhagic colitis and HUS.

**Evidence of transmission**

Evidence of transmission may include:

- Symptomatic household/close contacts (including contacts in childcare settings for those aged 5 years old and under) within 7 days before or after the cases’ date of onset, where STEC is the most likely cause of illness
- Positive screening stool sample result for a household/close contact (including contacts in childcare settings for those aged 5 years old and under)

**HUSEC (Haemolytic Uraemic Syndrome Associated E. Coli)**

STEC strains that have been frequently reported to cause HUS. They usually express stx2a, or 2c, or 2d shiga toxin subtypes together with eae or aggR virulence factors. The strains may also possess genes for stx1 subtypes.
Serogroup
Serogroup is the O (lipopolysaccharide) antigen e.g. O157

Serotype
Serotype is the combination of O (lipopolysaccharide) and H (flagella) antigen e.g. O157:H7

Shiga toxin (stx)
stx1 was previously described as VT1 (verotoxin)
stx2 was previously described as VT2 (verotoxin)

Virulence profile
The combination of stx and eae genes detected by GBRU in-house PCR tests is currently the best indicator of the potential virulence of the STEC, and its potential to cause serious illness (e.g. HUS). The majority of strains possessing toxin subtypes stx2a, or 2c, or 2d are also eae positive. There are a small number of isolates that are found to possess stx2a, 2c, 2d subtypes and to be eae negative.

For the purpose of minimising unnecessary public health actions associated with STEC strains that possess the lower risk subtypes (i.e. non stx2a, 2c or 2d), of which the majority do NOT possess the eae gene, the virulence profiles referred to in stages 2 and 3 of the algorithms that follow are defined as below.

<table>
<thead>
<tr>
<th>Virulence Profiles of HUSEC and lower risk STEC strains</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage of algorithm</strong></td>
</tr>
<tr>
<td>Stage 2 GBRU results</td>
</tr>
<tr>
<td>In-house PCR result</td>
</tr>
<tr>
<td>Potential HUSEC</td>
</tr>
<tr>
<td>Lower risk</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage 3 GBRU results</th>
<th>Stx1 subtypes (any)</th>
<th>Stx2 subtypes</th>
<th>eae</th>
<th>AggR</th>
</tr>
</thead>
<tbody>
<tr>
<td>WGS</td>
<td>HUSEC</td>
<td>(+/-)</td>
<td>Stx2a or stx2c or stx2d</td>
<td>(+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(+/-)</td>
<td>Stx2a or stx2c or stx2d</td>
<td>(-)</td>
</tr>
<tr>
<td></td>
<td>Lower risk</td>
<td>(+)</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(+/-)</td>
<td>stx2b or stx2e or stx2f or stx2g</td>
<td>(+/-)</td>
</tr>
</tbody>
</table>

NB It should be noted that ‘lower risk’ does not, however, imply no risk of potential to cause serious illness. Based on current evidence, public health action should be targeted towards those STEC strains with known HUSEC potential.
Introduction

The purpose of this guidance is to provide advice to public health practitioners on the public health management of Shiga toxin-producing *Escherichia coli* (*E. coli*) infections (STEC), also referred to as Verocytotoxin-producing *E. coli* (VTEC).

Diagnostic laboratories are required to notify Public Health England (PHE) Health Protection Teams (HPTs) once identification of *E. coli* STEC has been made, as according to the Health Protection (Notification) Regulations (2010). Similarly, clinically suspected cases of Haemolytic Uraemic Syndrome (HUS) should be urgently notified to HPTs.

In the UK, STEC belonging to serogroup O157 (STEC O157) is the commonest serogroup and the most likely to cause bloody diarrhoea and HUS in the UK. STEC other than serogroup O157 (non-O157 STEC) were historically under-ascertained but are now increasingly recognised for their ability to cause serious illness in infected individuals as well as their potential to cause outbreaks of infection.

This guidance is based on the available evidence for transmission and control of STEC infections and supersedes the 2011 Health Protection Agency VTEC Operational and Support manuals. Clinical management of STEC cases is outside the remit of these guidelines.

### Main recommendations and changes

| Case definitions for public health action | Case definitions for STEC have been amended to reflect an increase in the use of PCR methods for diagnosis of STEC infections |
| Definitions of groups at risk for ongoing transmission of gastrointestinal illness | Risk group definitions have been updated in line with amendments made to risk groups across PHE public health gastrointestinal guidelines |
| Updated (STEC O157) and new (non-O157 STEC) public health actions | Detailed actions have been included based on the available evidence of risk of severe infection and transmission for STEC serotypes, non-O157 serotypes and shiga toxin (stx) subtypes |
| A pragmatic approach to the management of cases and contacts in risk groups A, C and D | Completion of thorough risk assessments to support a pragmatic approach to clearance/screening and exclusion measures for cases and contacts in risk groups other than risk group B is recommended |
| Focus on cases and contacts in risk group B | Exclusion and clearance/screening measures for cases and contacts in risk group B are recommended based on the increased risk of severe infection and potential for onwards transmission amongst this group |
| PCR testing to demonstrate microbiological clearance of non-O157 cases is an acceptable strategy | Where diagnostic labs are using stx PCR methods, two consecutive negative PCR samples can be accepted as demonstration of microbiological clearance of non-O157 STEC infections with no further microbiological testing required |
**PCR screening of contacts of STEC O157 and non-O157 cases is an alternative to culture based methods**

A single negative PCR sample for contacts of O157 and non-O157 cases can be accepted as demonstration of negative screening with no further microbiological testing required.

**Inclusion of risk assessment proforma**

A risk assessment proforma has been included for use by Health Protection Teams to support case and contact management.

**Inclusion of template letters and fact sheets**

Template letters and fact sheets have been included for use by Health Protection Teams to support case and contact management.

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This guidance includes several changes to the public health management of cases and contacts of STEC, as detailed above. For the first time, detailed actions for Health Protection Teams (HPTs) managing cases and contacts of non-O157 are included.

**To capture HPTs experiences of the use of this guidance, please email any questions or queries on its implementation or the document itself to the email address below.** Clinical enquiries relating to the specific management of cases and/or contacts should be directed to local HPT Gastrointestinal (GI) Leads or PHE national services as usual.

An evaluation of the guidance will be conducted by members of the STEC network, on behalf of the PHE GI Leads Network, approximately 6 months after the publication of this document.

**Please email:** stecguidance@phe.gov.uk
Definitions for the public health management of STEC infections

Table 1 Definitions of cases of STEC infection

<table>
<thead>
<tr>
<th>STEC case definition</th>
<th>Clinical features</th>
<th>Epidemiological link to a CONFIRMED case</th>
<th>Laboratory findings</th>
<th>Action required</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONFIRMED (including STEC-related HUS)</td>
<td>Present or absent</td>
<td>Present or absent</td>
<td>GBRU Reference laboratory - positive STEC culture or PCR shiga toxin positive</td>
<td>Initiate or continue public health action (see STEC algorithm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HUS</td>
<td>Present or absent</td>
<td>GBRU Reference laboratory - positive STEC culture or PCR shiga toxin positive or serological confirmation of STEC* OR Diagnostic laboratory – clinical diagnosis AND PCR shiga toxin positive</td>
<td></td>
</tr>
<tr>
<td>PROBABLE</td>
<td>Local O157 culture positive</td>
<td>Present or absent</td>
<td>Present or absent</td>
<td>Diagnostic laboratory – positive culture presumptive STEC O157 regardless of PCR result</td>
</tr>
<tr>
<td></td>
<td>Probable STEC-related HUS</td>
<td>HUS</td>
<td>Present or absent</td>
<td>Awaiting laboratory testing</td>
</tr>
<tr>
<td></td>
<td>Epidemiological link</td>
<td>Acute diarrhoea (may be bloody) or absent</td>
<td>Present</td>
<td>Awaiting laboratory testing OR Diagnostic laboratory – PCR shiga toxin positive</td>
</tr>
<tr>
<td></td>
<td>PCR probable</td>
<td>Bloody diarrhoea or hospitalisation for acute diarrhoea</td>
<td>Absent</td>
<td>Diagnostic laboratory – PCR shiga toxin positive BUT negative culture for STEC O157</td>
</tr>
<tr>
<td>POSSIBLE</td>
<td>Clinical possible</td>
<td>Bloody diarrhoea or hospitalisation for acute diarrhoea</td>
<td>Absent</td>
<td>Awaiting laboratory testing</td>
</tr>
<tr>
<td></td>
<td>PCR possible</td>
<td>Absent</td>
<td>Absent</td>
<td>Diagnostic laboratory – PCR shiga toxin positive BUT negative culture for STEC O157</td>
</tr>
</tbody>
</table>

*Positive serology (O26, O55, O103, O111, O145, O157) + HUS = confirmed case. GBRU have robust validation data for O157 but not for the other serogroups.

The only other scenario that serology might be useful is during an outbreak where there is a strong epidemiological link.
### Table 2 Definitions of contacts of a case of STEC infection

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Household</strong></td>
<td>Someone who lives, or has stayed overnight, in the same household AND/OR ordinarily shared a bathroom/toilet facilities AND/OR ordinarily shared food with the case OR had other significant close contact with the case (e.g. sexual contact) during the infectious period</td>
</tr>
<tr>
<td><strong>Food handling</strong></td>
<td>Someone who has regularly eaten food prepared by the case OR has eaten food prepared by the case on a single occasion during the infectious period if there is concern about hygiene practices of the case OR if the case was symptomatic when preparing the food</td>
</tr>
<tr>
<td><strong>Caring duties</strong></td>
<td>Someone who has been involved in nappy changing or toileting assistance of the case OR who has been involved in close physical care of the case during the infectious period</td>
</tr>
<tr>
<td><strong>Shared exposure</strong></td>
<td>Someone who has been exposed to the suspected/identified source(s) of infection. This may include children who have shared bathroom/toilet facilities with the case AND/OR have had close contact with the case in a childcare setting during the infectious period</td>
</tr>
<tr>
<td>Risk Group</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Group A</strong></td>
<td>Any person who is unable to perform adequate personal hygiene due to their lack of capacity or ability to comply, OR lack of access to hygiene facilities</td>
</tr>
<tr>
<td><strong>Group B</strong></td>
<td>All children aged five years old or under (up to sixth birthday) who attend school, pre-school, nursery or other similar child care or minding groups</td>
</tr>
<tr>
<td><strong>Group C</strong></td>
<td>People whose work involves preparing or serving unwrapped ready to eat food (including drink)</td>
</tr>
<tr>
<td><strong>Group D</strong></td>
<td>Clinical, social care or nursery staff who work with young children, the elderly, or any other particularly vulnerable people, and whose activities increase the risk of transferring infection via the faecal-oral route</td>
</tr>
</tbody>
</table>
Algorithms for the local response to cases of STEC infection

Since 2013, many local NHS laboratories have introduced real-time Polymerase Chain Reaction (RT-PCR) testing kits as a gastrointestinal (GI) screening panel for faecal samples where infectious disease is suspected. These PCR GI 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 various non-O157 STEC serogroups may be identified. Referral of local culture negative samples is especially important for 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.

However, *E. coli* O157 is not grown from the vast majority of stx PCR positive specimens and since local laboratories cannot routinely isolate non-O157 STEC, there is a delay in confirmation with full laboratory results. Serotype and stx subtypes are usually reported by GBRU about 2-3 weeks after the HPT is first informed of the case.

The main aim of the public health response to cases is to prioritise the response to those cases most likely to be infected with viable STEC belonging to non-O157 HUS associated *E. coli* (HUSEC strains). This is likely to represent around 3% of all cases with stx PCR positive results, or 10% of all non-O157 STEC serotypes isolated.

In the interim, 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 when each new piece of information becomes available.
The aim is to provide a proportionate public health response that protects the public’s health whilst taking into consideration the workload implications for HPTs/local authorities, without imposing unnecessary restrictions on individuals.

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

- **Stage 1** - Diagnostic laboratory results (PCR and culture) and clinical history (HUS/bloody diarrhoea)
- **Stage 2** – GBRU in-house PCR results (stx and E. coli attachment and effacing (eae) gene)
- **Stage 3** – GBRU serogroup/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** – full / majority of public health actions recommended
- **Amber** – limited public health actions recommended
- **Green** – warn and inform public health actions only, or no public health actions
- **Blue** – questions for decision making process
- **White** – information only

The algorithms cover HUS and all STEC infections (O157 and non-O157). The STEC O157 public health management is described in the first part of this guidance and you will find references to HUS and O157 results in the algorithm sections that follow. This is to give a complete picture of results that come back to HPTs, but will direct you to the STEC O157 public health management where appropriate.

The algorithms should be used in conjunction with the following sections of this guidance as appropriate:

- **Section 2** - Public health management of STEC O157 (pages 33-38)
- **Section 3** – The principles of the public health management of stx PCR positive results and non-O157 STEC (pages 41-44)
**Stage 1**

**Note 1**

- Local culture *E. coli* O157 positive
- Clinical history of HUS
- Symptomatic contact with epi link to another case with HUS or HUSEC strain including *E. coli* O157

**PH actions:**
- If HUS and stx PCR positive define as CONFIRMED otherwise define as PROBABLE case
- Follow STEC O157 management (Section 2 of guidance)

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

**Note 3**

- Symptomatic contact with epi link to another case with potential HUSEC strain

**PH actions:**
- Define as POSSIBLE case
- Contact guardian by phone
- Give hygiene advice
- Exclude case until 48 hours symptom free
- Ask about potential transmission

- Send PCR letter and leaflet to case with copy to GP

**Case reports bloody diarrhoea or hospitalisation?**

**Note 10**

- Are there Symptomatic Contacts?

**Yes**

- Define as PROBABLE case

**No**

- Wait for GBRU in-house PCR result usually available about 8 days after initial frontline laboratory report to HPT or 11 days after original sample collected

**Go to Stage 2**
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 HUSEC strain (*stx*2a/2c/2d and *eae*/*aggR*)
- 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 HUSEC strain (*stx*2 and *eae*)
- Symptomatic contact with an epidemiological link to another case infected with culture confirmed lower risk STEC strain (non *stx*2a/2c/2d)

For notifications of infective bloody diarrhoea, unless there is a known epidemiological link to a case with HUSEC/potential HUSEC strain 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 *E. coli* O157 positive OR history of HUS

- Define case as PROBABLE
- Full public health actions as per O157 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 HUSEC strain, including O157 (*stx*2a/2c/2d and *eae*/*aggR*)

- Define case as PROBABLE
- Full public health actions as per O157 management for case and contacts are recommended

**Rationale**

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

**Note 3**

Local *stx* PCR positive, local *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.

**Rationale**

*Stx* PCR tests are very sensitive and specific. If positive DNA containing *stx* genetic material is present. The test does not distinguish between viable and dead non-viable organisms or even free *stx*-bacteriophages in the faeces. To date the experience of HPTs regularly receiving these results is that GBRU does not confirm STEC infection in about 30% of specimens. STEC strains are isolated from 40% of specimens and 20% of specimens are *stx* positive but STEC is not recoverable. About 3% of local *stx* PCR positive results are finally confirmed by GBRU as STEC belonging to HUSEC strains other than O157 STEC.

**Note 4**

Symptomatic contact with an epidemiological link to another case with potential HUSEC strain (*stx*2 and *eae* regardless of *stx1*)

- Follow the actions for cases with history of bloody diarrhoea (Note 8)

**Rationale**

The case associated with this symptomatic contact may not subsequently be confirmed by GBRU to be a HUSEC strain. The implementation of pragmatic precautions (exclusion while symptomatic and providing hygiene advice) and the completion of 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 *stx*2a/2c/2d)

- Define case as PROBABLE
  - Arrange diagnostic sample, give hygiene advice, provide PCR letter/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 *E. coli* O157 negative with history of HUS or epidemiological link to case infected with HUSEC strain

- *Stx* PCR positive and HUS, define case as CONFIRMED or
- Epidemiological link, define case as PROBABLE
- Full public health actions as per O157 management for case and contacts are recommended.

**Rationale**

Current case is *stx* PCR positive and is a contact of another case infected with a HUSEC strain. There is evidence of possible transmission. or case of diarrhoea associated HUS (D+ HUS), most cases of D+ HUS are caused by a HUSEC 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 HUSEC 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/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 (Table 6)
- If case is in risk group A-C do not automatically exclude case, carry out risk assessment (Table 6)
- If there are symptomatic contacts arrange single diagnostic sample, give hygiene advice and exclude them until 48 hours symptom free
- 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-D (Table 6)

Rationale

Although the case has bloody diarrhoea, most isolates are NOT subsequently confirmed by GBRU to be viable STEC belonging to HUSEC strains. However bloody diarrhoea is more frequently associated with infection with HUSEC strains. The implementation of pragmatic precautions (exclusion while symptomatic and providing hygiene advice) and the completion of 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 about confirmation of STEC

If local diagnostic laboratories do not routinely send stx PCR positive, local culture *E. coli* O157 negative samples to GBRU, HPTs are advised to agree criteria with local laboratories for sending samples to GBRU for in-house PCR and culture.

Suggested criteria:

- Cases with HUS
- Cases with bloody diarrhoea (with no other obvious cause)
- Cases hospitalised with acute diarrhoeal illness
- Cases aged 5 years and under (up to 6th birthday)
- HPT has information to suggest there is a potential outbreak

Note about hospitalisation

Hospitalisation for acute diarrhoeal illness may be an indicator of illness severity and risk of subsequent development of HUS. However, analysis of local HPT data has not shown that a history of hospitalisation is a reliable indicator of severe STEC infection. Most cases with a history of hospitalisation are admitted for other reasons and developed diarrhoeal symptoms during the admission or were screened as part of *C. difficile* control procedures. Analysis of national data to explore this is in progress.

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/guardian to confirm history and carry out a rapid risk assessment (Appendices II).
- Provide written information to case (or parent/guardian) and copy to the GP (Appendices III and IV)
- No other public health actions recommended at this stage
- Wait for GBRU in-house PCR and culture results

Rationale

There is a large amount of evidence showing that young children are particularly susceptible to acquiring and transmitting STEC infections and that they are also at greater risk of developing severe forms of infection eg 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 HUSEC strain as per Note 8 above.
- If case reports that contacts have been symptomatic:
  - Arrange single diagnostic sample, give hygiene advice and exclude contact until 48 hours symptom free
GBRU in-house PCR result
STEC isolated (STEC PCR+: culture +) OR stx genes detected (STEC PCR+: culture -)

No

Stx2 & eae (positive)

Yes

No

STEC isolated

Yes

HPT has already begun public health actions?

Yes

No

Stage 2

Note 11

1. All cases: reinforce hygiene advice, complete STEC questionnaire if not already done, seek evidence of transmission
2. HUS/probable E. coli O157:
   • All actions as per STEC O157 management (should have been completed/in progress)
3. Bloody diarrhoea:
   • Case in risk group A,C,D initiate clearance samples
4. Risk group B (regardless of bloody diarrhoea):
   • Continue clearance samples and continue exclusion until cleared

No further public health action required with contacts

Review both case and contacts and route of transmission

Wait for GBRU stx subtyping information usually available about 16 days after initial frontline laboratory report to HPT or 21 days after original sample taken

Go to Stage 3
Stage 2

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 HUSEC strains.

GBRU in-house PCR results

At this stage the GBRU in-house PCR results are reported on GDW and include the stx and eae results (Appendix I):

- 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 negative culture indicates that 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. It is important to note that between 30 to 40% of stx PCR positive results are not confirmed by GBRU, which may be due to a variety of reasons which include:
  - 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 actually dilutes the DNA.
  - Pathogens are not evenly distributed throughout a faecal sample.
  - Commercial PCR assays may be more sensitive than the GBRU PCR assay. There has not been a direct comparison of performance.

Note on PCR results

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.

Stx2 positive and eae positive (may also be stx1 positive)

- For all combinations of stx and eae results, change case definition to CONFIRMED.
- If the result is positive for both stx2 and eae regardless of stx1 go to the next question in the algorithm.
- For all other combinations of stx and eae there are no public health actions beyond ensuring case is excluded until 48 hours symptom free.

Note 13

STEC isolated

- If STEC is not isolated there are no public health actions usually recommended beyond ensuring case is excluded until 48 hours symptom free.
- If STEC is isolated the organism is viable and because it possesses genes for stx2a and eae it is also a potential HUSEC strain.
- If the result is positive for both stx2 and eae regardless of stx1 and organism is viable go to the next question in the algorithm.

Note 14

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. Potentially a further incubation period has passed since initial contact with the case.

HUS/probable E. coli O157:

- All actions as per STEC O157 management should have been completed or are in progress, including providing advice and the possible exclusion and screening of contacts (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) (Table 7)
  - symptomatic contacts (Table 7)

Children < 6yrs 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 (Table 6). However if there is evidence of transmission exclude until cleared.

Rationale

The STEC is viable and a potential HUSEC 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 GDW or from initial clinical history the case had been assessed to be low risk:
• Case is defined as CONFIRMED
• Complete the STEC questionnaire if not already done
• Re-inforce hygiene advice that may have been provided to the case in the letter/leaflet
• Assess for evidence of transmission
  o 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
  o if there is evidence of transmission then follow up is recommended.

Rationale
This case is infected with a potential HUSEC strain (serogroup/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

There is evidence of transmission or the case is aged 5 years and under and infected with potential HUSEC strain
• If case is in risk group B carry out risk assessment to determine need for exclusion until clearance has been achieved (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 (Table 6)
• Asymptomatic contacts in risk group B, exclude until the screening has been completed (Table 7)
• Asymptomatic contacts in risk group A,C,D screening not recommended (Table 7)
• Symptomatic contacts
  o manage as a PROBABLE case
  o arrange single diagnostic specimen and exclude until 48 hours symptom free
  o if symptomatic contact is in risk group A-D continue to exclude until the diagnostic/screening result is known (Table 7)

Rationale
Children aged 5 years and under can shed STEC for prolonged periods and onwards transmission is not uncommon and if a case has symptomatic contacts assume that transmission may have occurred.
Stage 3

GBRU WGS result
Note 18
Define as CONFIRMED case

STEC belongs to a HUSEC strain?
Note 19

Has GBRU advised that serotype has other markers eg aggR or is a serotype of concern?
Note 20

HPT has already begun public health actions?
Note 21

Evidence of transmission or case aged 5 years and under?
Note 22

Check that all PH actions have been completed

Update risk assessment

Complete STEC questionnaire
Reinforce hygiene advice

Is there evidence of transmission?
Note 25

Is case aged 5 years and under?
Note 26

Exclude until 48 hours symptom free
Risk assess both case and contacts and route of transmission
Consider seeking expert opinion to decide proportionate screening/clearance AND exclusion strategy

No further PH action required

Prepared by: Kevin Carroll, Lisa Harvey-Vince, Sooria Balasegaram
Updated: 02/03/2018
Stage 3

Note 18
GBRU WGS results
- Define case as CONFIRMED (if case not previously reported)

The stx subtypes stx2a/stx2c/stx2d are strongly associated with risk of HUS, particularly if positive for eae or aggR gene. Currently aggR is not routinely reported on GDW. From the preliminary analysis of the national data, approximately 14% of isolates with stx2a/stx2d are eae negative. The proportion of these that were aggR is not known.

Note 19
Serotype has the stx subtype stx2a/2c/2d (HUSEC strain)
- It is recommended that all isolates with stx2a/2c/2d regardless of eae, should be followed up for public health action.
- GBRU can provide the aggR result on a case by case basis.

Note 20
Serotype has a non HUSEC strain profile
Bacteria are constantly evolving and there have been documented instances when an E. coli strain of low pathogenicity has acquired stx genes eg STEC O26:H11 (stx1a, eae) acquired stx2a genes to become (stx1a, stx2a, eae) which significantly increased pathogenicity or EAEC O104:H4 (aggR) which also acquired stx2a genes and became (stx2a, aggR) causing a Europe wide outbreak with a high proportion of HUS cases in adults.

It is probable that other strains will emerge and GBRU will alert HPTs.

Note 21
Serotype has the stx subtype stx2a/2c/2d (HUSEC strain) and the HPT has commenced public health actions
If the strain has the stx subtype stx2a/2c/2d (HUSEC strain) and the STEC questionnaire has already been completed:
- For cases with HUS / bloody diarrhoea / probable O157 STEC 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. Seek advice from NIS about aggR status and the risk presented by the serotype, consider the time period since original sample was submitted/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,D follow guidance in Table 6

Note 24
Serotype has the stx subtype stx2a/2c/2d (HUSEC 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 NIS 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 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 NIS 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 and symptomatic contacts until 48 hours symptom free
- Complete risk assessment for case and contacts and route of transmission
- Seek advice from NIS taking into account the risk presented by the serotype, the time period since sample was submitted/disease onset date, and risk assessment information for both case and symptomatic contacts; to determine if further public health actions are advisable.
Section 1

General information on the public health management of STEC infections
1.1 Microbiological diagnosis and confirmation

Diagnostic laboratories should investigate all diarrhoeal specimens for the presence of STEC preferably using the procedures recommended in the UK Standards for Microbiology Investigations - Investigation of faecal specimens for enteric pathogens [1].

At present, diagnostic laboratories routinely test for *E. coli* O157, the most common STEC serogroup in the UK [1].

Specific procedures used by local diagnostic laboratories may vary, however most will carry out faecal culture, a morphological identification of *E. coli*, and a slide agglutination (or latex kit) test to identify *E. coli* O157. Diagnostic laboratories should refer samples to the Gastrointestinal Bacteria Reference Unit (GBRU) for further testing and confirmation as follows:

A) Cases of HUS:

- Laboratories using culture based methods for detection of STEC should refer faecal specimens from cases of HUS on the day of receipt to GBRU.
- Laboratories using PCR/enzyme-linked immunoabsorbent assay (EIA) for detection of STEC should refer all positive faecal specimens from cases of HUS urgently to GBRU to optimise isolation (non O157 and O157 STEC), characterisation of virulence and typing.
- Consider sending a serum specimen for detection of antibodies to *E. coli* from the case if culture / PCR results from GBRU are negative.

B) Cases without HUS:

- Presumptive (locally confirmed) isolates of *E. coli* O157 for confirmation of identity, shiga toxin gene detection and serotyping.
- Faecal samples testing positive for *stx* by PCR in local diagnostic laboratories where commercial PCR assays for gastrointestinal infections are used routinely and are culture negative locally for presumptive *E. coli* O157, particularly if the case is aged 5 years old or under or was admitted due to the severity of the diarrhoeal illness.
- Other strains of *E. coli* for confirmation of identity and shiga toxin gene detection if there is a high clinical suspicion of STEC infection.
• Faecal specimens from cases with bloody diarrhoea in whom conventional laboratory testing has failed to yield presumptive *E. coli* O157 or any other pathogen.

• Faecal samples from symptomatic contacts of cases of STEC infection or any STEC outbreak-associated case in whom conventional culture laboratory testing has failed to yield a pathogen. These should be discussed with GBRU prior to submission to ensure there is capacity for testing.

At present, results of GBRU *stx* PCR and culture testing are available approximately 11 days following the collection of the sample. Serotyping information from GBRU is available approximately 21 days after the sample was collected.

Where possible, clearance and screening samples should be submitted to a PHE collaborating laboratory. Where contacts are symptomatic, ensure GPs are informed and an assessment of their clinical condition is completed and samples submitted for diagnosis.

### 1.2 Notification of STEC infections

Diagnostic laboratories should notify PHE HPTs once a presumptive identification of STEC has been made as according to the Health Protection (Notification) Regulations (2010). This should be done verbally within 24 hours and followed up by written notification within 7 days. In order to enable urgent public health actions to be commenced, diagnostic laboratories should notify the local HPT of the following:

• Presumptive (locally confirmed) isolates ([see Appendix B – Microbiological diagnosis](#), p78)

• Detection of *stx* DNA from faeces via PCR methods (*stx* PCR positive)

Local arrangements between HPTs and diagnostic laboratories may be made to modify the notification procedures for *stx* PCR positive results, such as awaiting culture results before notification is made.
Prompt notification of cases of STEC infection is required to facilitate the commencement of public health action to prevent further cases and interrupt transmission. Clinical notification should be made the same day, including out of hours, via telephoning the appropriate HPT.

HPTs may be notified of cases of STEC infection via the following routes:

- Formal notification by a registered medical practitioner (RMP), such as a GP or hospital clinician. Haemolytic Uraemic Syndrome (HUS) and infectious bloody diarrhoea are notifiable by RMPs under the Health Protection (Notification) Regulations 2010
- Laboratory notification of identified organism from a local diagnostic or national reference laboratory

At the time of notification, in addition to the legally required demographic data about the case, the following information if available will assist in guiding public health action:

- Clinical picture – including symptoms (bloody diarrhoea, HUS) and their onset. Hospitalisation may be an indication of illness severity
- Known epidemiological link – this will be particularly important for RMP notifications of infectious bloody diarrhoea to distinguish between possible and probable cases
- Laboratory investigations – results of completed investigations and ensure appropriate testing for STEC infections is underway (including local and reference laboratory testing as appropriate)

The public health management of cases of STEC infection will be guided by whether a case meets the definition of a possible, probable or confirmed case as detailed in Table 1.

### 1.3 General principles of public health management

The following section outlines the general principles of the public health management of STEC infections.
Interim Public Health Operational Guidance for STEC

Enhanced Surveillance Questionnaire

The STEC enhanced surveillance questionnaire should be completed for all relevant cases to obtain a detailed history for the 7 days prior to onset of illness¹

The current version of the questionnaire from the PHE website below should be used:

https://www.gov.uk/government/publications/verocytotoxin-producing-escherichia-coli-questionnaire

The surveillance questionnaire should be completed within 24 hrs of the notification of a probable/confirmed case to the HPT. Completion of the questionnaire by HPTs or Environmental Health Officers (EHOs) will depend on local arrangements. If the case is notified out of hours, as a minimum, a rapid risk assessment by phone is recommended (see Appendix II) and the full questionnaire should be completed on the next working day.

Completed questionnaires should be submitted promptly to national Gastrointestinal teams via secure email to: vtec@phe.gov.uk

Risk assessment

An appropriate risk assessment of cases and their contacts should be conducted depending on the case definition and laboratory results as detailed in Sections 2 and 3 of this guidance. This may be conducted by HPTs or the local Environmental Health (EH) department depending on local arrangements.

An STEC risk assessment proforma may be found in Appendix II of this document. The information that may be required includes:

- Clinical condition including symptoms, symptom onset and duration
- Identify links to known cases, outbreaks or suspected outbreaks
- Determine whether case and/or contacts belong to a group at higher risk for ongoing transmission of gastrointestinal infections (see Table 3)

¹ The incubation period for STEC is usually 2-4 days so obtaining information on potential exposures in the 7 days prior to illness should capture most potential exposures. However, occasional reports of the incubation period being up to 14 days do exist so in some instances the history may be extended up to 14 days at the discretion of the investigating team.
• Establish hygiene standards and facilities which may help support measures to reduce secondary transmission
• Obtain details of contacts for assessment of need for public health action

Control measures

• Provision of information and hygiene advice

Cases should be provided with appropriate information and hygiene advice to prevent the onward transmission of STEC infections.

Written information on STEC can be found on the PHE website:

https://www.gov.uk/government/publications/vero-cytotoxin-producing-escherichia-coli-symptoms-how-to-avoid-how-to-treat

and NHS Choices pages at:

https://www.nhs.uk/conditions/e-coli/

• Exclusion and clearance samples for cases

For probable and confirmed cases, recommendations for exclusion and microbiological clearance should be commenced following completion of the initial risk assessment as according to Algorithms 1-3 of this guidance.

The local authority has statutory powers within the Public Health (Control of Disease) Act 1984 (as amended) [2] and the accompanying Health Protection (Local Authority Powers) Regulations 2010 [3]. Guidance on the use of these provisions has been issued jointly by the HPA (now PHE) and Chartered Institute of Environmental Health (CIEH) and Lewes District Council [4]. Exclusion may be arranged, either by the local authority where the case is resident, or by the local authority where they are in employment.

The schedule of exclusion and clearance for individual cases and/or screening of contacts should be agreed between HPTs and EH departments and should be shared with cases and their families to support any ongoing public health actions required.
Interim Public Health Operational Guidance for STEC

- Contact identification and management
  
  Close contacts of cases may need to be identified and managed as detailed in Algorithms 1-3 and Sections 2 and 3.

Communication

Relevant organisations and/or persons should be advised of probable and confirmed cases of STEC infection to support prevention and control measures. These may include the following:

- General Practitioners (GPs)
  
  If not already aware of the diagnosis, GPs of probable and confirmed cases should be advised of the suspected/confirmed diagnosis of STEC infection as detailed in Algorithms 1-3 and Sections 2 and 3. They may be provided with information on STEC infection, including guidance for exclusion and microbiological testing.

  The use of antibiotics and antidiarrheal medications is not generally recommended in the management of STEC infection due to an increased risk of HUS.

  Specific guidance relating to the management of acute bloody diarrhoea in children is available and GPs should be reminded to seek specialist support for any child presenting with a single acute episode of bloody diarrhoea. Guidance is available via the PHE website:
  

- Environmental Health (EH) Departments
  
  Local EH teams should be advised of probable and confirmed STEC cases as detailed in Algorithms 1-3 and Sections 2 and 3.

  Risk assessments, microbiological clearance and screening samples and investigations of potential sources of exposure should be conducted according to local agreements. Local authorities, rather than PHE, have the legal powers for exclusion.
• Local Authority Public Health teams
  Reporting arrangements to Local Authority Public Health teams should be agreed locally. These may include notification of cases in school or childcare settings or suspected or known clusters or outbreaks.

• PHE services
  Other local HPTs should be informed of any potential exposures or links to cases in other areas for local risk assessment and management.
  National Infection Services teams should be advised of probable and confirmed cases as detailed in Algorithms 1-3 and Sections 2 and 3 for the purposes of surveillance and further investigation and management as needed.

• Media
  Communications departments should be notified according to local agreements. These may include PHE, Local Authority and local NHS services communications teams. This may be especially relevant if there are particular features about the case that may attract attention such as severe illness or death, association with other cases or potential exposures or socially sensitive settings such as nurseries or schools.
Section 2
Public health management of STEC O157
2.1 Public health management of POSSIBLE cases (O157)

Cases may be defined as possible depending on their clinical, epidemiological and laboratory findings, as defined in Table 1 (page 11).

Table 4 – Public health management of POSSIBLE cases

<table>
<thead>
<tr>
<th>Clinical possible case</th>
<th>Public Health action</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diagnostic laboratories should initiate/complete diagnostic testing, notify HPT if presumptive O157 and ensure samples/isolates are sent to the GBRU as appropriate</td>
</tr>
<tr>
<td></td>
<td>Clinician to advise exclusion until 48 hours symptom free</td>
</tr>
<tr>
<td></td>
<td>No further public health action is required until results of microbiological testing are available</td>
</tr>
</tbody>
</table>

2.2 Public health management of PROBABLE and CONFIRMED cases (O157)

Cases may be defined as probable or confirmed depending on their clinical, epidemiological and laboratory findings, as defined in Table 1 (page 11).

Table 5 – Public health management of PROBABLE and CONFIRMED cases

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Public Health action</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROBABLE</td>
<td>FULL PUBLIC HEALTH ACTION</td>
</tr>
<tr>
<td>• Local O157 culture positive</td>
<td>Commence action on day of notification</td>
</tr>
<tr>
<td>• Probable HUS</td>
<td>Complete STEC <em>E. coli</em> enhanced surveillance questionnaire</td>
</tr>
<tr>
<td>• Epidemiological link</td>
<td>Ensure diagnostic laboratory initiates/completes diagnostic testing (see Section 1) and samples are sent to the GBRU as appropriate</td>
</tr>
<tr>
<td>CONFIRMED</td>
<td>Control measures</td>
</tr>
<tr>
<td>• All cases with positive culture for STEC O157</td>
<td>Provide information and hygiene advice</td>
</tr>
<tr>
<td>• STEC-related HUS</td>
<td>Advise exclusion and clearance samples for case according to risk group</td>
</tr>
<tr>
<td></td>
<td>Risk assess potential source(s) and consider further control measures as appropriate</td>
</tr>
<tr>
<td></td>
<td>Identify and risk assess contacts for exclusion and/or microbiological screening</td>
</tr>
<tr>
<td></td>
<td>Communication with relevant organisations/ person(s)</td>
</tr>
<tr>
<td></td>
<td>Including Environmental Health Officers (EHOs), GPs, child care settings and others</td>
</tr>
</tbody>
</table>
2.2.1 Exclusion and clearance of PROBABLE/ CONFIRMED cases (O157)

See Table 3 (page 13) Groups at risk for ongoing transmission of gastrointestinal (GI) illness

Exclusion and microbiological clearance is recommended for probable and confirmed STEC O157 infections, in accordance with recommendations and Algorithms 1-3 of these guidelines.

### Demonstration of microbiological clearance (cases)

Cases may be considered to have demonstrated microbiological clearance via the following **diagnostic laboratory methods:**

- Where the diagnostic laboratory uses stx PCR, clearance may be conducted via PCR methods.
  - If the case is found to be stx PCR negative on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required.
  - If the case is found to be stx PCR positive, local culture should be conducted and if negative for STEC O157 on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required.

- Where the diagnostic laboratory does not use PCR testing, clearance should be conducted via culture methods.
  - If the case is found to be culture negative for STEC O157 on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required.
Table 6 – Exclusion and microbiological clearance for **CASES** of STEC O157 infection, also applicable to non-O157 HUSEC strains *(see accompanying Notes below table)*

<table>
<thead>
<tr>
<th>RISK GROUP</th>
<th>SYMPTOMATIC</th>
<th>RECOVERED* OR ASYMPTOMATIC</th>
</tr>
</thead>
</table>
| Case NOT in a risk group | • Provide personal hygiene advice  
• Exclude until 48 hours symptom free  
• No microbiological clearance required | • No exclusion or microbiological clearance required |
| Case in risk group A, C or D | • Provide personal hygiene advice  
• Exclude until microbiological clearance completed  
• Arrange microbiological clearance  
  • 2 consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours | • Provide personal hygiene advice  
• Exclude and arrange microbiological clearance  
  • 2 consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours  
• Review risk assessment to determine whether restriction/redeployment may be appropriate whilst awaiting results of microbiological testing*²  
• If not appropriate, exclude case until microbiological clearance completed |
| Case in risk group B | • Provide personal hygiene advice  
• Exclude until microbiological clearance completed  
• Arrange microbiological clearance  
  • 2 consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours | • Provide personal hygiene advice  
• Exclude until microbiological clearance completed  
• Arrange microbiological clearance  
  • 2 consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours  
• Review risk assessment to determine whether a supervised return to childcare settings may be appropriate whilst waiting for results*³ |
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**NOTES- Table 6 Exclusion and microbiological clearance of cases of STEC**

1. **Recovered** – A person who has experienced symptoms consistent with STEC infection but for whom it has been at least 48 hours since symptoms resolved.

2. Results of the local risk assessment may determine whether restriction/redeployment within occupational settings is appropriate for cases in risk groups A, C and D whilst awaiting microbiological clearance. This may be guided by the duration and nature of symptoms, evidence of secondary transmission and an assessment of personal hygiene standards and facilities. This may include, for example, restriction of duties to exclude food handling or preparation or assistance with toileting of children but may facilitate redeployment to other duties. Such decisions should be made by HPTs in conjunction with relevant organisations, such as EH departments and following thorough discussion with the case and their responsible line manager. All cases should be excluded from all duties until symptom free for \( \geq 48 \) hours. Risk assessments should be regularly reviewed.

3. Children aged 5 years old and under may experience prolonged shedding of STEC however the evidence to support exclusion of recovered/asymptomatic prolonged shredders is limited and prolonged exclusion can cause significant disruption and burden to families. Results of the local risk assessment, including evidence of secondary transmission, age of the child, an assessment of personal hygiene standards and facilities to provide supervised toileting and handwashing in childcare settings may be used to determine whether a supervised return to a childcare setting whilst awaiting microbiological clearance is appropriate. Such decisions should be made by HPTs in conjunction with relevant organisations, such as EH departments and following thorough discussion with parents/guardians and childcare managers to ensure the public health benefit of continued exclusion is balanced against any potential harm from prolonged periods of exclusion. Risk assessments should be regularly reviewed.
2.3 Public health management of CONTACTS (O157)

See Table 2 (page 12) Definitions of contacts of a case of STEC infection
See Table 3 (page 13) Groups at risk for ongoing transmission of gastrointestinal (GI) illness

Exclusion and microbiological screening may be required for contacts of probable and confirmed STEC infections. This should be based on the findings of the initial risk assessment following notification of a probable or confirmed case and results of microbiological investigations.

The specific recommendations for exclusion and screening for contacts of cases are based on the available evidence of secondary transmission, carriage, groups at risk of severe disease and outbreak potential.

**Demonstration of microbiological screening (contacts)**
Contacts may be considered to have demonstrated microbiological screening via the following **diagnostic laboratory methods**:

- Where the diagnostic laboratory uses PCR for stx gene detection, screening may be conducted via PCR methods.
  - PCR is considered to have very high sensitivity. If the contact is found to be PCR negative on a single sample, no further microbiological testing is required.
  - If the contact is found to be PCR positive, local culture should be conducted and any isolate should be submitted to GBRU for further testing.
  - If local culture is negative, it is probable that the contact was infected but that the STEC is no longer viable or is present in very low numbers. HPTs may wish to discuss further testing with GBRU.

- Where the diagnostic laboratory does not use PCR testing, screening should be conducted via culture methods
  - If the contact is found to be culture negative for STEC O157 on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required.
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Table 7 - Exclusion and microbiological screening for CONTACTS of probable/confirmed cases of STEC O157 infection, also applicable to non-O157 HUSEC strains (see accompanying Notes below table)

<table>
<thead>
<tr>
<th>RISK GROUP</th>
<th>SYMPTOMATIC</th>
<th>RECOVERED(^*1) OR ASYMPTOMATIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact NOT in a risk group</td>
<td>• Provide personal hygiene advice&lt;br&gt;• Manage as a probable case</td>
<td>• No public health action required(^*2)</td>
</tr>
<tr>
<td>Contact in risk group A, C or D</td>
<td>• Provide personal hygiene advice&lt;br&gt;• Manage as a probable case</td>
<td>• Provide personal hygiene advice&lt;br&gt;• Exclusion and microbiological clearance are not routinely recommended(^*2)</td>
</tr>
<tr>
<td>Contact in risk group B</td>
<td>• Provide personal hygiene advice&lt;br&gt;• Manage as a probable case</td>
<td>• Provide personal hygiene advice&lt;br&gt;• Exclude and undertake microbiological screening(^*3) for STEC infection&lt;br&gt;• 2 consecutive negative faecal samples taken (\geq 24) hours apart&lt;br&gt;AND&lt;br&gt;Undertake a risk assessment to determine if a return to school/other childcare setting is possible whilst waiting for results. This may include:&lt;br&gt;• Reinforcing supervised hand washing by childcare staff&lt;br&gt;• Where there is no ongoing contact with the index case&lt;br&gt;Where contact with the index case is restricted and good personal hygiene can be maintained by the case (e.g. separate bathroom/toilet facilities, no food preparation/handling by the index case)</td>
</tr>
</tbody>
</table>
NOTES: Table 7 Exclusion and microbiological screening of CONTACTS of cases of STEC

*1 Recovered – A person who has experienced symptoms consistent with STEC infection but for whom it has been at least 48 hours since symptoms resolved

*2 Unless in an outbreak setting to aid epidemiological investigations, in which case, consider microbiological screening of individuals. In addition, those in risk group A who are unable to perform adequate personal hygiene, a risk assessment should be completed to assess the need for exclusion and/or microbiological screening.

*3 Microbiological screening of contacts should commence once the index case is symptom free. In instances where contacts do not have ongoing contact with the index case, screening may commence immediately. For cases with ongoing symptoms or prolonged excretion of STEC, a risk assessment may be conducted to agree the timing of when to commence contact screening as there may be continued exposure within the setting. This will involve assessment of likely compliance with personal hygiene measures and infection control in the home, access to use of separate bathroom/toilet facilities and restricting involvement in food preparation/handling by the index case. For contacts in risk group B (particularly where the case is also in risk group B), minimising the risk of transmission is challenging. Stringent personal hygiene and infection control should be in place for all cases and contacts in these risk groups including the supervision of their toileting and hand hygiene. Where there is continual contact between cases and contacts in risk group B, the screening of contacts should not start until the case has been symptom free for at least 48 hours. Should the case become symptomatic again before their clearance has been completed, then risk group B contact screening will need to recommence once the case has become symptom free again for at least 48 hours.
Section 3

Principles of public health management of stx PCR results and non-O157 STEC
3.1 The aims of public health management of cases that are \textit{stx} PCR positive

There is consensus that HPTs should target their public health actions to cases from whom STEC organisms have been isolated and also belong to HUSEC strains.

If the samples from a case are negative for STEC or confirmed by PCR only, it is reasonable to assume that the case is no longer infectious and unlikely to transmit the infection because the STEC is non-viable or present in very low numbers that are below the level of detection. This pragmatic approach means that only about 30\% of \textit{stx} PCR positive reports will require public health action when all microbiological tests have been completed. However it does presume that as well as notifying the local HPTs, the local hospital laboratories submit samples that are \textit{stx} PCR positive to GBRU for confirmation, at least for cases with HUS, bloody diarrhoea or who are 5 years of age and under.

If local diagnostic laboratories \textbf{do not} routinely send \textit{stx} PCR positive, local culture STEC O157 negative samples to GBRU, HPTs are advised to agree criteria with local laboratories for sending samples to GBRU for in-house PCR and culture.

\textbf{Suggested criteria:}

- Cases with HUS
- Cases with bloody diarrhoea (with no other obvious cause)
- Cases hospitalised with acute diarrhoeal illness
- Cases aged 5 years and under (up to their 6\textsuperscript{th} birthday)
- HPT has information to suggest there is evidence of transmission or a potential outbreak

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 \textit{stx} PCR positive result, local hospital laboratories can proceed to isolate and test for \textit{E. coli} O157. HPTs will usually receive reports of presumptive \textit{E. coli} O157 infections within 3 days of specimen collection. The public health response can be commenced quickly and the majority of isolates will be confirmed by GBRU to be STEC O157.
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However *E. coli* O157 is not isolated from the vast majority of *stx* PCR positive specimens. Local hospital laboratories cannot routinely isolate non-O157 STEC hence there will be a delay in getting confirmation. The main aim of the public health response to these cases is to prioritise the response to those that are most likely to be infected with viable STEC belonging to HUSEC strains. This is likely to represent about 3% of the cases reported. Another important aim of the response is to minimise unnecessary public health actions including microbiological clearance, screening of contacts and exclusion which can impose a considerable burden, including financial, on the cases and their households.

Bloody diarrhoea (haemorrhagic colitis), HUS and possibly admission due to acute diarrhoeal illness are predictors of STEC infections caused by HUSEC strains including O157. Children aged 5 years and under are the most vulnerable age group to severe illness and are most likely to acquire and transmit the infection. However, studies performed by local HPTs have shown that although bloody diarrhoea may be a predictor of HUSEC infections, HUSEC strains are not isolated from the majority of *stx* positive specimens obtained from cases presenting with bloody diarrhoea. In a modelling of different options, bloody diarrhoea/HUS or age 5 years old and under remain the best predictors of infection with STEC belonging to HUSEC strains.

HPTs should review the available clinical information for cases that are *stx* PCR positive. This may be obtained from a variety of sources depending upon local arrangements, such as via telephone notification, laboratory request forms, the referring clinician or parents of children aged 5 years old and under.
3.2 Public health management of POSSIBLE cases (stx PCR positive)

Cases may be defined as possible depending on their clinical, epidemiological and laboratory findings, as defined in Table 1 (page 11).

Table 8 – Public health management of POSSIBLE cases

<table>
<thead>
<tr>
<th>Stx PCR possible case</th>
<th>Public Health action</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diagnostic laboratories should initiate/complete diagnostic testing, notify HPT if stx PCR positive and culture negative for O157 and ensure samples/isolates are sent to the GBRU as appropriate</td>
</tr>
<tr>
<td></td>
<td>Clinician to advise exclusion until 48 hours symptom free</td>
</tr>
<tr>
<td></td>
<td>HPTs to review clinical history. Send written information to all cases and to contact parent/guardian if the case is a child aged 5 years old and under. No further public health action is recommended until the results of further microbiological testing are available.</td>
</tr>
</tbody>
</table>

3.3 Public health management of PROBABLE and CONFIRMED cases and their contacts

The practical management of probable and confirmed cases is essentially the same for all HUSEC including STEC O157 and the advice in Tables 5-7 should be followed for cases and contacts. However because confirmation of the HUSEC strain depends on the final stx subtyping results from WGS, the risk assessment and thus the response should be reviewed with each new result. For the majority of cases from whom lower risk strains are isolated, microbiological clearance and screening of contacts is not necessary.

Microbiological clearance and screening regimes for non-O157 HUSEC strains are also different to those for STEC O157 because most local hospital laboratories cannot routinely isolate non-O157 STEC organisms.
**Demonstration of microbiological clearance (cases) non-O157 STEC**

Cases may be considered to have demonstrated microbiological clearance via the following **diagnostic laboratory methods**:

- Where the diagnostic laboratory uses stx PCR, clearance may be conducted via PCR methods.
  - If the case is found to be stx PCR negative on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required
  - If the case is found to be stx PCR positive two approaches are possible:
    - Continue stx PCR testing at locally agreed intervals until 2 consecutive samples are PCR negative. If PCR remains positive after 4 weeks of testing, consider sending a faecal sample to GBRU to see if STEC can still be isolated
    - OR submit faecal specimens to GBRU and if the case is found to be culture negative for non-O157 STEC on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required
- Where the diagnostic laboratory does not use stx PCR testing, clearance should be conducted via culture methods
  - Samples should be submitted to GBRU and if the case is found to be culture negative for non-O157 STEC on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required

**Demonstration of microbiological screening (contacts) non-O157 STEC**

Contacts may be considered to have demonstrated microbiological screening via the following **diagnostic laboratory methods**:

- Where the diagnostic laboratory uses PCR for stx gene detection, screening may be conducted via PCR methods
  - PCR is very sensitive. If the contact is found to be PCR negative on a single sample, no further microbiological testing is required
  - If the contact is found to be PCR positive, local culture should be conducted and if negative for O157, the faecal sample should be submitted to GBRU for further testing.
- Where the diagnostic laboratory does not use PCR testing, screening should be conducted via culture methods at GBRU.
  - If the contact is found to be culture negative for non-O157 STEC on 2 consecutive samples taken at least 24 hours apart submitted to GBRU, no further microbiological testing is required.
Section 4
Outbreaks and clusters
4.1 Management of outbreaks and clusters

Outbreaks of STEC should be managed in accordance with agreed national and local Outbreak Plans and Memorandums of Understanding. The PHE national outbreak plan can be found at: https://www.gov.uk/government/publications/communicable-disease-outbreak-management-operational-guidance

Suspected clusters or outbreaks should be notified promptly to the relevant FES team, national GI team, and partner organisations such as local NHS, EH departments and Local Authority Public Health teams. If potential exposures may have occurred in another HPT catchment, the relevant HPTs should be notified promptly.

HPTs and relevant partners should maintain a low threshold for establishing an Outbreak Control Team (OCT) or Incident Management Team (IMT) if a cluster or outbreak is suspected to facilitate identification and control of potential sources and implement control measures to prevent onward transmission.

Food and water contamination are well recognised and documented sources of STEC outbreaks. Special consideration may be required for outbreaks in settings where behaviour may increase the risk of spread of infection, and/or the risk of severe infection in risk groups is increased.

4.1.1 Outbreaks associated with open farms

HPTs may consider the following when investigating and managing linked cases associated with an open farm:

- Key partners may include the Local Authority Environmental Health teams, HSE, DEFRA, APHA, FSA and other PHE divisions (such as Regional Microbiology, FES, GBRU, FWE) and Communications teams
- HPTs/Outbreak Control Teams (OCT) should work with enforcement agencies to facilitate business owners to protect the public’s health and reduce onward transmission amongst visitors and staff
- Restriction of public access to animals, animal faecal matter and surfaces contaminated with animal faecal matter should be considered, including the potential for farm closure
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- Sampling of potential sources may include animal faeces, manure, animal contact surfaces, water (particularly if there is potential for livestock contamination of private water supplies), fore-stream milk, primary filters or washings and raw milk on dairy farms where raw milk may have been consumed

- Business operators should be directed to Access to Farms Partnership Industry Code of Practice on Preventing or Controlling Ill health from Animal Contact at Visitor Attractions[5] which is available at: http://www.visitmyfarm.org/component/k2/339-industry-code-of-practice and includes advice on:
  - Premises layout and routes
  - Animal contact areas and livestock management
  - Eating areas
  - Play areas
  - Washing facilities
  - Visitor information and signage
  - Staff training and visitor supervision
  - Manure and compost heaps

- Information on avoiding ill health when visiting open farms should be accessible to all visitors. An information leaflet Avoiding infection on farm visits – advice for the public is available at: https://www.gov.uk/government/publications/farm-visits-avoiding-infection

4.1.2 Outbreaks associated with nurseries, primary schools and other childcare settings

HPTs may consider the following when investigating and managing linked cases associated with a nursery/primary school or other childcare setting:

- Work with enforcement agencies to facilitate early engagement with the manager/Head Teacher, key staff and parents which is important in ensuring cooperation and managing concern

- Other key partners may include the Local Authority (particularly the Education and Early Years teams and Environmental Health teams), other PHE divisions (such as Regional Microbiology, FES and GBRU) and Communications teams. Local Primary Care and Acute
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NHS Trust teams may also be included due to the increased risk of severe infection in younger children attending these settings

- Links between children and/or staff *within and outside* the institution should be investigated to develop hypotheses about the source of infection (e.g. common toileting facilities, common food source, school trips, after school clubs, social networks etc.). Mixing patterns, sharing of toys/play areas and the physical layout of the institution should also be assessed to determine potential routes for person-to-person transmission

- Cases and contacts in risk group B (children aged 5 years old and under attending childcare settings) should be excluded and microbiological testing and/or screening arranged as detailed in Sections 2 and 3 of this guidance. Additional testing and exclusion of older children and staff members will be determined by the OCT but may be implemented if a risk assessment suggests risk of ongoing environmental or person-to-person transmission

- Closure of all or part of the institution may be recommended by the OCT

- Information on hygiene measures within the institution and within the home should be provided to staff and parents to reduce onward transmission

- Communications should be agreed to provide advice and minimise concern amongst parents/families. This may be of particular importance in situations where children experience prolonged shedding STEC, requiring an extended period of exclusion from the childcare setting
Appendix A

Supporting documents
## Appendix I - Table of GBRU in-house PCR results

### GBRU - STEC isolated (STEC PCR:+ culture:+)

<table>
<thead>
<tr>
<th>Receipt date</th>
<th>Sample date</th>
<th>Report date</th>
<th>Foreign travel</th>
<th>Organism identified</th>
<th>Sero type</th>
<th>Phage Type</th>
<th>Clonal Complex</th>
<th>ST</th>
<th>EAE</th>
<th>STX1</th>
<th>STX2</th>
<th>STX subtype</th>
<th>SNP address</th>
</tr>
</thead>
<tbody>
<tr>
<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
<td></td>
<td>STEC isolated</td>
<td>STX genes detected (STEC PCR:+ culture:+)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>yyyy-mm-dd</td>
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<td>yyyy-mm-dd</td>
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<td>STEC isolated</td>
<td>STX genes detected (STEC PCR:+ culture:+)</td>
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<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
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<td>STEC isolated</td>
<td>STX genes detected (STEC PCR:+ culture:+)</td>
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<tr>
<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
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<td>STEC isolated</td>
<td>STX genes detected (STEC PCR:+ culture:+)</td>
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<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
<td></td>
<td>STEC isolated</td>
<td>STX genes detected (STEC PCR:+ culture:+)</td>
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<td>+</td>
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<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
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<td>STEC isolated</td>
<td>STX genes detected (STEC PCR:+ culture:+)</td>
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<td>+</td>
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</tr>
</tbody>
</table>

### GBRU - STX genes detected (STEC PCR:+ culture:-)

<table>
<thead>
<tr>
<th>Receipt date</th>
<th>Sample date</th>
<th>Report date</th>
<th>Foreign travel</th>
<th>Organism identified</th>
<th>Sero type</th>
<th>Phage Type</th>
<th>Clonal Complex</th>
<th>ST</th>
<th>EAE</th>
<th>STX1</th>
<th>STX2</th>
<th>STX subtype</th>
<th>SNP address</th>
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<tbody>
<tr>
<td>yyyy-mm-dd</td>
<td>yyyy-mm-dd</td>
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<td></td>
<td>STX genes detected</td>
<td>STX genes detected (STEC PCR:+ culture:-)</td>
<td>+</td>
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<td>-</td>
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<td>STX genes detected</td>
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<td>STX genes detected</td>
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</tbody>
</table>

51
## GBRU - STEC NOT isolated (STEC PCR:- culture:-)

<table>
<thead>
<tr>
<th>Receipt date</th>
<th>Sample date</th>
<th>Report date</th>
<th>Foreign travel</th>
<th>Organism identified</th>
<th>Sero type</th>
<th>Phage Type</th>
<th>Clonal Complex</th>
<th>ST</th>
<th>EAE</th>
<th>VT1</th>
<th>VT2</th>
<th>STX subtype</th>
<th>SNP address</th>
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<tr>
<td>yyyy-mm-dd</td>
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## GBRU - serogroup/serotype result

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<th>Report date</th>
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<th>Organism identified</th>
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<th>Phage Type</th>
<th>Clonal Complex</th>
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<th>EAE</th>
<th>STX1</th>
<th>STX2</th>
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<td>O26:H11</td>
<td>CC21</td>
<td>29</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<td>2a</td>
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## Appendix II - STEC risk assessment proforma

<table>
<thead>
<tr>
<th>Case name</th>
<th>HPZ No:</th>
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### Clinical Picture

Date of onset, symptoms (bloody diarrhoea), Date symptoms ceased or ongoing

### Key risks

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<th>CASE (Risk Group)</th>
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<tr>
<td>A. Doubtful hygiene</td>
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<tr>
<td>B. Children 5yrs and under</td>
<td>B. Children 5yrs and under</td>
<td>2</td>
</tr>
<tr>
<td>C. Food handler</td>
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</tr>
<tr>
<td>D. Direct patient contact</td>
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<tr>
<th>Employer / school / nursery</th>
<th>General hygiene standards, awareness etc.</th>
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### Hygiene Standards / Considerations

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<th>Activities attending</th>
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<table>
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<tr>
<th>If Child – nappies / toilet trained</th>
<th>Result of EH assessment (where undertaken)</th>
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### Decision

Rational for decision / who involved in decision

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<th>Assessor name</th>
<th>Signature</th>
<th>Date</th>
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Appendix III - Non-O157 STEC - PCR letter

Date

Our ref: HPZ

Private and confidential

Patient Address

Dear,

Re: Recent laboratory result on your poo sample

The Public Health England (PHE), Health Protection team for [insert name of HPT] has been informed by the local laboratory that the results on a poo sample that [you/your child] submitted may be positive for bacteria called Shiga toxin-producing *Escherichia coli* (STEC).

STEC is a notifiable disease. Clinicians and laboratories are required to report any illness where the suspected cause is STEC to Public Health England. Our role is to try and identify the source if possible and give advice to help prevent the spread of infection to other people.

The sample may have been sent to the PHE reference laboratory in London for further testing. If this was done the results should be available in several weeks and will be sent to the doctor who requested the sample.

In the meantime, please telephone us on [Insert HPT name and contact number] if:

- Your symptoms included bloody diarrhoea
  OR
- You attended hospital for your acute diarrhoeal illness
  OR
- Any other member of your household has experienced similar symptoms either 7 days before or 7 days after yours started

This will help us to gather more information on your illness and provide any relevant further advice.

Please read the accompanying leaflet which provides information about STEC and what actions you should now take, including information on how to prevent the spread of infection.

Kind regards,

Copy: Doctor
Appendix IV – Non-O157 STEC PCR leaflet

Shiga toxin-producing Escherichia coli non-O157 STEC PCR

An information leaflet for cases

Hearing from Public Health England

The Public Health England (PHE) local Health Protection Team is contacting you because the result of the poo sample submitted by you or your child is positive for a bacterium called Shiga toxin-producing *Escherichia coli* (STEC), previously known as VTEC.

The local laboratory test has detected genetic material (DNA) of STEC bacteria, and has confirmed that you are unlikely to have STEC O157, the most common strain of STEC in the UK which often causes more serious illness. It is likely that your infection is caused by another strain of STEC that usually causes mild illness.

Many NHS laboratories send samples to the PHE reference laboratory in London for further tests to identify the exact strain. If further testing has been done, then in a few weeks the result will be sent to the doctor who arranged for your sample; and the Health Protection team or Environmental Health team may contact you for further information.

In the meantime, because some strains can cause serious illness and can be passed from person to person, we are contacting you to:

- Identify potential sources of the infection
- Provide some information on the infection and how you can prevent the spread of infection to others

Next steps

Please read the leaflet. If you have any concerns or questions that are not answered after reading the rest of this leaflet please contact your local Health Protection Team

Symptoms

Most people get better within 5 to 7 days. Treatment involves drinking plenty of fluids as vomiting and diarrhoea can lead to dehydration. Antibiotics should not be used as there is no evidence that they are helpful to treat STEC infections and they may increase the risk of complications.

Rarely, symptoms may be severe or even life-threatening causing Haemolytic Uraemic Syndrome (HUS) which may occur up to 2 weeks after the start of the diarrhoea. If your symptoms do not go away or you develop easy bruising, feel you are passing less urine than usual or your urine is pink/brown in colour please urgently seek medical advice as these symptoms could indicate the start of HUS and you may need further tests.
**Staying away from work or school/nursery**

You should stay away from work/school or nursery until you have stopped having symptoms for **at least 48 hours** to avoid passing it on to others.

For some people, this time may be longer and further samples may be needed because of the higher chance of spreading the infection to others or spreading it to people who may be more likely to develop severe illness. This may include:

- Those that need help with their own personal hygiene at home, work or school
- Children aged 5 years and under, particularly those attending nursery or pre-school groups
- Those that prepare or serve unwrapped food that is not heated further
- Healthcare workers with direct contact with highly susceptible patients for whom an infection like STEC could have serious consequences

**Children aged 5 years and under (upto sixth birthday)**

Although rare, the risk of HUS is highest in children aged 5 years and under. Some children aged 5 years and under have also been shown to continue to pass STEC in their poo for longer than adults, sometimes for many weeks or even months.

For these reasons, children aged 5 years and under may need to stay away (be excluded) from childcare settings until their poo samples are clear of the infection. If there are other children aged 5 years and under in the household, they may also be excluded, whether they have symptoms or not, until poo samples show that they have not picked up the infection.

Your local PHE Health Protection or Environmental Health Officers will be in contact to advise you if exclusion is needed for you and/or your contacts. They will provide you with information on this clearance process and aim to support you to get you or your child back to normal activities as quickly as possible.

**Please read the rest of this leaflet and in particular follow the advice on ‘How can I prevent others from becoming ill?’ to minimise passing the infection on to others.**

**General information on STEC?**

**STEC (Shiga toxin-producing Escherichia coli)**

STEC (Shiga toxin-producing *Escherichia coli*) can cause illness ranging from mild diarrhoea to life threatening conditions. STEC O157 is the most common type in the UK and in a small number of people can cause very serious illness called Haemolytic Uraemic Syndrome (HUS). The risk of HUS is highest in children aged 5 years and under.
Interim Public Health Operational Guidance for STEC

We know that STEC is very infectious and can be easily passed to others. It has also been the cause of several outbreaks following eating infected food, contact with infected people and touching infected animals or their poo.

In some European countries, other types of STEC are the cause of serious illness and outbreaks.

**Becoming infected**

You may become infected with STEC in a variety of ways:

- **Eating infected/contaminated food** that has not been cooked all the way through, particularly minced meat products such as burgers and sausages, or salad items that have not been washed properly
- **Handling/preparation of food contaminated with soil** for example, potatoes and leeks where the soil has not been washed away
- **Drinking infected/contaminated water** such as from streams, rivers and lakes etc. which may contain animal poo
- **Close contact with animals**, particularly cattle, sheep and goats. Animal saliva may be infected because of the way animals clean themselves
- **Direct contact with animal poo** on the animal itself, in their pen or on the floor
- **Contact with an infected person**, particularly if you don't wash your hands thoroughly after using the toilet or before handling food

**Symptoms**

It usually takes between 2 and 4 days from being infected with STEC to develop symptoms which may be:

- No symptoms
- Very mild diarrhea
- Stomach pain
- Vomiting
- Fever
- Severe diarrhea with blood
- Passing less urine than normal
- Haemolytic uraemic syndrome (HUS)

**Preventing others from becoming ill**

Normal cooking temperatures kill STEC and it can be easily washed off your hands. For extra reassurance, you can use antibacterial gels/wipes AFTER washing your hands with soap and water.
Interim Public Health Operational Guidance for STEC

Important steps you can take include:

- **Wash hands thoroughly** with liquid soap and running water after using the toilet (or helping others including changing nappies), handling raw meat, before meals and after contact with animals. If you have false nails, pay particular attention to cleaning these thoroughly.

- **Clean hard surfaces** including toilet bowls, flush handles, taps and hand basins regularly with hot soapy water followed by a disinfectant/sanitiser.

- **Wash dirty clothes, bedding and towels** on the hottest wash cycle possible and do not share towels or face flannels with someone who is infected.

- **Clean animal faeces from footwear/buggy wheels** after visits to animal attractions and wash your hands after doing so.

- **Stay away from work/school/nursery** until 48 hours after you’ve stopped vomiting or having diarrhoea and **comply with any additional exclusions** recommended by the Environmental Health and/or Health Protection Teams.

Further information about STEC

Further information relating to STEC can be found on the following websites:

- NHS Choices  
  http://www.nhs.uk/conditions/Escherichia-Coli-O157/Pages/Introduction.aspx

- Public Health England  

- The UK E.coli Support Group called H.U.S.H (Haemolytic Uraemic Syndrome Help)  
  http://www.ecoli-uk.com/
Appendix V - STEC O157 leaflet

Shiga toxin-producing Escherichia coli O157 (STEC-O157)

An information leaflet for cases

Hearing from Public Health England

The Public Health England (PHE) local Health Protection Team is contacting you because the result of the poo sample submitted by you or your child is positive for a bacterium called Shiga toxin-producing *Escherichia coli* (STEC) O157, also known as *E.coli* O157. E.coli O157 is the most common strain of STEC found in the UK.

The local laboratory has sent your sample to the PHE reference laboratory in London for further investigations and the final results may not be available for several weeks.

In the meantime, because *E.coli* O157 can cause serious illness and can be passed from person to person, we are contacting you to:

- Identify potential sources of the infection
- Provide some information on the infection and how you can prevent the spread of infection to others

Next steps

Along with our colleagues in Environmental Health, we will complete a questionnaire with you to help identify the potential source(s) of your infection and risk to any of your contacts. This will include:

- The activities you have done and food you have eaten in the 7 days before your symptoms started
- Information on you and your household/close contacts
- Providing information on the infection and how you can prevent the spread of infection to others

Your personal identifiable information will be held confidentially and only shared with colleagues directly involved in managing this infection in accordance with General Data Protection Regulations (GDPR) (EU) 2016/679.
Symptoms

Most people get better within 5 to 7 days. Treatment involves drinking plenty of fluids as vomiting and diarrhoea can lead to dehydration. Antibiotics should not be used as there is no evidence that they are helpful to treat STEC infections and they may increase the risk of complications.

Rarely, symptoms may be severe or even life-threatening causing Haemolytic Uraemic Syndrome (HUS) which may occur up to 2 weeks after the start of the diarrhoea. If your symptoms do not go away or you develop easy bruising, feel you are passing less urine than usual or your urine is pink/brown in colour please urgently seek medical advice as these symptoms could indicate the start of HUS and you may need further tests.

Staying away from work or school/nursery

You should stay away from work/school or nursery until you have stopped having symptoms for at least 48 hours to avoid passing it on to others.

For some people, this time may be longer and further samples may be needed because of the higher chance of spreading the infection to others or spreading it to people who may be more likely to develop severe illness. This may include:

- Those that need help with their own personal hygiene at home, work or school
- Children aged 5 years and under, particularly those attending nursery or pre-school groups
- Those that prepare or serve unwrapped food that is not heated further
- Healthcare workers with direct contact with highly susceptible patients for whom an infection like STEC could have serious consequences

Children aged 5 years and under (upto sixth birthday)

Although rare, the risk of HUS is highest in children aged 5 years and under. Some children aged 5 years and under have also been shown to continue to pass STEC in their poo for longer than adults, sometimes for many weeks or even months.

For these reasons, children aged 5 years and under may need to stay away (be excluded) from childcare settings until their poo samples are clear of the infection. If there are other children aged 5 years and under in the household, they may also be excluded, whether they have symptoms or not, until poo samples show that they have not picked up the infection.

Your local PHE Health Protection or Environmental Health Officers will be in contact to advise you if exclusion is needed for you and/or your contacts. They will provide you with information on this clearance process and aim to support you to get you or your child back to normal activities as quickly as possible.
Interim Public Health Operational Guidance for STEC

Please read the rest of this leaflet and in particular follow the advice on ‘How can I prevent others from becoming ill?’ to minimise passing the infection on to others.

General information on STEC?

STEC (Shiga toxin-producing Escherichia coli)

STEC (Shiga toxin-producing *Escherichia coli*) can cause illness ranging from mild diarrhoea to life threatening conditions. STEC O157 is the most common type in the UK and in a small number of people can cause very serious illness called Haemolytic Uraemic Syndrome (HUS). The risk of HUS is highest in children aged 5 years and under.

We know that STEC is very infectious and can be easily passed to others. It has also been the cause of several outbreaks following eating infected food, contact with infected people and touching infected animals or their poo.

In some European countries, other types of STEC are the cause of serious illness and outbreaks.

Becoming infected

You may become infected with STEC in a variety of ways:

- **Eating infected/contaminated food** that has not been cooked all the way through, particularly minced meat products such as burgers and sausages, or salad items that have not been washed properly
- **Handling/preparation of food contaminated with soil** for example, potatoes and leeks where the soil has not been washed away
- **Drinking infected/contaminated water** such as from streams, rivers and lakes etc. which may contain animal poo
- **Close contact with animals**, particularly cattle, sheep and goats. Animal saliva may be infected because of the way animals clean themselves
- **Direct contact with animal poo** on the animal itself, in their pen or on the floor
- **Contact with an infected person**, particularly if you don't wash your hands thoroughly after using the toilet or before handling food
Interim Public Health Operational Guidance for STEC

Symptoms

It usually takes between 2 and 4 days from being infected with STEC to develop symptoms which may be:

- No symptoms
- Very mild diarrhea
- Stomach pain
- Vomiting
- Fever
- Severe diarrhoea with blood
- Passing less urine than normal
- Haemolytic haemolytic syndrome (HUS)

Preventing others from becoming ill

Normal cooking temperatures kill STEC and it can be easily washed off your hands. For extra reassurance, you can use antibacterial gels/wipes AFTER washing your hands with soap and water.

Important steps you can take include:

- **Wash hands thoroughly** with liquid soap and running water after using the toilet (or helping others including changing nappies), handling raw meat, before meals and after contact with animals. If you have false nails, pay particular attention to cleaning these thoroughly
- **Clean hard surfaces** including toilet bowls, flush handles, taps and hand basins regularly with hot soapy water followed by a disinfectant/sanitiser
- **Wash dirty clothes, bedding and towels** on the hottest wash cycle possible and do not share towels or face flannels with someone who is infected
- **Clean animal faeces from footwear/buggy wheels** after visits to animal attractions and wash your hands after doing so
- **Stay away from work/school/nursery** until 48 hours after you’ve stopped vomiting or having diarrhoea and comply with any additional exclusions recommended by the Environmental Health and/or Health Protection Teams

Further information about STEC

Further information relating to STEC can be found on the following websites:

- NHS Choices
  [http://www.nhs.uk/conditions/Escherichia-Coli-O157/Pages/Introduction.aspx](http://www.nhs.uk/conditions/Escherichia-Coli-O157/Pages/Introduction.aspx)
# Appendix VI – Guidance development

<table>
<thead>
<tr>
<th>Lead authors</th>
<th>STEC Guidelines Review Group</th>
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<td>Consultant in Communicable Disease Control, PHE North East</td>
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Appendix B

Background Information
Background

Shiga toxin-producing *Escherichia coli* (STEC), also called verocytotoxin-producing *E. coli*, are pathogenic strains of *E. coli*, characterised by the production of shiga toxins. The spectrum of symptoms of STEC infection is broad, ranging from mild or even absent (in asymptomatic carriage) to severe illness presenting with bloody diarrhoea or the development of haemolytic uraemic syndrome (HUS).

*E. coli* O157 is the most commonly identified serogroup worldwide. It was first identified as a pathogen in 1982 and since then has been identified as the source in multiple outbreaks of human gastrointestinal illness worldwide [6]. The majority of the information that is known about STEC infections is based on data from *E. coli* O157. However, Non-O157 STEC strains are being increasingly recognised as the cause of human illness and several serogroups have regularly been associated with outbreaks. International studies and recent population-based studies from the UK have found that for every one STEC O157 isolated there are approximately 4-7 other non-O157 STEC strains isolated, each possessing a combination of *stx1* and *stx2* subtypes and virulence factors (*eae/aggR*) that may give rise to illness ranging from mild symptoms to HUS.

The following provides information on the epidemiology and clinical burden of disease associated with O157 and non-O157 STEC infections. More detailed information on the emerging evidence related to non-O157 STEC may be found in ‘Non-O157 STEC Evidence Base June 2018’.

Clinical features

**STEC O157**

- **Incubation period**

  The incubation period has a reported range of 6 hours to 10 days, although 2-4 days is the most common [7-12]. The incubation period may depend on the number of organisms ingested.
- **Clinical presentation and sequelae**

  Infection with STEC may be asymptomatic or cause a spectrum of illness from mild non-bloody diarrhoea to bloody diarrhoea, haemolytic uraemic syndrome (HUS) and death.

  In addition to non-bloody diarrhoea, symptoms of milder infection may include fever, abdominal pain or cramps and vomiting.

  More severe symptoms may reflect haemorrhagic colitis, with patients developing bloody diarrhoea and severe abdominal pain. The GBRU surveillance data study (England and Wales) reported symptoms of bloody diarrhoea in 61% and abdominal pain in 79.2% of patients with STEC O157 infection [13]. The illness is usually self-limiting with recovery in less than 10 days [7].

  HUS is characterised by acute renal failure, thrombocytopenia and microangiopathic haemolytic anaemia. Up to 10% of STEC cases are estimated to develop HUS, although this may differ for cases of non-O157 STEC infection [7,13].

  Children aged less than 5 years of age are at greatest risk of developing HUS, which usually occurs approximately 1 week after the onset of bloody diarrhoea [14]. Those aged 1-4 years are specifically at highest risk [15]. Other groups at risk of the development of HUS include hospitalised patients aged >60 years. The majority of patients recover from HUS, although around 50% may develop chronic renal complications (usually mild) and mortality is estimated to be between 3-5% [7].

- **Use of antibiotics**

  The use of antibiotics to treat infection with STEC is not routinely recommended. Although there has been some disagreement in the literature about the use of antibiotics in this condition, a recently conducted meta-analysis identified that when considering only those studies with a low risk of bias and appropriate definition of HUS, a significant association was found between the use of antibiotics and the risk of developing HUS [16].
Period of shedding
The period of shedding of STEC organisms is considered to be up to around 7 days in adults [7]. Although the precise duration of excretion is not known, it is recognised that in children, prolonged shedding may occur. In a UK study of confirmed cases of STEC in children aged ≤5 years attending childcare facilities, the average duration of shedding was 31 days [17], with other studies reporting similar results of 29 days (range 11-57 days) [18]. In the study of children attending childcare facilities in the UK, 24% were found to be continuing to shed for as long as ≥6 weeks [17].

The duration of shedding may be affected by age and severity of illness and may differ between cases of STEC O157 and non-O157 STEC serotypes.

Non-O157 STEC

Incubation period
The evidence that is available has found that the incubation periods for various non-O157 STEC serogroups are similar to those quoted for STEC O157. However, in the German outbreak of O104:H4 (stx2a, aggR) in 2011, in one study based on 91 cases, the median incubation period was 8 days (interquartile range, 6 to 10) [19].

Clinical presentation, sequelae and determinants of virulence
Most strains of O157:H7 STEC are eae positive and possess stx2a/2c genotypes with or without stx1a genotype. Non-O157 STEC serogroups are a heterogeneous group of organisms that cause a similar spectrum of illnesses to STEC O157. Over 100 serogroups have been documented to cause human illness, with the majority of reported cases associated with non-O157 STEC having diarrhoeal illness of short duration. However, it has been recognised from numerous observational studies that several serogroups are regularly associated with more severe forms of human illness. In the USA, CDC data shows that 75-80% of reported and serogrouped non-O157 STEC isolates from humans with severe symptoms (including bloody diarrhoea and HUS) belong to serogroups O26, O45, O103, O111, O121, and O145 [19-21]. Advances made in molecular biology have shown that particular serotypes belonging to these serogroups possess combinations of shiga toxin subtypes and other virulence factors that are associated with the development of HUS and bloody diarrhoea [22]. The combination of shiga toxin subtype stx2a and the
Interim Public Health Operational Guidance for STEC

virulence factor eae has the strongest association with toxicity. Observational studies have also demonstrated an association between HUS or bloody diarrhoea with stx2d and stx2c shiga toxin subtypes, although not as strong as the association with stx2a. In vitro studies have shown that stx subtypes stx2a, stx2d (in particular elastase-activatable stx2d) are very potent toxins. Stx1, stx2b, stx2e, stx2f are the least potent toxins. Stx2c has intermediate potency but is 25 times less potent than stx2a. Epidemiological studies suggest that STEC infections caused by strains possessing both stx1a and stx2a genes may be less likely to cause HUS than strains with stx2a only. In vivo studies using mice have provided an explanation at the molecular level. Stx1a interferes with the expression of stx2a toxicity in the kidneys possibly by competing for common receptors [23]. In 2011, a hybrid STEC strain (O104:H4, stx2a, aggR) emerged that caused a large Europe wide outbreak with a high incidence of HUS affecting mainly adults [24]. This strain possesses an adherence factor aggR that is distinct from eae and significantly enhances the virulence of the strain. In England during 2014, an STEC strain (O55:H7, stx2a, eae) emerged that caused an outbreak in which 42% of cases developed HUS [25] and in France, an STEC serotype O80:H2 has become a significant problem, with 91% of cases developing HUS [26]. The strains possessed combinations of stx2a, stx2c and stx2d with eae [27].

Significance for public health response

The significance of these findings for public health is that most non-O157 STEC strains can cause diarrhoeal illnesses and any organism producing shiga toxin has the potential to cause HUS. However, most strains commonly causing severe illness in humans possess stx subtypes stx2a, stx2c or stx2d and eae or aggR virulence factors – collectively referred to as HUS-associated E. coli (HUSEC) strains. In South East England, it is estimated that around 10% of successfully serotyped isolates belong to HUSEC strains other than STEC O157. Public health actions should be prioritised to cases infected with these strains [22, 28]. It is likely that other factors are involved in adapting the organisms for human transmission e.g. O157:H7 and O104:H4.

- Use of antibiotics

The use of antibiotics to treat infection with STEC O157 is not routinely recommended. During the O104:H4 outbreak in Germany antibiotics were widely used to treat the complications of severe disease e.g. HUS [29, 30]. The antibiotic most commonly used was
azithromycin and median shedding duration for HUS patients was significantly shorter than for those not treated with antibiotics. In at least one study it has been shown that in an in vitro system azithromycin reduced the concentration of stx2a toxin produced by bacteria belonging to STEC O80:H2 whereas ciprofloxacin significantly increased the concentration of free stx2a toxin [27]. More studies are required to identify the conditions that should be present before antibiotics are used to treat non-O157 STEC infections or to treat long term carriers.

- **Period of shedding**

Most of our understanding about the infectious dose, transmissibility and duration of shedding of STEC by human cases has been derived from investigations conducted in response to cases of STEC O157. In contrast to STEC O157 there is much less information regarding transmission and duration of shedding associated with non-O157 STEC infections, which is further complicated by their heterogeneity. There is consensus however that prolonged shedding in young children is common and many studies report median durations of shedding of about 30-40 days, but the range is broad. There is an inverse relationship between age and duration of shedding. There does not appear to be any differences related to sex, severity of disease, or stx subtype in the median duration of shedding [31].

Observational studies have been reported suggesting that non-O157 STEC serogroups behave in a similar way to STEC O157 and the factors affecting duration of shedding are likely to be similar. Secondary case rates between 7 and 21% for STEC O157 associated outbreaks have been reported. Similar transmission rates have been seen in outbreaks associated with non-O157 STEC serogroups [31, 32]. In households the highest rates of transmission are generally seen when the sources are young children. The youngest children are also those at greatest risk of acquiring the infection in households [33].

**Sources and Transmission**

**STEC O157**

STEC are recognised to colonise the gastrointestinal tracts of farm animals, primarily cattle, usually without causing illness. Sheep, goats and deer are also recognised to be significant reservoirs, with other wild and domestic animals including pigs, dogs and birds amongst
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others also able to act as vectors for disease for both STEC O157 and non-O157 STEC serotypes.

Any food, water or environmental surface contaminated by the excreta of an animal or human case, including asymptomatic carriers, is a potential source of infection.

The organism is highly virulent and the infectious dose is low, possibly less than 100 organisms [34], facilitating its potential to cause large outbreaks of human illness.

- **Food**

  Human infection with STEC is most commonly due to consumption of contaminated foods, particularly raw or undercooked ground meat products [7]. The surface of meat can be contaminated during slaughter and processing, which when spread through the whole product, as in hamburgers and other ground meat products, poses a particular risk if inadequately cooked. Unpasteurised or inadequately pasteurised milk also poses a risk from faecal contamination. Contamination of ready-to-eat foods, via cross-contamination from raw meat products, is an important cause of foodborne STEC infections.

  In a review of outbreaks of STEC across 9 countries, food was identified as the most common source of primary transmission (42%) [35]. Food vehicles implicated in large-scale outbreaks worldwide include meat and dairy products[36], salad products such as lettuce [37], sprouted seeds, such as fenugreek [38], raw fruits and vegetables and associated products such as apple juice [36].

  Primary prevention of transmission via food products therefore involves minimising contamination of animal carcasses during slaughter, good kitchen practices to avoid cross-contamination of raw and cooked foods, thorough cooking of meat products, pasteurisation of milk and dairy products and ensuring personal hygiene, most specifically thorough handwashing [34].

- **Water**

  Both surface water and private water supplies have the potential for contamination with STEC via animal excreta. Sporadic cases and outbreaks linked to waterborne sources have
been documented worldwide. These have been associated with exposure to bacteria via swimming in lakes, pools and consumption of water from farm wells and private water supplies [36].

- Livestock and farms
Due to the recognised reservoir of STEC amongst animals, especially ruminants, human infection may follow occupational or recreational exposure to animals, their excreta or the environment contaminated by them.

A large-scale outbreak of *E. coli* O157 linked to an open farm in the UK in 2009 highlighted the importance of minimising or eliminating visitor contact with animal excreta and raising public awareness of the importance of hand hygiene during recreational farm visits [39]. Cases of non-O157 STEC have also been associated with contact with farm animals [13]. Visits to petting farms and agricultural fairs have also been implicated in outbreaks of STEC infection [36]. Farm workers are also at risk of infection with STEC through occupational exposure.

- Person-to-person spread
Transmission of STEC from person-to-person is via the faecal-oral route and is a recognised cause of outbreaks of STEC infection worldwide. A review of 90 outbreaks across 9 countries identified the most common mode of secondary transmission to be person-to-person spread within household settings (46%) [35].

The evidence for food handlers acting as the primary source of transmission within outbreaks in the UK is limited. A large outbreak of STEC O157 cases linked to a restaurant in Northern Ireland in 2012 identified a food handler as a possible source of transmission, however there were significant caveats to the potential association and results from Whole Genome Sequencing (WGS) suggested a contaminated food source was more likely [40]. A 2014 review of UK STEC O157 outbreaks between the 1980s and 2013 did not identify food handlers as the primary source of transmission in any of the included outbreaks [41].

For outbreaks with secondary transmission via person-to-person spread in nursery settings, higher rates of secondary cases were noted which are likely to reflect a combination of
factors including prolonged shedding in this age group, poor/under-developed personal hygiene measures and immature immune systems amongst this age group [35]. Other studies of sporadic cases of STEC infection have also identified contact with symptomatic young children (aged <5 years) as being a risk factor for transmission [42].

**Non-O157 STEC**

Ruminants have been identified as the major reservoir of *E. coli* O157 and also appear to be the main reservoir of non-O157 STEC strains [43-45]. STEC have been isolated from cattle, sheep, goats, and deer. In a novel ecological study from Germany [46], a positive association was found for the incidence of five HUS-relevant STEC serogroups in paediatric patients (O26, O103, O111, O145, O157) and cattle density in the geographical area of residence. STEC have also been isolated from other wild and domestic animals. A survey of wildlife meat in Germany found a number of non-O157 STEC serotypes present in deer, wild boar, and wild rabbit meats [47]. Of the 140 STEC strains examined in the study 80 (57.1%) belonged to 18 serotypes previously associated with human pathogenicity. Genes linked to high virulence for humans (*stx*2a, *stx*2d, and *eae*) were present in 46 (32.8%) STEC strains from game. It is believed that, in many cases, they are transiently colonised and the STEC acquired from foods or water contaminated by faecal material from ruminants. Nevertheless, some of these transient hosts may be vehicles of infection for humans and have been associated with outbreaks. In experiments some strains of the non-O157 STEC serogroups O26 and O111 have been reported to survive in untreated well water for over 56 days at 10ºC. Bacteria died more quickly at 22ºC but did persist in significant numbers for four weeks [43].

Most large outbreaks associated with non-O157 STEC have been associated with contaminated food or water as the main vehicle of infection. An analysis of outbreaks in the USA [48] found that of 38 single-aetiology outbreaks, 66% were caused by non-O157 and 84% and transmitted through food or person-to-person spread. The authors found that food vehicles included dairy products, vegetable produce, and meats. Childcare centres were the most common setting for person-to-person spread. Person to person spread has been reported more often in association with non-O157 STEC infections (Table 2) [43].
Contaminated food is a recognised source of STEC O157 infections, and is often responsible for large outbreaks. Outbreaks caused by non-O157 STEC serogroups have been associated with contaminated dairy products [49, 50], salad vegetables, bean sprouts, fenugreek seeds [24] and recently in flour and cookie dough. There were fewer reports of non-O157 STEC outbreaks caused by meat products.

There are also fewer reports of water associated outbreaks [51, 52] caused by non-O157 STEC serogroups than for STEC O157. Several outbreaks have been reported involving children playing or swimming in pool water, infected children may have been the source of bacteria for these cases. Other outbreaks have been traced to water consumed at summer camps and faecal material from domestic and/or wild ruminant animals may have contaminated lakes, rivers, and some drinking water sources. In the Republic of Ireland outbreaks caused by O26 STEC serotypes are regularly associated with private water sources [53, 54].

There is little information about the transmission of non-O157 STEC infections related to animal contact. A meta-analysis has indicated that infections from undercooked or raw meat occur more often with O157 strains while non-O157 strains are more often associated with animal contact but only 6 out of 31 studies contained sufficient information to enable this comparison to be done [55].

<table>
<thead>
<tr>
<th>Vehicle</th>
<th>non-O157:H7 STEC</th>
<th>E. coli O157:H7(64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal contact</td>
<td>6.2%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Water</td>
<td>10.0%</td>
<td>25.6%</td>
</tr>
<tr>
<td>Person–person contact</td>
<td>28.8%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Dairy</td>
<td>10.0%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Meat</td>
<td>11.2%</td>
<td>24.6%</td>
</tr>
<tr>
<td>Produce</td>
<td>6.2%</td>
<td>9.2%</td>
</tr>
<tr>
<td>Other food</td>
<td>8.8%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Unknown</td>
<td>18.8%</td>
<td>5.8%</td>
</tr>
</tbody>
</table>
• Person-to-person spread

There have been numerous reports of outbreaks probably caused by person-to-person spread of non-O157 STEC in day-care [31-33, 56], schools and senior care facilities, and it appears that this form of spread might be a more common route for non-O157 STEC infections. Transmission by infected food handlers is a recognised risk and there are reports in the published literature. One outbreak was reported involving a prison and epidemiological investigations implicated an infected food handler, the outbreak was caused by STEC serogroup O45 \( (stx1) \) [57].

There were 341 probable cases during a large restaurant associated outbreak caused by O111 STEC in Oklahoma and epidemiological evidence suggested the outbreak resulted from cross-contamination of restaurant food from food preparation equipment or surfaces, or from an unidentified infected food handler [58]. During the O104:H4 outbreak in Germany a cluster of 23 cases in a family party associated with a restaurant is postulated to have been caused by a food handler contaminating several food items from which the organism was isolated [59].

**Epidemiology**

**STEC O157**

*E. coli* O157 is the most common serogroup of STEC causing infections in the UK. It is also the most likely *E.coli* serogroup to cause bloody diarrhoea in the UK, and HUS/TMA worldwide [60]. Non-sorbitol fermenting (NSF) O157 are the only strains that can be routinely screened for in the majority of UK diagnostic laboratories by current methods, so the true incidence of non-O157 STEC is not known. There are more than 300 serogroups of STEC. Most serogroups are not known to be pathogenic to humans [61].

In the late 1980s confirmed human isolates of STEC O157 in England and Wales increased markedly, peaking in the late 1990s. Since 2005, between 630 and 1091 isolates of STEC O157 have been confirmed annually from human sources.

A small number of STEC strains (<10) per year in addition to NSF STEC O157 are isolated annually from faeces, and some of these are linked to serious illness. In Scotland more than
97% of STEC isolates are serogroup O157 but isolations of other serogroups have increased in recent years. This pattern has also been seen in the Republic of Ireland. The most common serogroups other than O157 in England are O26 and O103 [62].

The annual incidence of STEC O157 in England and Wales is shown in Figure 1. There were 630 isolates of STEC O157 confirmed in 2015 in England and Wales [62]. Reported incidence of STEC O157 varies within England and Wales, with the highest rates occurring in the north and south west of England (Figure 2).

Around 62% of cases are regarded as sporadic, 19% as part of household clusters and 19% are part of general outbreaks (PHE data). 21% of cases reported to national surveillance reported foreign travel between 2009 and 2015 although the numbers differ by phage type with PT21/28 being the predominant indigenously acquired UK strain [63].

Almost 50% of cases are in children under 16 [64], and rates of infection are highest in children under 5 years with the peak incidence in the 1-4 age group (Figure 3) [63]. Some of this excess may reflect screening policies as young children are routinely screened for STEC following a case in a household, whereas adult contacts may not be screened unless they are in a risk group, although we also know that clinical illness more commonly occurs in children aged 5 years and under. Around a third (34.3%) of STEC O157 cases are hospitalised and the median duration of hospitalisation was 3 days (IQR 1–21) [63].

HUS occurs in up to 11% of cases and 85% of patients with HUS are under 16 years of age [64]. The percentage chance of progressing to HUS are being 1-4 years of age, being female, being infected with PT21/28 or PT2, receiving β-lactam antibiotics or presenting with vomiting or bloody diarrhoea. The chances are increased when all of these factors are present [15].

Seasonality of STEC O157 infections in England and Wales has been reported since 1989 and shows a peak in the third quarter with very few infections in the first quarter. Monthly data (Figure 4) shows that variation in isolates confirmed per month during the summer and autumn periods is introduced by general outbreak activity.
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Figure 1: Number of culture positive STEC O157 isolates from England and Wales (2010-2015)

![Figure 1](image1.png)

Figure 2: Regional rates of culture positive STEC O157 laboratory isolations from England & Wales 2015

![Figure 2](image2.png)
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Figure 3: Average rate per 100,000 population of culture positive STEC O157 laboratory isolations by age group and gender, England & Wales, 2010-2015

![Figure 3: Average rate per 100,000 population of culture positive STEC O157 laboratory isolations by age group and gender, England & Wales, 2010-2015](image)

**Figure 4: Monthly confirmations of STEC O157 from human infections in England & Wales, 2010 - 2015**

![Figure 4: Monthly confirmations of STEC O157 from human infections in England & Wales, 2010 - 2015](image)

**Non-O157 STEC**

In England all STEC infections are notifiable but little is known about the epidemiology and true incidence of non-O157 STEC infections. Analysis of surveillance data has been
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published by the Gastrointestinal Bacteria Reference Unit [13]. A twenty fold increase in non-O157 STEC serotypes isolated has been seen, from fewer than 18 in 2011 to over 370 isolated in 2016 (see Figure 5). The increase is attributable to the increased detection of these organisms by local hospital laboratories implementing stx PCR testing, mainly in London and the South East of England.

Figure 5
Confirmed non-O157 STEC infections: Data from Gastrointestinal Bacteria Reference Unit. Jan 2009 – Dec 2016

The most common serogroups, accounting for 68% of all isolates were O26, O146, O55, O91, O103, O128, O145, O104, O111, O121, O80. The most frequently isolated serogroups were O26(22%), O146(12%) and O55(9.0%). Serogroups O26 and O55 were isolated from 73% of HUS cases. All the O55 cases were associated with two outbreaks in the South East and South West of England.

From late 2013 several front-line laboratories in Kent, Surrey and Sussex introduced PCR screening of faecal samples. By the end of 2015 five out of the ten local hospital laboratories, serving a population of over 1.8 million had implemented PCR testing for diagnostic purposes. Surveillance information has been collected on over 700 stx PC positive results from local hospital laboratories. The epidemiology of STEC infections in this population has been described.
The overall annualised incidence rate of STEC infections (PCR or culture confirmed) was 7.6 cases per 100,000 population. The annualised incidence rate of confirmed STEC O157 was 0.7 cases per 100,000. The annual incidence of all non-O157 serotypes was 4.3 cases per 100,000. The ratio of STEC O157 to non-O157 STEC was 1 to 6.2. These findings are comparable with two large prospective, population-based studies of infectious intestinal disease (IID) incidence and aetiology conducted in the UK in 1993–1996 (IID1) and in 2008–2009 (IID2) [65]. Culture based techniques were used for STEC O157 and PCR-based procedures for the detection of stx genes were also employed. In the IID2 study STEC O157 was detected in one out of 866 patients and non-O157 STEC in seven out of 866 patients with diarrhoea, an estimated ratio of STEC O157 to non-O157 STEC infections of 1 to 7. The Republic of Ireland STEC surveillance system is well developed and has also observed a significant increase in the incidence of STEC infections since 2012, coinciding with the implementation of stx PCR screening of faecal samples by front line laboratories [66]. In 2015 the overall incidence of STEC was estimated as 16.0 per 100,000 (inclusive of PCR confirmed but culture negative results) or 13.7 per 10⁵ if confirmed by isolation. The incidence of STEC O157 was 3.2 per 100,000 population. The ratio of STEC O157 to non-O157 STEC infections is estimated to be about 1 to 4.3. Although these rates are significantly higher than those found in the UK study, the ratio is similar and confirms that non-O157 STEC infections are also more frequent in Ireland than infections with O157 serogroup. Analysis of the cohort also showed that non-O157 STEC infections have an older age distribution than STEC O157 infections (see Figure 6). In contrast to STEC O157 infections non-O157 STEC infections appear to have a different seasonal distribution and the incidence in December to February is much higher, suggesting that different exposures are responsible (see Figure 7).
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Figure 6
Age distribution of STEC infections: Corrected annual age specific rates per 100000, Kent, Surrey and Sussex. November 2013 - March 2017. (N=338)

Figure 7
Rationale for public health action

As described, human infection with STEC is predominantly acquired via the consumption of contaminated foods, with several large-scale foodborne outbreaks being documented in the published literature. Person-to-person spread within household and nursery settings has also been well documented and there is evidence that younger children, particularly those aged under 6 years and attending nursery or other childcare settings are at both an increased risk of developing severe infection and facilitating onward transmission [17, 67].

What is less well-documented, however is evidence of outbreaks in settings involving secondary transmission amongst other risk group populations, such as healthcare workers or food handlers.

The increased incidence of STEC infections in children may in part reflect enhanced detection of cases in this group due to a greater likelihood that medical advice may be sought for younger children with diarrhoeal symptoms but may also reflect an increase in risk factors for developing gastrointestinal illnesses within this cohort, such as inadequate personal hygiene habits [67]. In contrast, it is more likely, although not inevitable, that adults in risk groups such as food handling, caring or healthcare roles will have increased levels of hand hygiene and access to handwashing facilities to help prevent the onward transmission of gastrointestinal illness.

To help support the development of the recommendations in these guidelines, guidelines on the management of STEC infections and HUS in Western countries other than the UK were reviewed [68-78]. Although the public health management of cases and contacts of STEC or HUS varies between regions, the majority of guidelines support the exclusion and/or microbiological screening of cases in children. However, the management of cases and contacts within other risk groups is less standardised, with guidelines including the use of measures to redeploy or restrict staff within these settings.

As a result of the current picture within the UK and internationally, the guidelines development group has established recommendations for the public health management of cases and contacts within risk groups which aim to balance protecting those groups at greatest risk of developing severe illness and facilitating onward transmission with a pragmatic approach to
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supporting those in risk group settings where the risk of onward transmission appears to be lower. As such, these guidelines stress the importance of focussing public health actions on children aged 5 years old and under, whilst facilitating health protection teams to carry out detailed risk assessments for those in other risk groups to establish whether restrictions to working patterns or redeployment to other roles may be possible. Where this is not feasible, however, these guidelines stress the need to continue to focus on protecting public health via exclusion and microbiological testing methods as required.

**Microbiological diagnosis**

Recommended procedures for the investigation of diarrhoea by diagnostic/diagnostic laboratories are detailed in the *UK Standards for Microbiology Investigations* - *Investigation of faecal specimens for enteric pathogens* [1].

As described, specific procedures used by diagnostic laboratories may vary, however most will carry out a morphological identification, a slide agglutination (or latex kit) test and a biochemical test to identify the organism.

When all 3 procedures have been completed and are positive, this may be referred to in laboratory terms as *presumptive (locally confirmed) isolate* which satisfies the following conditions:

- Positive typical colony morphology on appropriate selective medium
- Positive O157 (by slide agglutination OR latex kit)
- Positive biochemical identification of *E. coli*

It should be noted that the term “presumptive (locally confirmed) isolate” refers to laboratory isolates only and not human cases. Please refer to Table 1 for definitions of human cases of STEC infection based on laboratory, clinical and epidemiological information.

PCR methods for the detection of shiga toxin (stx) are increasingly used by diagnostic laboratories for the identification of STEC infections. The use of PCR methods has made a significant impact on the ability to identify and estimate the burden of STEC infections caused by non-O157 serotypes. Where diagnostic laboratories report PCR positive, culture negative results, this may reflect numbers of organisms below detection limits for culture measures or
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the presence of organisms that are non-culturable by diagnostic laboratory methods, including non-O157 STEC serotypes. The management of these cases is detailed in the main Public Health STEC guidelines.

Referral to the GBRU Reference Laboratory

Diagnostic laboratories should refer the following to the Gastrointestinal Bacteria Reference Unit (GBRU):

A) Cases of HUS:

- Laboratories using culture based methods for detection of STEC should refer faecal specimens from cases of HUS on the day of receipt to GBRU.
- Laboratories using PCR/EIA for detection of STEC should refer all positive faecal specimens from cases of HUS urgently to GBRU to optimise isolation (non-O157 and STEC O157), characterisation of virulence and typing.
- Consider sending a serum specimen for detection of antibodies to E. coli from the case if culture / PCR results from GBRU are negative.

B) Cases without HUS:

- Presumptive (locally confirmed) isolates of E. coli O157 for confirmation of identity, shiga toxin gene detection and serotyping
- Faecal samples testing positive by PCR in local diagnostic laboratories where commercial PCR assays for GI infections are used routinely and are culture negative locally for presumptive E. coli O157.
- Other strains of E. coli for confirmation of identity and shiga toxin gene detection if there is a high clinical suspicion of STEC infection
- Faecal specimens from cases with bloody diarrhoea in whom conventional laboratory testing has failed to yield presumptive E. coli O157 or any other pathogen
- Faecal samples from symptomatic contacts of cases of STEC infection or any STEC outbreak-associated case in whom conventional culture laboratory testing has failed to yield a pathogen. These should be discussed with GBRU prior to submission to ensure there is capacity for testing

The GBRU sends results to the diagnostic laboratory in paper form but in urgent cases also telephone results. HPTs have access to STEC reports from the GBRU via the Gastro Data
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Warehouse (GDW). The diagnostic laboratory should forward all results from the GBRU to their local HPT by telephone. HPTs should be informed irrespective of whether the results are positive or negative for STEC infection.
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