

NATIONAL STANDARD METHOD

# RECOMMENDATIONS FOR THE SCREENING OF SPECIMENS FOR *CORYNEBACTERIUM* SPECIES

QSOP 53

Issued by Standards Unit, Department for Evaluations, Standards and Training  
Centre for Infections



Association of Medical Microbiologists  
*Association of Medical Microbiologists*  
Association of Medical Microbiologists



RECOMMENDATIONS FOR THE SCREENING OF SPECIMENS FOR *CORYNEBACTERIUM* SPECIES

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# STATUS OF NATIONAL STANDARD METHODS

National Standard Methods, which include standard operating procedures (SOPs), algorithms and guidance notes, promote high quality practices and help to assure the comparability of diagnostic information obtained in different laboratories. This in turn facilitates standardisation of surveillance underpinned by research, development and audit and promotes public health and patient confidence in their healthcare services. The methods are well referenced and represent a good minimum standard for clinical and public health microbiology. However, in using National Standard Methods, laboratories should take account of local requirements and may need to undertake additional investigations. The methods also provide a reference point for method development.

National Standard Methods are developed, reviewed and updated through an open and wide consultation process where the views of all participants are considered and the resulting documents reflect the majority agreement of contributors.

Representatives of several professional organisations, including those whose logos appear on the front cover, are members of the working groups which develop National Standard Methods. Inclusion of an organisation's logo on the front cover implies support for the objectives and process of preparing standard methods. The representatives participate in the development of the National Standard Methods but their views are not necessarily those of the entire organisation of which they are a member. The current list of participating organisations can be obtained by emailing [standards@hpa.org.uk](mailto:standards@hpa.org.uk).

The performance of standard methods depends on the quality of reagents, equipment, commercial and in-house test procedures. Laboratories should ensure that these have been validated and shown to be fit for purpose. Internal and external quality assurance procedures should also be in place.

Whereas every care has been taken in the preparation of this publication, the Health Protection Agency or any supporting organisation cannot be responsible for the accuracy of any statement or representation made or the consequences arising from the use of or alteration to any information contained in it. These procedures are intended solely as a general resource for practising professionals in the field, operating in the UK, and specialist advice should be obtained where necessary. If you make any changes to this publication, it must be made clear where changes have been made to the original document. The Health Protection Agency (HPA) should at all times be acknowledged.

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More details can be found on the website at [www.evaluations-standards.org.uk](http://www.evaluations-standards.org.uk). Contributions to the development of the documents can be made by contacting [standards@hpa.org.uk](mailto:standards@hpa.org.uk).

The reader is informed that all taxonomy in this document was correct at time of issue.

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## Citation for this document:

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# AMENDMENT PROCEDURE

Controlled document reference	QSOP 53
Controlled document title	Recommendations for the screening of specimens for <i>Corynebacterium</i> species

Each National Standard Method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from [standards@hpa.org.uk](mailto:standards@hpa.org.uk).

On issue of revised or new pages each controlled document should be updated by the copyholder in the laboratory.

Amendment Number/ Date	Issue no. Discarded	Insert Issue no.	Page	Section(s) involved	Amendment
2/ 29/09/08	2	2.1	All	<b>All</b>	Department name changed
			2	<b>Status page</b>	Taxonomy sentence inserted.

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# RECOMMENDATIONS FOR THE SCREENING OF SPECIMENS FOR *CORYNEBACTERIUM* SPECIES

Type of specimen: Throat swab

## INTRODUCTION

The National Standard Methods (NSMs) [BSOP 9 - Investigation of throat swabs](#), and [BSOPID 2 - Identification of \*Corynebacterium diphtheriae\*, \*Corynebacterium ulcerans\* and \*Corynebacterium pseudotuberculosis\*](#) may be relevant to this document.

### **Toxigenic *Corynebacterium diphtheriae* and *Corynebacterium ulcerans***

Globally, toxigenic *Corynebacterium diphtheriae* is the most common cause of diphtheria. Toxigenic strains of *Corynebacterium ulcerans* have been reported to cause illnesses similar to diphtheria, with formation of pseudomembranes and cardiac and neurological complications, but generally this is rare<sup>2,3</sup>.

The principal virulence factor of this group of organisms is the ability to produce diphtheria toxin. In a fully developed case of diphtheria, this toxin damages the pharyngeal epithelium to produce a leathery membrane, giving the disease its name. This membrane may occlude the airway, sometimes causing death by respiratory obstruction. Systemic absorption of the toxin from the primary site of replication may damage a wide range of host cells, including those of the heart and nervous system. Myocarditis and neurological dysfunction may cause or contribute to disability or death.

The usual site of carriage or infection is the throat or nasopharynx, occasionally the nose. *C. diphtheriae* may also cause cutaneous infections.

### **Non-toxigenic *Corynebacterium diphtheriae* and *Corynebacterium pseudotuberculosis***

*Corynebacterium pseudotuberculosis* as a cause of human infection is mainly reported from Australia and is zoonotic in nature; it will not be further considered here.

Non-toxigenic *C. diphtheriae* may be a cause of sore throat, but not a true diphtheritic membrane and/or symptoms attributable to systemic absorption of toxin. Non-toxigenic strains of *C. diphtheriae* may be encountered in clinical specimens, especially those taken from persons previously immunised against diphtheria toxin. On re-introduction of the necessary gene, these organisms may express toxin production. Circulation of these organisms has led to public health concern.

Occasionally, humans will develop invasive infections with non-toxigenic strains of *C. diphtheriae*. These conditions appear to be rare, and will be detected by blood culture rather than by culture of throat or nasopharyngeal swabs. It is thought that *C. diphtheriae* has additional virulence factors because invasive disease caused by non-toxigenic strains has been reported<sup>4,5</sup>.

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# 1 EPIDEMIOLOGY

In 1991, following the collapse of the former Soviet Union, an epidemic of diphtheria occurred in Eastern and Central Europe. All countries of the newly independent states of the former Soviet Union were affected<sup>6</sup>.

Following enhancement or introduction of appropriate Public Health interventions, such as immunisation, case-finding and treatment of cases and carriers within these countries, there is now evidence that the situation is improving<sup>7,8</sup>.

The outbreak did not spread outside the former Soviet bloc to any significant extent<sup>9</sup>. One case was imported into the United Kingdom<sup>10</sup>. Most cases of toxigenic *C. diphtheriae* reported in the UK are imported from South East Asia and the Indian sub-continent.

# 2 IMMUNISATION

Immunisation against diphtheria toxin prevents disease, and has led to a virtual disappearance of toxigenic *C. diphtheriae* amongst some populations. The epidemic in Eastern and Central Europe encouraged enhanced surveillance of pathogenic *Corynebacterium* species in the UK. In a drive to enhance the herd immunity of the population, a low dose booster of diphtheria toxoid combined with tetanus toxoid was recommended for school leavers by the UK Departments of Health from 1994<sup>9</sup>. In 1985 diphtheria vaccine coverage, for 2 year olds of diphtheria vaccine in England and Wales, was 85%; by 1998, this had risen to 95% and in 2003-4 it was 94%<sup>11</sup>.

# 3 CRITERIA FOR SCREENING THROAT SWABS FOR *CORYNEBACTERIUM DIPHTHERIAE* OR *CORYNEBACTERIUM ULCERANS*

There are specific exposures which, if reported on request forms, should trigger examination of specimens for *C. diphtheriae* or *C. ulcerans*. These are based on recognised risk factors and information from enhanced diphtheria surveillance. [BSOP 9 - Investigation of throat swabs](#) recommends screening for *Corynebacterium* species in the following circumstances:

## 1. Throat or nose swabs from a patient with one or more of the following risk factors reported:

- Membranous or pseudomembranous pharyngitis/tonsillitis
- Travel overseas (especially Russia and Former Soviet States, Africa, South America and South-East Asia) within the last 10 days
- Recent contact with someone who has travelled overseas recently (especially Russia and Former Soviet States, Africa, South America and South-East Asia)\*
- Recent consumption of raw milk products (*C. ulcerans*)
- Recent contact with farms/farm animals or domestic animals (*C. ulcerans*)
- The patient works in a clinical microbiology laboratory, or similar, where *Corynebacterium* species may be handled

\* Travel or contact with travellers in the past 10 days is most likely to be relevant to the risk of diphtheria.

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**2. Swabs from chronic non-healing ulcers or skin lesions with one of the following risk factors reported:**

- Recent travel overseas (especially tropical regions)
- Recent contact with someone who has travelled overseas recently (especially Russia and Former Soviet States, Africa, South America and South-East Asia)
- The patient works in a clinical microbiology laboratory, or similar, where *Corynebacterium* species may be handled

It is recommended that those laboratories with a specific public health remit such as the Health Protection Agency laboratories continue to screen throat swabs for *Corynebacterium* species: this ensures that surveillance of the disease continues (See [BSOP 9 - Investigation of throat swabs](#)).

**Table 1. Toxigenic *Corynebacterium* species isolates - risk factors identified in England and Wales 1995-2006**

**Toxigenic *C. diphtheriae* isolates: 1995 – 2006 (total 22\*)**

	<b>Skin lesion</b>	<b>Throat/nose</b>
Travel	100 % (11/11)	58 % (7/12)
Contact with traveller	9 % (1**/11)	25 % (3***/12)
Membrane	0 % (0/11)	8 % (1/12)
Lab worker	0 % (0/11)	17 % (2/12)
Raw milk/farm animal	n/a	n/a
None of the above	0 %	8 % (1/12)

**Toxigenic *C. ulcerans* isolates : 1995 - 2006 (total 37)**

	<b>Skin lesion</b>	<b>Throat/nose</b>
Travel	0 % (0/4)	12 % (4/33)
Contact with traveller	0 % (0/4)	3 % (1*/33)
Membrane	0 % (0/4)	12 % (6/33)
Lab worker	0 % (0/4)	0 % (0/33)
Raw milk/farm animal/rural connection	0 % (0/4)	42 % (15/33)
None of the above	100 % (4/4)	27 % (9/33)
(mention of domestic animals)	25 % (1/4)	42 % (14/33)

\* Includes one patient with both skin and throat isolates

\*\* Patient also had travel history

\*\*\*2/3 patients also had travel history

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## 4 PUBLIC HEALTH

It is recommended that laboratories with a specific public health remit, particularly Health Protection Agency laboratories, continue to screen throat swabs for *Corynebacterium* species, therefore ensuring that surveillance of the disease continues and appropriate public health action is taken.

## 5 CLINICAL DETAILS

The onus is on the attending physician to supply relevant information, and consideration should be given to cascading periodic reminders about diphtheria down the medical and scientific hierarchies.

## 6 QUALITY ASSURANCE

It is suggested that laboratories should continue to undertake external quality assessment, such as that provided by UK NEQAS, for the isolation of this group of bacteria. Laboratories should also maintain their own internal quality control measures.

## 7 RELEVANT NATIONAL STANDARD METHODS

For additional details on specific areas of diagnosis refer to the relevant NSMs available through the Evaluations and Standards Laboratory web page ([www.hpa-standardmethods.org.uk](http://www.hpa-standardmethods.org.uk)).

Other documents of relevance to this NSM are:

[BSOP 9 - Investigation of throat swabs](#)

[BSOPID 2 - Identification of \*Corynebacterium diphtheriae\*, \*Corynebacterium ulcerans\* and \*Corynebacterium pseudotuberculosis\*](#)

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## 8 ACKNOWLEDGEMENTS AND CONTACTS

This National Standard Method has been developed, reviewed and revised by the National Standard Methods Working Group for Clinical Bacteriology ([http://www.hpa-standardmethods.org.uk/wg\\_bacteriology.asp](http://www.hpa-standardmethods.org.uk/wg_bacteriology.asp)). The contributions of many individuals in clinical bacteriology laboratories and specialist organisations who have provided information and comment during the development of this document, and final editing by the Medical Editor are acknowledged.

The National Standard Methods are issued by Standards Unit, Evaluations and Standards Laboratory, Centre for Infections, Health Protection Agency, London.

For further information please contact us at:

Standards Unit  
Evaluations and Standards Laboratory  
Centre for Infections  
Health Protection Agency  
Colindale, London  
NW9 5EQ

Email: [standards@hpa.org.uk](mailto:standards@hpa.org.uk)

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## REFERENCES

1. Department of Health NHS Executive: The Caldicott Committee. Report on the review of patient-identifiable information. London. December 1997.
2. Efstratiou A, George RC. Laboratory guidelines for the diagnosis of infections caused by *Corynebacterium diphtheriae* and *C. ulcerans*. World Health Organization. Commun Dis Public Health 1999;2:250-7.
3. Lipsky BA, Goldberger AC, Tompkins LS, Plorde JJ. Infections caused by nondiphtheria corynebacteria. Rev Infect Dis 1982;4:1220-35.
4. Efstratiou A, Tiley SM, Sangrador A, Greenacre E, Cookson BD, Chen SC, et al. Invasive disease caused by multiple clones of *Corynebacterium diphtheriae*. Clin Infect Dis 1993;17:136.
5. Reacher M, Ramsay M, White J, De Zoysa A, Efstratiou A, Mann G, et al. Nontoxigenic corynebacterium diphtheriae: an emerging pathogen in England and Wales? Emerg Infect Dis 2000;6:640-5.
6. De Zoysa A, Efstratiou A. Eighth International Meeting of the European Laboratory Working Group on Diphtheria and the Diphtheria Surveillance Network - June 2004 : Progress is needed to sustain control of diphtheria in European Region. Euro Surveill 2004;9.
7. Nekrassova LS, Chudnaya LM, Marievski VF, Oksiuk VG, Gladkaya E, Bortnitska II, et al. Epidemic diphtheria in Ukraine, 1991-1997. J Infect Dis 2000;181 Suppl 1:S35-S40.
8. Markina SS, Maksimova NM, Vitek CR, Bogatyreva EY, Monisov AA. Diphtheria in the Russian Federation in the 1990s. J Infect Dis 2000;181 Suppl 1:S27-S34.
9. Salisbury DM, Begg NT, editors. Immunisation against infectious diseases. London: HMSO; 1996. p. 67-76
10. CDR Weekly. CDR. diphtheria acquired during a cruise in the Baltic sea. PHLS CDSC. <http://www.hpa.org.uk/cdr/archives/cdr97/cdr2497.pdf>. 207.
11. Diphtheria Notifications, laboratory isolates of *Corynebacterium diphtheriae*, deaths and vaccine uptake rates. [http://www.hpa.org.uk/infections/topics\\_az/diphtheria/data\\_death\\_vaccine.htm](http://www.hpa.org.uk/infections/topics_az/diphtheria/data_death_vaccine.htm).

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