UK Health Security Agency

UK Standards for Microbiology Investigations

Identification of *Actinomyces* and reclassified species

National Institute for Health and Care Excellence (NICE) has renewed accreditation of the process used by the **UK Health Security Agency** to produce **UK Standards for Microbiology Investigations (UK SMIs)**. The renewed accreditation is valid until **30 June 2026** and applies to guidance produced using the processes described in '**UK Standards for Microbiology Investigations Development Process' (2021)**. The original accreditation term began on 1 July 2011.

Issued by the Standards Unit, Specialised Microbiology and Laboratories, UKHSA

Acknowledgments

UK Standards for Microbiology Investigations (UK SMIs) are developed under the auspices of UKHSA working in partnership with the partner organisations whose logos are displayed below and listed on the UK SMI website. UK SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see the Steering Committee page on GOV.UK).

The contributions of many individuals in clinical, specialist and reference laboratories who have provided information and comments during the development of this document are acknowledged. We are grateful to the medical editors for editing the medical content.

UK SMIs are produced in association with:

Displayed logos correct as of March 2021

UKHSA publications gateway number:

Contents

Amendment table

Each UK SMI document has an individual record of amendments. The amendments are listed on this page. The amendment history is available from standards@ukhsa.gov.uk.

Any alterations to this document should be controlled in accordance with the local document control process.

Amendment number/date	x/dd.mm.yy
Issue number discarded	
Insert issue number	
Anticipated next review date	dd.mm.yy
Section(s) involved	**Amendment**
Title	The title has been changed from 'Identification of Anaerobic *Actinomyces* species' to 'Identification of *Actinomyces* and reclassified species'

1 General information

View general information related to UK SMIs.

2 Scientific information

View scientific information related to UK SMIs.

3 Scope of document

This UK Standards for Microbiology Investigations (UK SMI) document describes the identification of *Actinomyces* species and includes routine culture, MALDI-TOF MS and gene sequencing for identification. This document does not provide information on antimicrobial susceptibility testing of *Actinomyces* species.

Some of the *Actinomyces* species have been reclassified, and the updated nomenclature of these species have been included in this document for reference.

UK SMIs should be used in conjunction with other relevant UK SMIs.

4 Introduction

4.1 Taxonomy and characteristics

Actinomyces species are gram-positive, filamentous, microaerophilic to facultative anaerobes with high G-C DNA content. The genus *Actinomyces* is in the family *Actinomycetaceae* of the order *Actinomycetales* which belongs to the phylum *Actinomycetota* (*Actinobacteria*) - one of the largest and most diverse phyla among the bacteria (1-3).

Currently, there are 58 *Actinomyces* species validly published with the correct nomenclature and taxonomic status (2). Please refer to the most up to date nomenclature available as changes within the genus are commonplace and may occur following the publication of this UK SMI.

The genus was revised in 2018 and a number of clinically significant species have been designated to alternative genera (see Table 1). For simplicity the original nomenclature has been retained throughout this UK SMI.

Actinomyces species are opportunistic pathogens that form part of the usual microbiota of humans, they typically colonise the oral cavity, gastrointestinal tract, and female urogenital tract. Actinomycosis is a relatively rare and generally polymicrobial infection caused by *Actinomyces* species especially in immunocompromised individuals (4,5).

The main causative agent is *Actinomyces israelii* but other *Actinomyces* species have also been reported including *Actinomyces odontolyticus*, *Actinomyces viscosus*, *Actinomyces gerencseriae* and *Actinomyces naeslundii*. The clinical presentation of the actinomycosis can vary depending on the severity and site of infection (6-11).

Species within this group have also been identified as clinically significant pathogens in breast abscesses and other non-classical actinomycosis infections (12), of particular note Arachnia propionica is associated with canaliculitis (13).

5 Technical information and limitations

Advancements in technology and gene sequencing have significantly contributed to the evolving taxonomy of *Actinomyces*, leading to numerous reclassification and changes in nomenclature of these species (2,3,14). Refer to section 7, table 1 for the reclassified *Actinomyces* species to date.

The complex taxonomy of *Actinomyces* species can lead to uncertainty and inconsistency in their identification, therefore it is important that clinicians stay up to date with the latest taxonomic revisions and resources and incorporate them into their interpretation of laboratory results. It is also important that the databases of identification methods such as MALDI-TOF MS and 16S rRNA gene sequencing reflect any changes in the taxonomy of *Actinomyces* (15).

6 Safety considerations

The section covers specific safety considerations (16-37) related to this UK SMI, and should be read in conjunction with the general safety considerations on GOV.UK.

Actinomyces species and associated Gram-positive species are Hazard group 2 organisms. The processing of diagnostic samples should be carried out at Containment Level 2.

Refer to current guidance on the safe handling of all organisms documented in this UK SMI.

Laboratory procedures that give rise to infectious aerosols must be conducted in a microbiological safety cabinet (25).

The above guidance should be supplemented with local COSHH and risk assessments. Compliance with postal and transport regulations is essential.

7 Target organisms

Table 1. *Actinomyces* species reported to have caused human infection (38-54)

Previous nomenclature	Current nomenclature
Actinomyces israelii	*Actinomyces israelii*
Actinomyces graevenitzii	*Actinomyces graevenitzii*
Actinomyces gerencseriae	*Actinomyces gerencseriae*
Actinomyces naeslundii	*Actinomyces naeslundii*
Actinomyces odontolyticus	*Schaalia odontolytica*
Actinomyces viscosus	*Actinomyces viscosus*
Actinomyces funkei	*Schaalia funkei*
Actinomyces europaeus	*Gleimia europaea*
Actinomyces urogenitalis	*Actinomyces urogenitalis*
Actinomyces meyeri	*Schaalia meyeri*
Actinomyces neuii	*Winkia neuii*
Actinomyces neuii subsp *neuii*	*Winkia neuii* subsp. *neuii*
Actinomyces neuii subsp *anitratus*	*Winkia neuii* subsp. *anitrata*
Actinomyces radingae	*Schaalia radingae*
Actinomyces turicensis	*Schaalia turicensis*
Actinomyces radicidentis	*Actinomyces radicidentis*
Actinomyces cardiffensis	*Schaalia cardiffensis*
Actinomyces oricola	*Actinomyces oricola*
Actinomyces nasicola	*Bowdeniella nasicola*
Actinomyces massiliensis	*Actinomyces massiliensis*
Actinomyces johnsonii	*Actinomyces johnsonii*
Actinomyces dentalis	*Actinomyces dentalis*
Actinomyces hongkongensis	*Pauljensenia hongkongensis*
Actinomyces hominis	*Gleimia hominis*
Actinomyces oris	*Actinomyces oris*
Actinomyces timonensis	*Actinomyces timonensis*
Actinomyces georgiae	*Schaalia georgiae*

Table 2. Other organisms which may be misidentified as *Actinomyces* species

Previous nomenclature	Current nomenclature
(Pseudo)Propionibacterium propionicum	*Arachnia propionica*
Scardovia wiggsiae	*Scardovia wiggsiae*
Nocardia species	*Nocardia* species

8 Identification

Culture-based methods remain the gold standard for identification, however laboratories have increasingly integrated faster identification techniques such as MALDI-TOF MS. There is also a growing shift towards molecular methods for identification. However, these techniques require specialised laboratories, trained staff and expensive reagents which may not be available to all routine laboratories.

8.1 Culture methods

Culture methods provide presumptive identification of *Actinomyces* species based on colony morphology, Gram stain and other phenotypic characteristics followed by identification via MALDI-TOF MS and if necessary, confirmation using 16S rRNA gene sequencing.

8.1.1 Bacterial growth media

Some *Actinomyces* species are fastidious and slow growing (for example, *A israelii, A. gerencseriae*) and require enriched medium, with growth enhanced by the addition of carbon dioxide. Anaerobic conditions are favoured but some species can be cultured aerobically or in air plus 5 to 10% CO_2 (55).The optimum growth temperature is 35 to 37ºC (54,55). Colonies may appear after 3 to 7 days of incubation, but detection may require 10 to 14 days of incubation (54). Refer to section 8.1.3, table 3 for colony morphology.

Note: The majority of *Actinomyces* species are facultative anaerobes, with the exception of *A israelii*, *A gerencseriae* and *A meyeri* which are strict anaerobes (56).

8.1.1.1 Primary isolation media

Fastidious anaerobic agar or equivalent agar **without neomycin** incubated anaerobically at 35 to 37ºC for 5 to 10 days (55).

Note: Many *Actinomyces* species may be inhibited by neomycin.

8.1.1.2 Selective media

Actinomyces selective agar with metronidazole 10mg/L and nalidixic acid 30mg/L (deep fill) incubated anaerobically at 35 to 37ºC for 5 to 10 days (55). Growth in air and in air plus 5 to 10% CO_2 is variable. Broth enrichment is rarely beneficial.

Note: Some species may require longer incubation

8.1.2 Colonial appearance

Actinomyces species exhibit various appearances (54,57). Only a few species produce the classic breadcrumb/molar tooth colonies, refer to section 8.2, table 3. The majority are white or grey in colour, with some producing pigmentation following prolonged incubation periods.

8.2 Microscopic appearance

Actinomyces colonies can be examined directly and/or following Gram staining to assess their colony and cellular morphology. Members of the genus demonstrate considerable variation in cellular and colony morphology, which can make their recognition and identification challenging (54,57,58). A combination of different laboratory techniques can aid in their accurate identification.

Note: Clinical specimens such as pus can also be examined directly under the microscope to detect sulphur granules suggesting Actinomycosis (55)

8.2.1 Gram stain

Refer to TP 39 - Staining procedures

Branching, beaded, filamentous or diphtheroid-shaped or coccobacillary Gram positive bacilli.

Note: *Propionibacterium and Cutibacterium* species are pleomorphic bacilli that may appear to branch. *Nocardia* species are morphologically indistinguishable from *Actinomyces* species on Gram stain (59).

Table 3. Microscopic and colonial morphology of *Actinomyces* species (2)

The information here provides general characteristics of colony appearance, which can vary among different strains and culture conditions.

Species	Colonies	Comments
A. israelii	White to cream, breadcrumb, or molar tooth, gritty, pitting	Slow growing
A. gerensceriae	Bright white, breadcrumb, or molar tooth, pitting and softer than *A. israelii*	Slow growing

A. naeslundii	White, cream, or pinkish, smooth, convex, entire edged	Occasional rough forms occur. Acid production may affect viability in older cultures.
A. odontolyticus	Cream to red, smooth, convex, entire edged	Old colonies may be dark brown. Acid production may affect viability in older cultures.
A. meyeri	Small, white, smooth, convex, entire edged	Slow growing
A. georgiae	White or cream, smooth, convex, entire edged	
A. neuii sub sp. *neuii* and *anitratius*	White or cream, smooth, convex, entire edged	
A. radingae	Grey to white, semi-translucent, smooth, low convex, entire edge	
A. turicensis	Grey, semi translucent, smooth, low convex, entire edged	
A. europaeus	Whitish, semi translucent, smooth, low convex, entire edged	
*A. graevenitzii**	White pronounced molar tooth or smooth, convex	Red fluorescence. Rough and smooth forms occur together. Old colonies may become dark brown
A. radicidentis	Cream to pink, smooth, convex, entire edged	Old colonies may become red
A. urogenitalis	Cream to-pink, with darker rings, smooth	Old colonies may become red. Acid production may affect viability in older cultures.
A. funkei	Grey, semi translucent, opaque centre (fried egg), low convex, entire edged	
A. cardiffensis	Cream to pink, smooth, convex, entire edged	
A. nasicola	White or grey, smooth, convex, entire edged	
A. oricola	White, breadcrumb, pitting on the agar	
A. viscosus	The two types of colonies: large and smooth colonies with V, Y and T configurations or small and rough colonies with short branching filaments.	
A. johnsonii	Colonies are similar to *A. naeslundii*	Acid production may affect viability in older cultures.
A. oris	Colonies are similar to *A. naeslundii*	Acid production may affect viability in older cultures.
A. massiliensis	white, pinpoint, circular and shiny with entire edges	

A. dentalis	tiny, white and breadcrumb-like and pitting on the agar	
A. hongkongensis	non-haemolytic, pinpoint colonies	
A. hominis	white–greyish, convex, entire edges	
A. timonensis	α-haemolytic, pinpoint, circular, white, dry and embedded in the agar	
*P. propionicum**	Off white to buff, breadcrumb, gritty, pitting, or smooth, convex, entire edged	Red fluorescence, rough and smooth forms occur together
Scardovia wiggsiae	White to cream, breadcrumb, or molar tooth, gritty, pitting.	Very slow growing. May not identify by conventional methods.
*Colonies of *A. graevenitzii* and *P. propionicum* on blood containing media fluoresce red under long-wave (366 nm) UV illumination.		

8.3 Matrix-assisted laser desorption/ionisation - time of flight mass spectrometry (MALDI-TOF MS)

MALDI-TOF MS is currently used as the primary method for the identification of *Actinomyces* species, while 16S rRNA gene sequencing serves as an alternative identification approach or is employed as a confirmatory method.

However, the changing taxonomy and reclassification of *Actinomyces* species poses a challenge for species-level identification (2,3,14). The reference database used by MALDI-TOF MS instruments need to be reviewed regularly and updated with the evolving nomenclature and classification of *Actinomyces* species to ensure accurate identification (15,58,60,63).

Also, closely related *Actinomyces* species exhibit similar protein profiles, making it difficult to distinguish between them, which can lead to misidentification (15,60,61). Additional confirmatory testing with molecular methods such as 16S rRNA gene sequencing may be required.

In addition, the performance of MALDI-TOF MS can be influenced by colony age and morphology. Older colonies or colonies with drier and ‘chalkier’ morphology can negatively impact the quality of the mass spectral output and subsequently reduce the accuracy of identification of *Actinomyces* species (58,64).

Overall, MALDI-TOF MS is a valuable tool for the identification of *Actinomyces* species, but the factors that limit its effectiveness need to be taken into consideration and tackled by the continual improvement of reference databases and sample preparation processes as well as confirmatory testing when required.

8.4 Further identification

8.4.1 Biochemical tests and commercial identification systems

Biochemical tests including commercial identification kits provide basic biochemical information that can aid in the identification of *Actinomyces* species. However, relying solely on these tests is insufficient for accurate identification of *Actinomyces* species. Therefore, these tests are either not considered reliable for the identification of *Actinomyces* species or employed as part of a multi-step approach that combines alternative identification techniques to achieve more accurate results.

Refer to manufacturer's guidance or Manual of Clinical Microbiology for the biochemical properties of *Actinomyces* species and associated gram-positive species (65).

8.4.1 Indole test

Refer to TP 19 – Indole test

Actinomyces species are spot indole negative

Note: *Propionibacterium/Cutibacterium acnes* is indole positive

8.4.2 Catalase test

Refer to TP 8 – Catalase test

All *Actinomyces* species are catalase negative except *Actinomyces viscous*, *Actinomyces neuii* subsp *neuii*, *Actinomyces neuii* subsp *anitratus* and *Actinomyces radicidentis* and *Actinomyces bonmis* (57,66).

Laboratories should follow manufacturers' instructions and rapid tests and kits should be validated and be shown to be fit for purpose prior to use.

Results should be interpreted with caution and in conjunction with other test results. To achieve accurate results with biochemical tests, it is advisable to use taxonomic keys and not rely on the identification given by the code. This is because the databases contain out of date information, are incomplete or due variation in reaction strengths/occasional weak enzymatic and sugar fermentation reactions (67,68). This is particularly true as molecular techniques enable more species to be identified than was previously possible (68).

8.4.2 Molecular methods

Molecular techniques have made identification of many species more rapid and precise than is possible with phenotypic techniques. The routine implementation of molecular methods can be challenging, as not all clinical laboratories have access to the different molecular methods.

Therefore, in such cases significant isolates identified by MALDI-TOF MS should be sent to appropriate reference labs for further testing and confirmation of results if required.

8.4.2.1 16S rRNA gene sequencing

The utilisation of 16S rRNA gene sequencing has transformed the identification and taxonomy of *Actinomyces* species (3,14).

Although MALDI-TOF MS is the primary technique for the identification of *Actinomyces* species, 16S rRNA gene sequencing is employed in laboratories as a confirmatory method to resolve any discrepancies and provide more accurate identification of *Actinomyces* species.

However, 16S rRNA gene sequencing also has limitations, these include the challenge of differentiating between some closely related *Actinomyces* species such as *Actinomyces naeslundii*, *Actinomyces viscosus* and *Actinomyces oris*, which can lead to misidentification (58). Within 16S sequencing databases erroneous sequences exist that may appear as the top match. Therefore, it is important to corroborate results using a different identification method such as MALDI-TOF MS and to continue improving and expanding the reference databases to include a comprehensive range of *Actinomyces* species including novel species to reflect current classifications (15,58).

The implementation of 16S rRNA gene sequencing for *Actinomyces* identification can be challenging, as not all clinical laboratories have access to this sequencing technique. In this case any significant isolates should be sent to appropriate reference laboratory.

8.4.2.2 Next generation sequencing (NGS)

With the increased availability of NGS technologies, there may be a shift towards their utilisation for the identification and prediction of antimicrobial susceptibility of *Actinomyces* alongside other target pathogens in future. However currently these technologies are largely restricted to reference units.

Whole genome sequencing (WGS) is routinely used by UKHSA and has greatly improved surveillance capabilities and monitoring trends in antimicrobial resistance. WGS has replaced traditional phenotypic and polymerase chain reaction (PCR) methods for routine surveillance. It also has high discriminatory power and can provide in-depth genetic analysis and identification (69). Therefore, it has the potential to be an alternative to techniques like MALDI-TOF MS for the identification of *Actinomyces* species and associated Gram-positive species.

8.5 Storage and referral

If required, inoculate the pure isolate into anaerobic broth culture or scrape pure growth on to a charcoal transport swab (or anaerobic transport swab) for referral to the appropriate reference laboratory.

9 Reporting

9.1 Infection Specialist

Inform the infection specialist of presumptive or confirmed *Actinomyces* when the request bears relevant information.

9.2 Presumptive identification

If appropriate growth characteristics, colonial appearance and Gram stain of the culture are demonstrated and the isolate is metronidazole non-susceptible.

9.3 Confirmation of identification

If MALDI-TOF MS and/or 16S rRNA gene sequencing identify *Actinomyces* spp.

For further confirmation and identification please refer to section 10.

9.4 Health Protection Team (HPT)

N/A

9.5 UK Health Security Agency

N/A

9.6 Infection prevention and control team

N/A

10 Referral to reference laboratories

For information on the tests offered, turnaround times, transport procedure and the other requirements of the reference laboratory see user manuals and request forms

Contact appropriate reference laboratory for information on the tests available, turnaround times, transport procedure and any other requirements for sample submission:

England

Wales

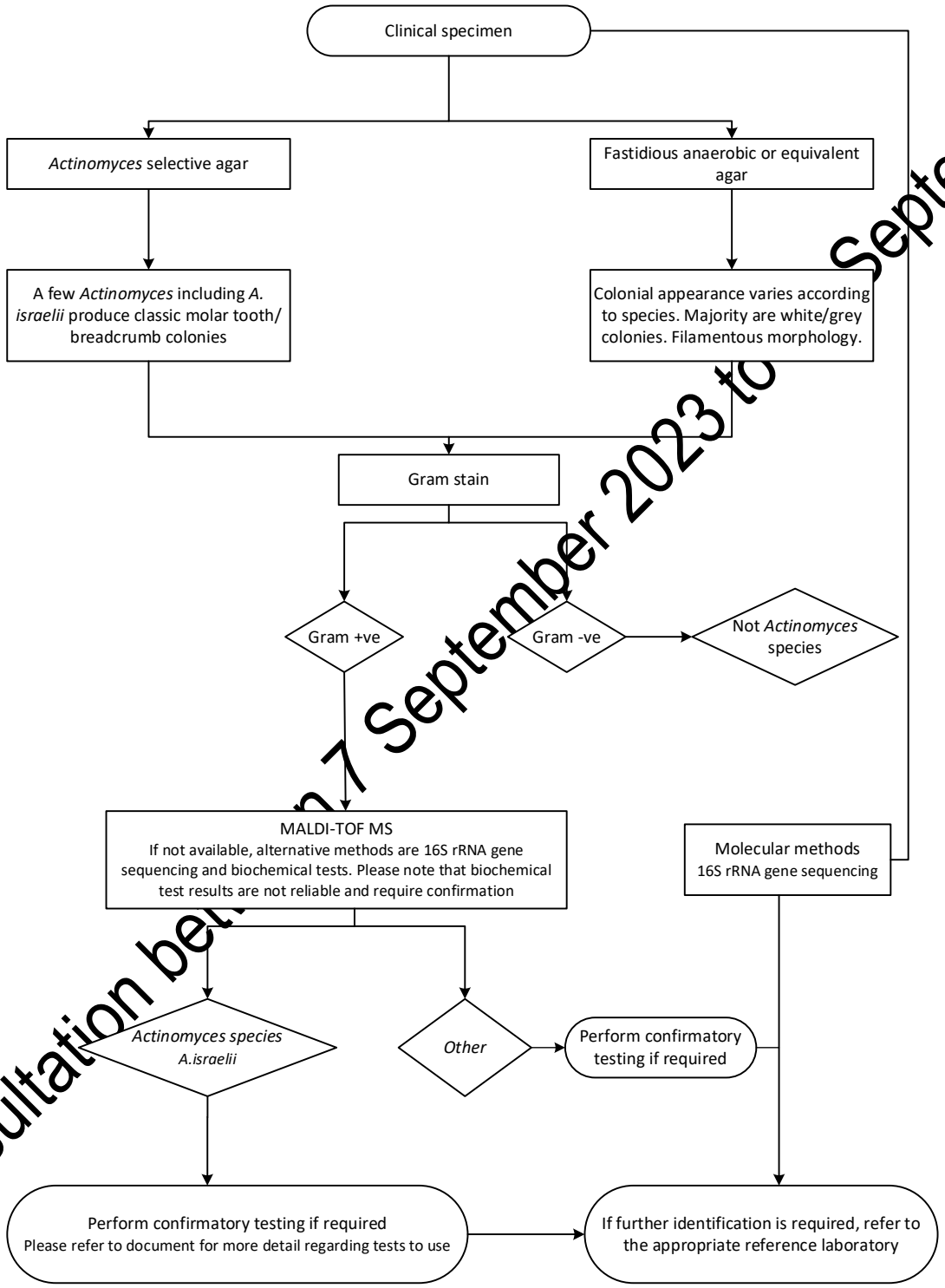
Scotland

Northern Ireland

Note: In case of sending away to laboratories for processing, ensure that specimen is placed in appropriate package and transported accordingly.

Algorithm: Identification of *Actinomyces* and reclassified species

An accessible text description of this flowchart is provided with this document



The flowchart is for guidance only.

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An explanation of the reference assessment used is available in the scientific information section on the UK SMI website.

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