ANNEX II

4. CASE DEFINITIONS OF SPECIAL HEALTH ISSUES

4.1. GENERAL CASE DEFINITION OF NOSOCOMIAL INFECTION (OR 'HEALTHCARE-ASSOCIATED INFECTION (HAI)')

A nosocomial infection associated to the current hospital stay is defined as infection that matches one of the case definitions AND

— the onset of symptoms was on day 3 or later (day of admission = day 1) of the current hospital admission OR

— the patient underwent surgery on day 1 or day 2 and develops symptoms of a Surgical Site Infection before day 3 OR

— an invasive device was placed on day 1 or day 2 resulting in an HAI before day 3

A nosocomial infection associated to a previous hospital stay is defined as an infection that matches one of the case definitions

AND

— the patient presents with an infection but has been readmitted less than 48 hours after a previous admission to an acute care hospital

OR

— the patient has been admitted with an infection that meets the case definition of a Surgical Site Infection i.e. the SSI occurred within 30 days of the operation (or in the case of surgery involving an implant was a deep or organ/space SSI that developed within 90 days of the operation) and the patient either has symptoms that meet the case definition and/or is on antimicrobial treatment for that infection

OR

— the patient has been admitted (or develops symptoms within 2 days) with *Clostridium difficile* infection less than 28 days from a previous discharge from an acute care hospital.

Note: For the purpose of point prevalence surveys, an active nosocomial infection present on the day of the survey is defined as an infection for which signs and symptoms of the infection are present on the survey date or signs and symptoms were present in the past and the patient is (still) receiving treatment for that infection on the survey date. The presence of symptoms and signs should be verified until the start of the treatment in order to determine whether the treated infection matches one of the case definitions of nosocomial infection

4.1.1. **BJ: Bone and joint infection**

BJ-BONE: Osteomyelitis

Osteomyelitis must meet at least one of the following criteria:

— Patient has organisms cultured from bone

— Patient has evidence of osteomyelitis on direct examination of the bone during a surgical operation or histopathologic examination

— Patient has at least 2 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), localized swelling, tenderness, heat, or drainage at suspected site of bone infection

AND at least 1 of the following:

— organisms cultured from blood

— positive blood antigen test (for example, *Haemophilus influenzae*, *Streptococcus pneumoniae*)
— radiographic evidence of infection (for example, abnormal findings on X-ray, CT scan, MRI, radiolabel scan (gallium, technetium, etc.)).

Note reporting instruction

Report mediastinitis following cardiac surgery that is accompanied by osteomyelitis as surgical site infection-organ/space (SSI-O).

BJ-JNT: Joint or bursa

Joint or bursa infections must meet at least one of the following criteria:

— Patient has organisms cultured from joint fluid or synovial biopsy
— Patient has evidence of joint or bursa infection seen during a surgical operation or histopathologic examination
— Patient has at least two of the following signs or symptoms with no other recognized cause: joint pain, swelling, tenderness, heat, evidence of effusion or limitation of motion

AND at least one of the following:
— organisms and white blood cells seen on Gram's stain of joint fluid
— positive antigen test on blood, urine, or joint fluid
— cellular profile and chemistries of joint fluid compatible with infection and not explained by an underlying rheumatologic disorder
— radiographic evidence of infection (for example, abnormal findings on X-ray, CT scan, MRI, radiolabel scan (gallium, technetium, etc.))

BJ-DISC: Disc space infection

Vertebral disc space infection must meet at least one of the following criteria:

— Patient has organisms cultured from vertebral disc space tissue obtained during a surgical operation or needle aspiration
— Patient has evidence of vertebral disc space infection seen during a surgical operation or histopathologic examination
— Patient has fever (> 38 °C) with no other recognized cause or pain at the involved vertebral disc space

AND radiographic evidence of infection (for example, abnormal findings on X-ray, CT scan, MRI, radiolabel scan (gallium, technetium, etc.)).
— Patient has fever (> 38 °C) with no other recognized cause and pain at the involved vertebral disc space

AND positive antigen test on blood or urine (for example, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, or Group B *Streptococcus*).

4.1.2. **BSI: Bloodstream infection**

BSI: Laboratory-confirmed bloodstream infection

One positive blood culture for a recognised pathogen

OR

Patient has at least one of the following signs or symptoms: fever (> 38 °C), chills, or hypotension

AND Two positive blood cultures for a common skin contaminant (from 2 separate blood samples, usually within 48 hours)

Skin contaminants = coagulase-negative staphylococci, *Micrococcus* spp., *Propionibacterium acnes*, *Bacillus* spp., *Corynebacterium* spp.

Source of bloodstream infection:

— Catheter-related: the same micro-organism was cultured from the catheter or symptoms improve within 48 hours after removal of the catheter (C-PVC: peripheral catheter, C-CVC: central venous catheter (*Note:* report C-CVC or C-PVC BSI as CRI3-CVC or CRI3-PVC respectively if microbiologically confirmed, see CRI3 definition)).

— Secondary to another infection: the same micro-organism was isolated from another infection site or strong clinical evidence exists that bloodstream infection was secondary to another infection site, invasive diagnostic procedure or foreign body
  — Pulmonary (S-PUL)
  — Urinary tract infection (S-UTI)
  — Digestive tract infection (S-DIG)
  — SSI (S-SSI): surgical site infection
  — Skin and soft tissue (S-SST)
  — Other (S-OTH)

— Unknown origin (UO): None of the above, bloodstream infection of unknown origin (verified during survey and no source found)

— Unknown (UNK): No information available about the source of the bloodstream infection or information missing

4.1.3. **CNS: Central nervous system infection**

CNS-IC: Intracranial infection (brain abscess, subdural or epidural infection, encephalitis)

Intracranial infection must meet at least one of the following criteria:

— Patient has organisms cultured from brain tissue or dura

— Patient has an abscess or evidence of intracranial infection seen during a surgical operation or histopathologic examination

— Patient has at least 2 of the following signs or symptoms with no other recognized cause: headache, dizziness, fever (> 38 °C), localizing neurologic signs, changing level of consciousness, or confusion

  AND at least 1 of the following:
  — organisms seen on microscopic examination of brain or abscess tissue obtained by needle aspiration or by biopsy during a surgical operation or autopsy
  — positive antigen test on blood or urine
  — radiographic evidence of infection (for example, abnormal findings on ultrasound, CT scan, MRI, radionuclide brain scan, or arteriogram)
  — diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen

  AND if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy.

Note reporting instruction

If meningitis and a brain abscess are present together, report the infection as IC

CNS-MEN: Meningitis or ventriculitis

Meningitis or ventriculitis must meet at least one of the following criteria:

— Patient has organisms cultured from cerebrospinal fluid (CSF)

— Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), headache, stiff neck, meningeal signs, cranial nerve signs, or irritability

AND at least one of the following:

— increased white cells, elevated protein, and/or decreased glucose in CSF

— organisms seen on Gram's stain of CSF

— organisms cultured from blood

— positive antigen test of CSF, blood, or urine

— diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen

AND if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy.

Note reporting instructions

— Report CSF shunt infection as SSI if it occurs <=90 days of placement; if > 90 days or after manipulation/access of the shunt, report as CNS-MEN if the infection meets the general case definition of HAI

— Report meningoencephalitis as MEN

— Report spinal abscess with meningitis as MEN

CNS-SA: Spinal abscess without meningitis

An abscess of the spinal epidural or subdural space, without involvement of the cerebrospinal fluid or adjacent bone structures, must meet at least one of the following criteria:

— Patient has organisms cultured from abscess in the spinal epidural or subdural space

— Patient has an abscess in the spinal epidural or subdural space seen during a surgical operation or at autopsy or evidence of an abscess seen during a histopathologic examination

— Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), back pain, focal tenderness, radiculitis, paraparesis, or paraplegia

AND at least 1 of the following:

— organisms cultured from blood

— radiographic evidence of a spinal abscess (for example, abnormal findings on myelography, ultrasound, CT scan, MRI, or other scans (gallium, technetium, etc.))

AND if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy

Note reporting instruction

Report spinal abscess with meningitis as meningitis (CNS-MEN)

4.1.4. **CRI: Catheter-related infection**[(1)]

CRI1-CVC: Local CVC-related infection (no positive blood culture)

— quantitative CVC culture ≥ 10^3 CFU/ml or semi-quantitative CVC culture > 15 CFU

— AND pus/inflammation at the insertion site or tunnel

CRI1-PVC: Local PVC-related infection (no positive blood culture)

— quantitative PVC culture ≥ 10^3 CFU/ml or semi-quantitative PVC culture > 15 CFU

— AND pus/inflammation at the insertion site or tunnel

CRI2-CVC: General CVC-related infection (no positive blood culture)

— quantitative CVC culture ≥ 10^3 CFU/ml or semi-quantitative CVC culture > 15 CFU

— AND clinical signs improve within 48 hours after catheter removal

CRI2-PVC: General PVC-related infection (no positive blood culture)

— quantitative PVC culture ≥ 10^3 CFU/ml or semi-quantitative PVC culture > 15 CFU

— AND clinical signs improve within 48 hours after catheter removal

CRI3-CVC: microbiologically confirmed CVC-related bloodstream infection

— BSI occurring 48 hours before or after catheter removal (if any)

AND positive culture with the same micro-organism of either:

— quantitative CVC culture ≥ 10^3 CFU/ml or semi-quantitative CVC culture > 15 CFU

— quantitative blood culture ratio CVC blood sample/peripheral blood sample > 5

— differential delay of positive blood cultures: CVC blood sample culture positive 2 hours or more before peripheral blood culture (blood samples drawn at the same time)

— positive culture with the same micro-organism from pus from insertion site

CRI3-PVC: microbiologically confirmed PVC-related bloodstream infection

BSI occurring 48 hours before or after catheter removal (if any)

AND positive culture with the same micro-organism of either:

— quantitative PVC culture ≥ 10^3 CFU/ml or semi-quantitative PVC culture > 15 CFU

— positive culture with the same micro-organism from pus from insertion site

4.1.5. **CVS: Cardiovascular system infection**

CVS-VASC: Arterial or venous infection

Arterial or venous infection must meet at least one of the following criteria:

— Patient has organisms cultured from arteries or veins removed during a surgical operation

AND blood culture not done or no organisms cultured from blood

— Patient has evidence of arterial or venous infection seen during a surgical operation or histopathologic examination

— Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), pain, erythema, or heat at involved vascular site

AND more than 15 colonies cultured from intravascular cannula tip using semiquantitative culture method

AND blood culture not done or no organisms cultured from blood

— Patient has purulent drainage at involved vascular site

AND blood culture not done or no organisms cultured from blood

Note reporting instructions

Report infections of an arteriovenous graft, shunt, or fistula or intravascular cannulation site without organisms cultured from blood as CVS-VASC. Report CVS-VASC matching the third criterion as CRI1 or CRI2, as appropriate.

CVS-ENDO: Endocarditis

Endocarditis of a natural or prosthetic heart valve must meet at least one of the following criteria:

— Patient has organisms cultured from valve or vegetation

— Patient has two or more of the following signs or symptoms with no other recognized cause: fever (> 38 °C), new or changing murmur, embolic phenomena, skin manifestations (for example, petechiae, splinter hemorrhages, painful subcutaneous nodules), congestive heart failure, or cardiac conduction abnormality

AND at least one of the following:

— organisms cultured from two or more blood cultures

— organisms seen on Gram's stain of valve when culture is negative or not done

— valvular vegetation seen during a surgical operation or autopsy

— positive antigen test on blood or urine (for example, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, or Group B *Streptococcus*)

— evidence of new vegetation seen on echocardiogram

AND if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy

CVS-CARD: Myocarditis or pericarditis

Myocarditis or pericarditis must meet at least one of the following criteria:

— Patient has organisms cultured from pericardial tissue or fluid obtained by needle aspiration or during a surgical operation

— Patient has at least two of the following signs or symptoms with no other recognized cause: fever (> 38 °C), chest pain, paradoxical pulse, or increased heart size

AND at least one of the following:

— abnormal EKG consistent with myocarditis or pericarditis

— positive antigen test on blood (for example, *Haemophilus influenzae*, *Streptococcus pneumoniae*)

— evidence of myocarditis or pericarditis on histologic examination of heart tissue

— 4-fold rise in type-specific antibody with or without isolation of virus from pharynx or feces

— pericardial effusion identified by echocardiogram, CT scan, MRI, or angiography

CVS-MED: Mediastinitis

Mediastinitis must meet at least one of the following criteria:

— Patient has organisms cultured from mediastinal tissue or fluid obtained during a surgical operation or needle aspiration

— Patient has evidence of mediastinitis seen during a surgical operation or histopathologic examination

— Patient has at least one of the following signs or symptoms with no other recognized cause: fever (> 38 °C), chest pain, or sternal instability

AND at least 1 of the following:

— purulent discharge from mediastinal area

— organisms cultured from blood or discharge from mediastinal area

— mediastinal widening on X-ray

Note reporting instruction

Report mediastinitis following cardiac surgery that is accompanied by osteomyelitis as SSI-O

4.1.6. **EENT: Eye, ear, nose, throat, or mouth infection**

EENT-CONJ: Conjunctivitis

Conjunctivitis must meet at least one of the following criteria:

— Patient has pathogens cultured from purulent exudate obtained from the conjunctiva or contiguous tissues, such as eyelid, cornea, meibomian glands, or lacrimal glands

— Patient has pain or redness of conjunctiva or around eye

AND at least 1 of the following:

— WBCs and organisms seen on Gram's stain of exudates

— purulent exudates

— positive antigen test (for example, ELISA or IF for *Chlamydia trachomatis*, herpes simplex virus, adenovirus) on exudate or conjunctival scraping

— multinucleated giant cells seen on microscopic examination of conjunctival exudate or scrapings

— positive viral culture

— diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen

Note reporting instructions

— Report other infections of the eye as EYE

— Do not report chemical conjunctivitis caused by silver nitrate ($AgNO_3$) as a health care-associated infection

— Do not report conjunctivitis that occurs as a part of a more widely disseminated viral illness (such as measles, chickenpox, or a URI)

EENT-EYE: Eye, other than conjunctivitis

An infection of the eye, other than conjunctivitis, must meet at least one of the following criteria:

— Patient has organisms cultured from anterior or posterior chamber or vitreous fluid

— Patient has at least 2 of the following signs or symptoms with no other recognized cause: eye pain, visual disturbance, or hypopyon

AND at least 1 of the following:

— physician diagnosis of an eye infection

— positive antigen test on blood (for example, *Haemophilus influenzae*, *Streptococcus pneumoniae*)

— organisms cultured from blood

EENT-EAR: Ear mastoid

Ear and mastoid infections must meet at least one of the following criteria:

Otitis externa must meet at least one of the following criteria:

— Patient has pathogens cultured from purulent drainage from ear canal

— Patient has at least one of the following signs or symptoms with no other recognized cause: fever (> 38 °C), pain, redness, or drainage from ear canal

— and organisms seen on Gram's stain of purulent drainage

Otitis media must meet at least one of the following criteria:

— Patient has organisms cultured from fluid from middle ear obtained by tympanocentesis or at surgical operation

— Patient has at least two of the following signs or symptoms with no other recognized cause: fever (> 38 °C), pain in the eardrum, inflammation, retraction or decreased mobility of eardrum, or fluid behind eardrum

Otitis interna must meet at least one of the following criteria:

— Patient has organisms cultured from fluid from inner ear obtained at surgical operation

— Patient has a physician diagnosis of inner ear infection

Mastoiditis must meet at least one of the following criteria:

— Patient has organisms cultured from purulent drainage from mastoid

— Patient has at least two of the following signs or symptoms with no other recognized cause: fever (> 38 °C), pain, tenderness, erythema, headache, or facial paralysis

AND at least 1 of the following:

— organisms seen on Gram's stain of purulent material from mastoid

— positive antigen test on blood

EENT-ORAL: Oral cavity (mouth, tongue, or gums)

Oral cavity infections must meet at least one of the following criteria:

— Patient has organisms cultured from purulent material from tissues of oral cavity

— Patient has an abscess or other evidence of oral cavity infection seen on direct examination, during a surgical operation, or during a histopathologic examination

— Patient has at least 1 of the following signs or symptoms with no other recognized cause: abscess, ulceration, or raised white patches on inflamed mucosa, or plaques on oral mucosa

AND at least one of the following:

— organisms seen on Gram's stain

— positive KOH (potassium hydroxide) stain

— multinucleated giant cells seen on microscopic examination of mucosal scrapings

— positive antigen test on oral secretions

— diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen

— physician diagnosis of infection and treatment with topical or oral antifungal therapy

Note reporting instruction

Report health care-associated primary herpes simplex infections of the oral cavity as ORAL; recurrent herpes infections are not healthcare-associated

EENT-SINU: Sinusitis

Sinusitis must meet at least 1 of the following criteria:

— Patient has organisms cultured from purulent material obtained from sinus cavity

— Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), pain or tenderness over the involved sinus, headache, purulent exudate, or nasal obstruction

AND at least 1 of the following:

— positive transillumination

— positive radiographic examination (including CT scan)

EENT-UR: Upper respiratory tract, pharyngitis, laryngitis, epiglottitis

Upper respiratory tract infections must meet at least 1 of the following criteria:

— Patient has at least two of the following signs or symptoms with no other recognized cause: fever (> 38 °C), erythema of pharynx, sore throat, cough, hoarseness, or purulent exudate in throat

  AND at least 1 of the following:
  - — organisms cultured from the specific site
  - — organisms cultured from blood
  - — positive antigen test on blood or respiratory secretions
  - — diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen
  - — physician diagnosis of an upper respiratory infection

— Patient has an abscess seen on direct examination, during a surgical operation, or during a histopathologic examination

4.1.7. **GI: Gastrointestinal system infection**

GI-CDI: Clostridium difficile infection

A *Clostridium difficile* infection (previously also referred to as *Clostridium difficile* associated diarrhoea or CDAD) must meet at least one of the following criteria:

— Diarrhoeal stools or toxic megacolon, AND a positive laboratory assay for *Clostridium difficile* toxin A and/or B in stools or a toxin-producing *C. difficile* organism detected in stool via culture or other means for example, a positive PCR result;

— Pseudomembranous colitis revealed by lower gastro-intestinal endoscopy

— Colonic histopathology characteristic of *Clostridium difficile* infection (with or without diarrhoea) on a specimen obtained during endoscopy, colectomy or autopsy

GI-GE: Gastroenteritis (excl. CDI)

Gastroenteritis must meet at least one of the following criteria:

— Patient has an acute onset of diarrhea (liquid stools for more than 12 hours) with or without vomiting or fever (> 38 °C) and no likely noninfectious cause (for example, diagnostic tests, therapeutic regimen other than antimicrobial agents, acute exacerbation of a chronic condition, or psychologic stress)

— Patient has at least 2 of the following signs or symptoms with no other recognized cause: nausea, vomiting, abdominal pain, fever (> 38 °C), or headache

  AND at least 1 of the following:
  - — an enteric pathogen is cultured from stool or rectal swab
  - — an enteric pathogen is detected by routine or electron microscopy
  - — an enteric pathogen is detected by antigen or antibody assay on blood or feces
  - — evidence of an enteric pathogen is detected by cytopathic changes in tissue culture (toxin assay)
  - — diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen

GI-GIT: Gastrointestinal tract (esophagus, stomach, small and large bowel, and rectum) excluding gastroenteritis and appendicitis

Gastrointestinal tract infections, excluding gastroenteritis and appendicitis, must meet at least 1 of the following criteria:

— Patient has an abscess or other evidence of infection seen during a surgical operation or histopathologic examination
— Patient has at least 2 of the following signs or symptoms with no other recognized cause and compatible with infection of the organ or tissue involved: fever (> 38 °C), nausea, vomiting, abdominal pain, or tenderness

AND at least 1 of the following:
— organisms cultured from drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain
— organisms seen on Gram's or KOH stain or multinucleated giant cells seen on microscopic examination of drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain
— organisms cultured from blood
— evidence of pathologic findings on radiographic examination
— evidence of pathologic findings on endoscopic examination (for example, *Candida* spp. esophagitis or proctitis)

GI-HEP: Hepatitis

Hepatitis must meet the following criterion:

Patient has at least 2 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), anorexia, nausea, vomiting, abdominal pain, jaundice, or history of transfusion within the previous 3 months

AND at least 1 of the following:
— positive antigen or antibody test for hepatitis A, hepatitis B, hepatitis C, or delta hepatitis
— abnormal liver function tests (for example, elevated ALT/AST, bilirubin)
— cytomegalovirus (CMV) detected in urine or oropharyngeal secretions

Note reporting instructions
— Do not report hepatitis or jaundice of non-infectious origin (alpha-1 antitrypsin deficiency, etc.)
— Do not report hepatitis or jaundice that results from exposure to hepatotoxins (alcoholic or acetaminophen-induced hepatitis, etc.)
— Do not report hepatitis or jaundice that results from biliary obstruction (cholecystitis)

GI-IAB: Intraabdominal, not specified elsewhere including gallbladder, bile ducts, liver (excluding viral hepatitis), spleen, pancreas, peritoneum, subphrenic or subdiaphragmatic space, or other intraabdominal tissue or area not specified elsewhere

Intraabdominal infections must meet at least one of the following criteria:
— Patient has organisms cultured from purulent material from intraabdominal space obtained during a surgical operation or needle aspiration
— Patient has abscess or other evidence of intraabdominal infection seen during a surgical operation or histopathologic examination
— Patient has at leasttwo of the following signs or symptoms with no other recognized cause: fever (> 38 °C), nausea, vomiting, abdominal pain, or jaundice

AND at least one of the following:
— organisms cultured from drainage from surgically placed drain (for example, closed suction drainage system, open drain, T-tube drain)
— organisms seen on Gram's stain of drainage or tissue obtained during surgical operation or needle aspiration

— organisms cultured from blood and radiographic evidence of infection (for example, abnormal findings on ultrasound, CT scan, MRI, or radiolabel scans (gallium, technetium, etc.) or on abdominal X-ray)

Note reporting instruction

Do not report pancreatitis (an inflammatory syndrome characterized by abdominal pain, nausea, and vomiting associated with high serum levels of pancreatic enzymes) unless it is determined to be infectious in origin

4.1.8. **LRI: Lower respiratory tract infection, other than pneumonia**

LRI-BRON: Bronchitis, tracheobronchitis, bronchiolitis, tracheitis, without evidence of pneumonia

Patient has no clinical or radiographic evidence of pneumonia

AND patient has at least two of the following signs or symptoms with no other recognized cause: fever (> 38 °C), cough, new or increased sputum production, rhonchi, wheezing

AND at least one of the following:

— positive culture obtained by deep tracheal aspirate or bronchoscopy

— positive antigen test on respiratory secretions

Note reporting instruction

Do not report chronic bronchitis in a patient with chronic lung disease as an infection unless there is evidence of an acute secondary infection, manifested by change in organism

LRI-LUNG: Other infections of the lower respiratory tract

Other infections of the lower respiratory tract must meet at least one of the following criteria:

— Patient has organisms seen on smear or cultured from lung tissue or fluid, including pleural fluid

— Patient has a lung abscess or empyema seen during a surgical operation or histopathologic examination

— Patient has an abscess cavity seen on radiographic examination of lung

Note reporting instruction

Report lung abscess or empyema without pneumonia as LUNG

4.1.9. **NEO: Specific neonatal case definitions**

NEO-CSEP: Clinical Sepsis

ALL of the three following criteria:

— Supervising physician started appropriate antimicrobial therapy for sepsis for at least 5 days

— No detection of pathogens in blood culture or not tested

— No obvious infection at another site

AND 2 of the following criteria (without other apparent cause):

— Fever (> 38 °C) or temperature instability (frequent post-set of the incubator) or hypothermia (< 36,5 °C)

— Tachycardia (> 200/min) or new/increased bradycardia (< 80/min)

— Capillary refilling time (CRT) > 2s

— New or increased apnoea (s) (> 20s)

— Unexplained metabolic acidosis

— New-onset hyperglycemia (> 140 mg/dl)

— Another sign of sepsis (skin colour (only if the CRT is not used), laboratory signs (CRP, interleukin), increased oxygen requirement (intubation), unstable general condition of the patient, apathy)

NEO-LCBI: Laboratory-confirmed BSI

at least two of: temperature > 38 °C or < 36,5 °C or temperature instability, tachycardia or bradycardia, apnoea, extended capillary refilling time (CRT), metabolic acidosis, hyperglycaemia, other sign of BSI such as apathy

AND

a recognised pathogen other than coagulase-negative staphylococci cultured from blood or cerebrospinal fluid (CSF; this is included because meningitis in this age group is usually haematogenous, so positive CSF can be regarded as evidence of BSI even if blood cultures are negative or were not taken)

Note reporting instructions

— in order to be consistent with BSI reporting in adults (including secondary BSI), the criterion 'the organism is not related to an infection at another site' was removed from the Neo-KISS definition for the purposes of the EU PPS

— report the origin of the neonatal BSI in the field BSI origin

— if both the case definitions for NEO-LCBI and NEO-CNSB are matched, report NEO-LCBI

NEO-CNSB: Laboratory-confirmed BSI with coagulase-negative staphylococci

— at least two of: temperature > 38 °C or < 36,5 °C or temperature instability, tachycardia or bradycardia, apnoea, extended recapillarisation time, metabolic acidosis, hyperglycaemia, other sign of BSI such as apathy

— AND coagulase-negative staphylococci is cultured from blood or catheter tip

— AND patient has one of: C-reactive protein > 2,0 mg/dL, immature/total neutrophil ratio (I/T ratio) > 0,2, leukocytes < 5/nL, platelets < 100/nL

Note reporting instructions

— in order to be consistent with BSI reporting in adults (including secondary BSI), the criterion 'the organism is not related to an infection at another site' was removed from the Neo-KISS definition for the purposes of the EU PPS

— report the origin of the neonatal BSI in the field BSI origin

— if both the case definitions for NEO-LCBI and NEO-CNSB are matched, report NEO-LCBI

NEO-PNEU: Pneumonia

— respiratory compromise

— AND new infiltrate, consolidation or pleural effusion on chest X ray

— AND at least four of: temperature > 38 °C or < 36,5 °C or temperature instability, tachycardia or bradycardia, tachypnoea or apnoea, dyspnoea, increased respiratory secretions, new onset of purulent sputum, isolation of a pathogen from respiratory secretions, C-reactive protein > 2,0 mg/dL, I/T ratio > 0,2

NEO-NEC: Necrotising enterocolitis

Histopathological evidence of necrotising enterocolitis

OR

at least one characteristic radiographic abnormality (pneumoperitoneum, pneumatosis intestinalis, unchanging 'rigid' loops of small bowel) plus at least two of the following without other explanation: vomiting, abdominal distention, prefeeding residuals, persistent microscopic or gross blood in stools

4.1.10. **PN: Pneumonia**

Two or more serial chest X-rays or CT-scans with a suggestive image of pneumonia for patients with underlying cardiac or pulmonary disease. In patients without underlying cardiac or pulmonary disease one definitive chest X-ray or CT-scan is sufficient

AND at least one of the following symptoms

— Fever > 38 °C with no other cause

— Leukopenia (< 4 000 WBC/mm^3) or leucocytosis (≥ 12 000 WBC/mm^3)

AND at least one of the following (or at least two if clinical pneumonia only = PN 4 and PN 5)

— New onset of purulent sputum, or change in character of sputum (colour, odour, quantity, consistency)

— Cough or dyspnea or tachypnea

— Suggestive auscultation (rales or bronchial breath sounds), ronchi, wheezing

— Worsening gas exchange (for example, O_2 desaturation or increased oxygen requirements or increased ventilation demand)

and according to the used diagnostic method

(a) *Bacteriologic diagnostic performed by:*

Positive quantitative culture from minimally contaminated LRT[(2)] specimen (PN 1)

— Broncho-alveolar lavage (BAL) with a threshold of ≥ 10^4 CFU[(3)]/ml or ≥ 5 % of BAL obtained cells contains intracellular bacteria on direct microscopic exam (classified on the diagnostic category BAL)

— Protected brush (PB Wimberley) with a threshold of ≥ 10^3 CFU/ml

— Distal protected aspirate (DPA) with a threshold of ≥ 10^3 CFU/ml

Positive quantitative culture from possibly contaminated LRT specimen (PN 2)

— Quantitative culture of LRT specimen (for example, endotracheal aspirate) with a threshold of 10^6 CFU/ml

(b) *Alternative microbiology methods (PN 3)*

— Positive blood culture not related to another source of infection

— Positive growth in culture of pleural fluid

— Pleural or pulmonary abscess with positive needle aspiration

— Histologic pulmonary exam shows evidence of pneumonia

— Positive exams for pneumonia with virus or particular germs (for example, *Legionella*, *Aspergillus*, mycobacteria, mycoplasma, *Pneumocystis jirovecii*):

  — Positive detection of viral antigen or antibody from respiratory secretions (for example, EIA, FAMA, shell vial assay, PCR)

  — Positive direct exam or positive culture from bronchial secretions or tissue

  — Seroconversion (for example, influenza viruses, *Legionella*, *Chlamydia*)

  — Detection of antigens in urine (*Legionella*)

(c) *Others*

— Positive sputum culture or non-quantitative LRT specimen culture (PN 4)

— No positive microbiology (PN 5)

Notes:

— One definitive chest X-ray or CT-scan for the current pneumonia episode may be sufficient in patients with underlying cardiac or pulmonary disease if comparison with previous X-rays is possible.

— PN 1 and PN 2 criteria were validated without previous antimicrobial therapy. However, this does not exclude the diagnosis of PN 1 or PN 2 in case of previous antimicrobial use.

Intubation-associated pneumonia (IAP)

A pneumonia is defined as intubation-associated (IAP) if an invasive respiratory device was present (even intermittently) in the 48 hours preceding the onset of infection

Note: Pneumonia for which intubation was started on the day of onset without additional information on the sequence of the events is not considered as IAP

4.1.11. **REPR: Reproductive tract infection**

REPR-EMET: Endometritis

Endometritis must meet at least 1 of the following criteria:

— Patient has organisms cultured from fluid or tissue from endometrium obtained during surgical operation, by needle aspiration, or by brush biopsy

— Patient has at least 2 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), abdominal pain, uterine tenderness, or purulent drainage from uterus

Note reporting instruction

Report postpartum endometritis as a health care-associated infection unless the amniotic fluid is infected at the time of admission or the patient was admitted 48 hours after rupture of the membrane

REPR-EPIS: Episiotomy

Episiotomy infections must meet at least 1 of the following criteria:

— Postvaginal delivery patient has purulent drainage from the episiotomy

— Postvaginal delivery patient has an episiotomy abscess

REPR-VCUF: Vaginal cuff

Vaginal cuff infections must meet at least 1 of the following criteria:

— Posthysterectomy patient has purulent drainage from the vaginal cuff

— Posthysterectomy patient has an abscess at the vaginal cuff

— Posthysterectomy patient has pathogens cultured from fluid or tissue obtained from the vaginal cuff

Note reporting instruction

Report vaginal cuff infections as SSI-O if other SSI criteria are met (within 30 days following hysterectomy).

REPR-OREP: Other infections of the male or female reproductive tract (epididymis, testes, prostate, vagina, ovaries, uterus, or other deep pelvic tissues, excluding endometritis or vaginal cuff infections)

Other infections of the male or female reproductive tract must meet at least 1 of the following criteria:

— Patient has organisms cultured from tissue or fluid from affected site

— Patient has an abscess or other evidence of infection of affected site seen during a surgical operation or histopathologic examination

— Patient has 2 of the following signs or symptoms with no other recognized cause: fever (> 38 °C), nausea, vomiting, pain, tenderness, or dysuria

AND at least 1 of the following:

— organisms cultured from blood

— physician diagnosis

Note reporting instructions

— Report endometritis as EMET

— Report vaginal cuff infections as VCUF

4.1.12. **SSI: Surgical site infection**

Note: All definitions are to be assumed to be confirmed for the purposes of surveillance reporting.

Superficial incisional (SSI-S)

Infection occurs within 30 days after the operation AND infection involves only skin and subcutaneous tissue of the incision AND at least one of the following:

— Purulent drainage with or without laboratory confirmation, from the superficial incision

— Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision

— At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat AND superficial incision is deliberately opened by surgeon, unless incision is culture-negative

— Diagnosis of superficial incisional SSI made by a surgeon or attending physician

Deep incisional (SSI-D)

Infection occurs within 30 days after the operation if no implant is left in place or within 90 days if implant is in place AND the infection appears to be related to the operation AND infection involves deep soft tissue (for example, fascia, muscle) of the incision AND at least one of the following:

— Purulent drainage from the deep incision but not from the organ/space component of the surgical site

— A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (> 38 °C), localized pain or tenderness, unless incision is culture-negative

— An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination

— Diagnosis of deep incisional SSI made by a surgeon or attending physician

Organ/Space (SSI-O)

Infection occurs within 30 days after the operation if no implant is left in place or within 90 days if implant is in place AND the infection appears to be related to the operation AND infection involves any part of the anatomy (for example, organs and spaces) other than the incision which was opened or manipulated during an operation AND at least one of the following:

— Purulent drainage from a drain that is placed through a stab wound into the organ/space

— Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space

— An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination

— Diagnosis of organ/space SSI made by a surgeon or attending physician

4.1.13. **SST: Skin and soft tissue infection**

SST-SKIN: Skin infection

Skin infections must meet at least one of the following criteria:

— Patient has purulent drainage, pustules, vesicles, or boils

— Patient has at least two of the following signs or symptoms with no other recognized cause: pain or tenderness, localized swelling, redness, or heat

AND at least one of the following:

— organisms cultured from aspirate or drainage from affected site; if organisms are normal skin flora (for example, diphtheroids (*Corynebacterium* spp.), *Bacillus* (not *B. anthracis*) spp., *Propionibacterium* spp., coagulase-negative staphylococci (including *Staphylococcus epidermidis*), viridans group streptococci, *Aerococcus* spp., *Micrococcus* spp.), they must be a pure culture

— organisms cultured from blood

— positive antigen test performed on infected tissue or blood

— multinucleated giant cells seen on microscopic examination of affected tissue

— diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen

Note reporting instructions

— Report infected decubitus ulcers as DECU

— Report infected burns as BURN

— Report breast abscesses or mastitis as BRST

SST-ST: Soft tissue (necrotizing fascitis, infectious gangrene, necrotizing cellulitis, infectious myositis, lymphadenitis, or lymphangitis)

Soft tissue infections must meet at least 1 of the following criteria:

— Patient has organisms cultured from tissue or drainage from affected site

— Patient has purulent drainage at affected site

— Patient has an abscess or other evidence of infection seen during a surgical operation or histopathologic examination

— Patient has at least 2 of the following signs or symptoms at the affected site with no other recognized cause: localized pain or tenderness, redness, swelling, or heat

AND at least 1 of the following:

— organisms cultured from blood

— positive antigen test performed on blood or urine (for example, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, Group B *Streptococcus*, *Candida* spp.)

— diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for pathogen

Note reporting instructions

— Report infected decubitus ulcers as DECU

— Report infection of deep pelvic tissues as OREP

SST-DECU: Decubitus ulcer, including both superficial and deep infections

Decubitus ulcer infections must meet the following criterion:

— Patient has at least 2 of the following signs or symptoms with no other recognized cause: redness, tenderness, or swelling of decubitus wound edges

AND at least one of the following:
— organisms cultured from properly collected fluid or tissue
— organisms cultured from blood

SST-BURN: Burn

Burn infections must meet at least 1 of the following criteria:
— Patient has a change in burn wound appearance or character, such as rapid eschar separation, or dark brown, black, or violaceous discoloration of the eschar, or edema at wound margin
— and histologic examination of burn biopsy shows invasion of organisms into adjacent viable tissue
— Patient has a change in burn wound appearance or character, such as rapid eschar separation, or dark brown, black, or violaceous discoloration of the eschar, or edema at wound margin

AND at least one of the following:
— organisms cultured from blood in the absence of other identifiable infection
— isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsies or lesion scrapings
— Patient with a burn has at least two of the following signs or symptoms with no other recognized cause: fever (> 38 °C) or hypothermia (< 36 °C), hypotension, oliguria (< 20 cc/hr), hyperglycemia at previously tolerated level of dietary carbohydrate, or mental confusion

AND at least one of the following:
— histologic examination of burn biopsy shows invasion of organisms into adjacent viable tissue
— organisms cultured from blood
— isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsies or lesion scrapings

SST-BRST: Breast abscess or mastitis

A breast abscess or mastitis must meet at least one of the following criteria:
— Patient has a positive culture of affected breast tissue or fluid obtained by incision and drainage or needle aspiration
— Patient has a breast abscess or other evidence of infection seen during a surgical operation or histopathologic examination
— Patient has fever (> 38 °C) and local inflammation of the breast

AND physician diagnosis of breast abscess

4.1.14. **SYS: Systemic infection**
SYS-DI: Disseminated infection

Disseminated infection is infection involving multiple organs or systems, without an apparent single site of infection, usually of viral origin, and with signs or symptoms with no other recognized cause and compatible with infectious involvement of multiple organs or systems
Note reporting instructions

— Use this code for viral infections involving multiple organ systems (for example, measles, mumps, rubella, varicella, erythema infectiosum). These infections often can be identified by clinical criteria alone.
— Do not use this code for healthcare-associated infections with multiple metastatic sites, such as with bacterial endocarditis; only the primary site of these infections should be reported
— Do not report fever of unknown origin (FUO) as DI
— Report viral exanthems or rash illness as DI

SYS-CSEP: treated unidentified severe infection

Patient has at least one of the following
— clinical signs or symptoms with no other recognized cause
— fever (> 38 °C)
— hypotension (systolic pressure < 90 mm/Hg)
— or oliguria (20 cm^3 (ml)/hr)

And blood culture not done or no organisms or antigen detected in blood

And no apparent infection at another site

And physician institutes treatment for sepsis

Note reporting instructions

Do not use this code unless absolutely needed

For CSEP in neonates, use NEO-CSEP case definition (see below)

4.1.15. **UTI: Urinary tract infection**

UTI-A: microbiologically confirmed symptomatic UTI

Patient has at least one of the following signs or symptoms with no other recognized cause: fever (> 38 °C), urgency, frequency, dysuria, or suprapubic tenderness

AND

patient has a positive urine culture, that is, $\geq 10^5$ microorganisms per ml of urine with no more than two species of microorganisms.

UTI-B: not microbiologically confirmed symptomatic UTI

Patient has at least two of the following with no other recognized cause: fever (> 38 °C), urgency, frequency, dysuria, or suprapubic tenderness

AND

at least one of the following:
— Positive dipstick for leukocyte esterase and/or nitrate
— Pyuria urine specimen with $\geq 10^4$ WBC/ml or ≥ 3 WBC/high-power field of unspun urine
— Organisms seen on Gram stain of unspun urine
— At least two urine cultures with repeated isolation of the same uropathogen (Gram-negative bacteria or *Staphylococcus saprophyticus*) with $\geq 10^2$ colonies/ml urine in nonvoided specimens

— $\leq 10^5$ colonies/ml of a single uropathogen (Gram-negative bacteria or *Staphylococcus saprophyticus*) in a patient being treated with effective antimicrobial agent for a urinary infection
— Physician diagnosis of a urinary tract infection
— Physician institutes appropriate therapy for a urinary infection

Asymptomatic bacteriuria should not be reported, but bloodstream infections secondary to asymptomatic bacteriuria are reported as BSI with source (origin) S-UTI

A urinary tract infection is defined as catheter-associated if an indwelling urinary catheter was present (even intermittently) in the 7 days preceding the onset of infection

4.2. GENERAL CASE DEFINITION OF BLOOD STREAM INFECTION DUE TO SPECIFIC PATHOGENS

Clinical criteria

Not relevant for surveillance purposes

Laboratory criteria

At least one blood culture positive for *Staphylococcus aureus* or *Klebsiella pneumoniae* or *Escherichia coli* or *Enterococcus faecium* or *Enterococcus faecalis* or *Pseudomonas aeruginosa* or *Acinetobacter* species or *Streptococcus pneumoniae*.

Epidemiological criteria

Not relevant for surveillance purposes

Case classification

A. Possible case NA

B. Probable case NA

C. Confirmed case

Antimicrobial resistance

The results of antimicrobial susceptibility tests must be reported according to the methods and criteria agreed between ECDC and Member States as specified by ECDC's European Antimicrobial Resistance Surveillance Network (EARS-Net)[(4)], and in particular:

— for *Staphylococcus aureus*: susceptibility to meticillin and other anti-staphylococcal beta-lactams;
— for *Enterococcus faecium* and *Enterococcus faecalis*: susceptibility to glycopeptides;
— for *Klebsiella pneumoniae* and *Escherichia coli*: susceptibility to carbapenems, and susceptibility to colistin in carbapenem-resistant isolates;
— for *Pseudomonas aeruginosa* and *Acinetobacter* species: susceptibility to carbapenems.

4.3. GENERIC CASE DEFINITION AND CLASSIFICATION OF ANTIMICROBIAL REISTANCE TO ANTIMICROBIAL AGENTS

Clinical resistance to antimicrobial agents

Definition

A micro-organism is classified as clinically susceptible, clinically intermediate, or clinically resistant to an antimicrobial agent by applying the appropriate EUCAST clinical breakpoints in a standardized methodology (or a methodology calibrated to a standardized methodology)[(5)], i.e. clinical minimum inhibitory concentration (MIC) breakpoints and their inhibition zone diameter correlates. Breakpoints may be altered with legitimate changes in circumstances.

Classification
Clinically Susceptible (S)
— a micro-organism is defined as susceptible (S) by a level of antimicrobial exposure associated with a high likelihood of therapeutic success.
Clinically Intermediate (I)
— a micro-organism is defined as intermediate (I) by a level of antimicrobial agent activity associated with uncertain therapeutic effect. It implies that an infection due to the isolate may be appropriately treated in body sites where the drugs are physically concentrated or when a dosage regimen of drug producing higher exposure can be used; it also indicates a buffer zone that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations.
Clinically Resistant (R)
— a micro-organism is defined as resistant (R) by a level of antimicrobial exposure associated with a high likelihood of therapeutic failure.

Clinical breakpoints[5] are presented as:
— S: MIC ≤ x mg/L; disk diffusion zone diameter ≥ σ mm
— I: MIC > x, ≤ y mg/L; disk diffusion zone diameter ≥ ρ mm, < σ mm
— R: MIC > y mg/L; disk diffusion zone diameter < ρ mm
Pandrug-resistant (PDR)
— for *Staphylococcus aureus*, *Enterococcus* species, Enterobacteriaceae including *Klebsiella pneumoniae* and *Escherichia coli*, *Pseudomonas aeruginosa* and *Acinetobacter* species, an isolate is defined as pandrug-resistant (PDR) based on the fact that it is resistant to all antimicrobial agents, as in the international expert proposal for interim standard definitions for acquired resistance[6]
— an isolate is defined as confirmed PDR when it is non-susceptible (i.e. intermediate — I, or resistant — R) to all agents in all antimicrobial categories, confirmed by a reference or other clinical microbiology laboratory testing a supplemental panel of antimicrobial agents beyond those routinely tested, in accordance with the definitions by microorganism in the international expert proposal for interim standard definitions for acquired resistance[7]
— an isolate is defined as possibly PDR when it is non-susceptible (i.e. intermediate — I, or resistant — R) to all the antimicrobial agents tested in the laboratory
— an isolate is defined as not PDR when it is susceptible to at least one of the tested antimicrobial agents

Microbiological resistance to antimicrobial agents
Phenotypic definition

A microorganism is classified as having a wild-type phenotype or a non-wild-type phenotype for a species according to the EUCAST epidemiological cut-off concentrations (ECOFFs) in a standardized methodology (or a methodology calibrated to a standardized methodology)[8][9] based on species-specific MIC distributions and their inhibition zone diameter correlates.
Phenotypic classification
Wild-type (WT) phenotype
— a micro-organism is defined as wild-type (WT) for a species or species complex when it is devoid of phenotypically-detectable acquired resistance mechanism
Non-wild-type (NWT) phenotype
— a micro-organism is defined as non-wild-type (NWT) for a species when it expresses at least one phenotypically-detectable acquired resistance mechanism

ECOFFs are presented as[9]

— WT: ECOFF ≤ x mg/L; disk diffusion zone diameter ≥ σ mm

— NWT: ECOFF > x mg/L; disk diffusion diameter < σ mm

Identification of an acquired antimicrobial resistance mechanism (for example, drug inactivating enzyme, modification of drug target protein type, efflux pump)

Expression of an acquired antimicrobial resistance mechanism by a micro-organism can be determined in vitro and the type of mechanism identified using standardized methodology according to the EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance[10]

Genotypic definition

A microorganism is classified as harbouring or lacking a genetic determinant or combination of determinants conferring to it a non-wild type susceptibility phenotype in relation to antimicrobial agent (transferable gene or core gene mutation). The presence of a genetic determinant or combination of determinants conferring to it a non-wild type susceptibility phenotype in relation to one or several antimicrobial agents can be shown by detecting and identifying the corresponding nucleic acid sequence(s) in a bacterial genome.

Genotypic classification

Genotypes are reported as:

— Positive: presence of [name of resistance gene or core gene mutation]

— Negative: absence of [name of resistance gene] or wild-type core gene sequence

(**1**) CVC = central vascular catheter, PVC = peripheral vascular catheter. Central vascular catheter colonisation should not be reported. A CRI3 (-CVC or -PVC) is also a bloodstream infection with source C-CVC or C-PVC respectively; however when a CRI3 is reported, the BSI should not be reported in the point prevalence survey; microbiologically confirmed catheter-related BSI should be reported as CRI3

(**2**) LRT = Lower Respiratory Tract

(**3**) CFU = Colony Forming Units

(**4**) The criteria for reporting are published each year as part of the Antimicrobial resistance (AMR) reporting protocol. See: Antimicrobial resistance (AMR) reporting protocol. European Antimicrobial Resistance Surveillance Network (EARS-Net). www.ecdc.europa.eu

(**5**) http://www.eucast.org/clinical_breakpoints/. Equivalent quantitative antimicrobial susceptibility testing (AST) methods may be used instead of MIC or disk diffusion if endorsed by EUCAST.

(**6**) Magiorakos AP, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012 Mar;18(3):268-81. http://www.sciencedirect.com/science/article/pii/S1198743X14616323

(**7**) Magiorakos AP, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012 Mar;18(3):268-81. http://www.sciencedirect.com/science/article/pii/S1198743X14616323

(**8**) http://www.eucast.org/ast_of_bacteria/

(**9**) http://www.eucast.org/mic_distributions_and_ecoffs/

(**10**) http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Resistance_mechanisms/EUCAST_detection_of_resistance_mechanisms_v1.0_20131211.pdf

Changes to legislation:
There are currently no known outstanding effects for the Commission Implementing Decision (EU) 2018/945, Division 4..