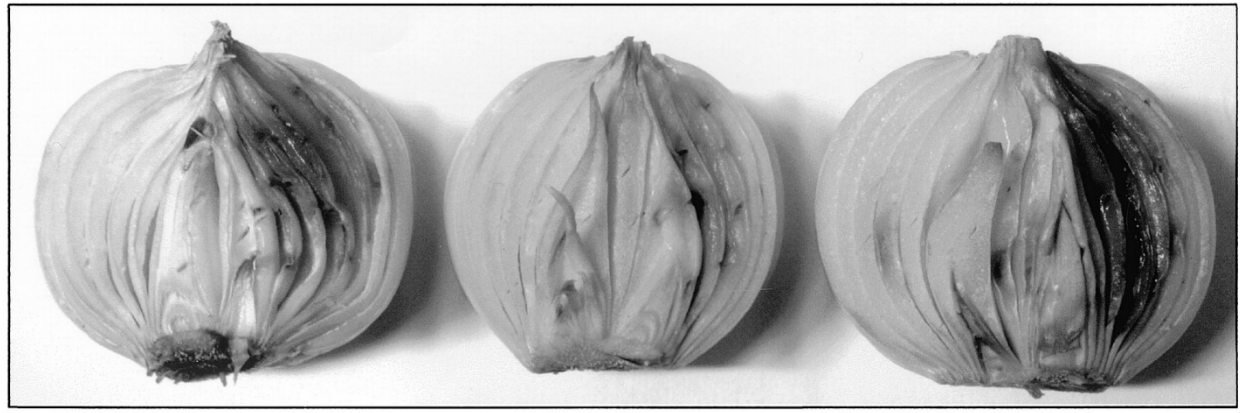
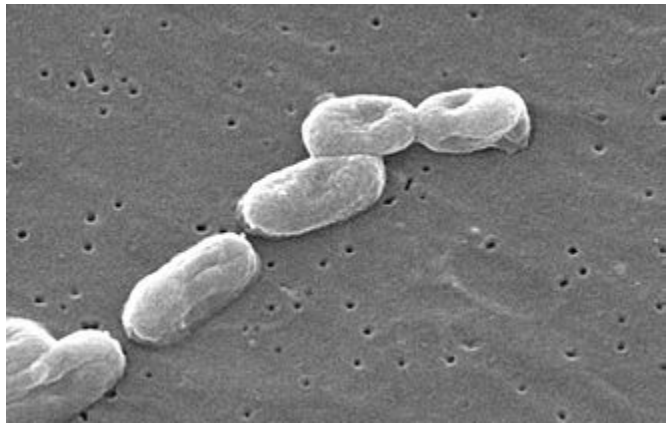
Burkholderia cepacia complex 洋蔥伯克氏菌



B. cepacia ATCC 25416 | *B. cepacia* 25416-I | *B. cepacia* 25416-I (pMPIR)

- Formerly known as *Pseudomonas cepacia*
- A group of closely related Gram-negative, non-lactose fermenting bacteria
- Found in natural environments including soil, water, plants and animals
- First Discovered in 1949 as the cause of onion skin rot, first described as a human pathogen in the 1950s
- Opportunistic human pathogen that most commonly causes pneumonia in immunocompromised patients and patients with cystic fibrosis or chronic granulomatous disease (CGD)
- Nine genomovars, *Burkholderia cenocepacia* (genomovar III) and *Burkholderia multivorans* (genomovar II) are the most common causes of *B. cepacia* colonization and infection in cystic fibrosis patients
- Naturally resistant to multiple antibiotics including polymixin B and aminoglycoside



Photos from Wikipedia and Applied and Environmental Microbiology Mar 2003, 69 (3) 1739-1747;

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Department of Health

Burkholderia lata Infections from Intrinsically Contaminated Chlorhexidine Mouthwash, Australia, 2016.
Leong LEX, Lagana D, Carter GP, Wang Q, Smith K, Stinear TP, Shaw D, Sintchenko V, Wesselingh SL, Bastian I, Rogers GB.
Emerg Infect Dis. 2018 Nov;24(11):2109-2111. doi: 10.3201/eid2411.171929.

Outbreak of **Burkholderia cepacia** pseudobacteraemia caused by intrinsically contaminated commercial 0.5% chlorhexidine solution in neonatal intensive care units.
Song JE, Kwak YG, Um TH, Cho CR, Kim S, Park IS, Hwang JH, Kim N, Oh GB.
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Morillo Á, Torres MJ, Alonso Salas MT, Conde M, Aznar J.
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de Frutos M, López-Urrutia L, Domínguez-Gil M, Arias M, Muñoz-Bellido JL, Eiros JM, Ramos C.
Enferm Infecc Microbiol Clin. 2017 Dec;35(10):624-629. doi: 10.1016/j.eimc.2016.06.016. Epub 2016 Aug 3. English, Spanish.

[Outbreak due to **Serratia marcescens** associated with intrinsic contamination of aqueous chlorhexidine].
Hervé B, Chomali M, Gutiérrez C, Luna M, Rivas J, Blamey R, Espinoza R, Izquierdo G, Cabezas C, Alvarez C, de la Fuente S.
Rev Chilena Infectol. 2015 Oct;32(5):517-22. doi: 10.4067/S0716-10182015000600004. Spanish.

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Ko S, An HS, Bang JH, Park SW.
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An outbreak of **Burkholderia cenocepacia** associated with contaminated chlorhexidine solutions prepared in the hospital.
Lee S, Han SW, Kim G, Song DY, Lee JC, Kwon KT.
Am J Infect Control. 2013 Sep;41(9):e93-6. doi: 10.1016/j.ajic.2013.01.024. Epub 2013 Apr 19.

Hospital outbreak of **Burkholderia stabilis** bacteraemia related to contaminated chlorhexidine in haematological malignancy patients with indwelling catheters.
Heo ST, Kim SJ, Jeong YG, Bae IG, Jin JS, Lee JC.
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Outbreak of **Burkholderia cepacia** bacteremia caused by contaminated chlorhexidine in a hemodialysis unit.
Romero-Gómez MP, Quiles-Melero MI, Peña García P, Gutiérrez Altes A, García de Miguel MA, Jiménez C, Valdezate S, Sáez Nieto JA.
Infect Control Hosp Epidemiol. 2008 Apr;29(4):377-8. doi: 10.1086/529032. No abstract available.

Outbreak of **Achromobacter xylosoxidans** pseudobacteremia in a neonatal care unit related to contaminated chlorhexidine solution.
Molina-Cabrillana J, Santana-Reyes C, González-García A, Bordes-Benítez A, Horcajada I.
Eur J Clin Microbiol Infect Dis. 2007 Jun;26(6):435-7. No abstract available.

OUTBREAKS/PSEUDO-OUTBREAKS IN CONTAMINATED CHG SOLUTION

Chlorhexidine gluconate (CHX) and benzalkonium chloride (BZK) formulations are frequently used as antiseptics in healthcare and consumer products. *Burkholderia cepacia* complex (BCC) contamination of pharmaceutical products could be due to the use of contaminated water in the manufacturing process, over-diluted antiseptic solutions in the product, and the use of outdated products, which in turn reduces the antimicrobial activity of CHX and BZK. To establish a "safe use" period following opening containers of CHX and BZK, we measured the antimicrobial effects of CHX (2–10 μg/ml) and BZK (10–50 μg/ml) at sublethal concentrations on six strains of *Burkholderia cenocepacia* using chemical and microbiological assays. CHX (2, 4, and 10 μg/ml) and BZK (10, 20, and 50 μg/ml) stored for 42 days at 23°C showed almost the same concentration and toxicity compared with freshly prepared CHX and BZK on *B. cenocepacia* strains. When 5 μg/ml CHX and 20 μg/ml BZK were spiked to six *B. cenocepacia* strains with different inoculum sizes (10^0–10^5 CFU/ml), their toxic effects were not changed for 28 days. *B. cenocepacia* strains in diluted CHX
10^2 CFU/ml after incubation for 28 days at 23°
toxicity of both antiseptics were not observed, our results indicate that *B. cenocepacia* strains could remain viable in CHX and BZK for 28 days, which in turn, indicates the importance of control measures to monitor BCC contamination in pharmaceutical products.

Concentrations below 0.05% may be insufficient to kill or inhibit the growth of B. cenocepacia.

J. Microbiol. Biotechnol. (2017), 27(12), 2211–2220
https://doi.org/10.4014/jmb.1706.06034

750-bed, secondary care hospital in Daegu, Republic of Korea

Chlorhexidine was purchased by the hospital pharmacy as a 5% solution and diluted with water to 0.05%, 0.5%, 2%, and 4% solutions by health care workers in the manufacturing laboratory of the hospital pharmacy. The water used to dilute chlorhexidine was purified by the purification system (Millipore, Billerica, MA) in the hospital's manufacturing laboratory.

This system was equipped with a 0.22-μm pore sized filter, which was satisfactory to industry standards for sterile drug products. However, environmental cultures displayed that the water supplied by the purification system was contaminated with *B cenocepacia*. The guidance for the industry on sterile drug products states that every process of dilution must perform aseptic techniques and terminal sterilization of drug products,[10] but they were not performed in the hospital laboratory. This might result in outbreak of *B cenocepacia*.

BCC infection sites include SSI, resp tract, CABSI and chemoport insertion site

From October to December 2007, an outbreak of *Burkholderia cenocepacia* occurred in a secondary care hospital. The 19 *B cenocepacia* isolated from the patients, the chlorhexidine solutions of each different ward, and the purified water that diluted these solutions exhibited an identical pulsed-field gel electrophoresis pattern. Inadequate preparation of chlorhexidine solutions diluted with contaminated purified water may have resulted in an outbreak of *B cenocepacia*. Adequate preparation of chlorhexidine solutions should be emphasized.

An outbreak of Burkholderia cenocepacia associated with contaminated chlorhexidine solutions prepared in the hospital. American Journal of Infection Control Volume 41, Issue 9, September 2013, Pages e93-e96
https://www.sciencedirect.com/science/article/pii/S0196655313001867?via%3Dihub

Burkholderia lata Infections from Intrinsically Contaminated Chlorhexidine Mouthwash, Australia, 2016

Lex E.X. Leong, Diana Lagana, Glen P. Carter, Qinning Wang, Kija Smith, Tim P. Stinear, David Shaw, Vitali Sintchenko, Steven L. Wesselingh, Ivan Bastian, Geraint B. Rogers

Author affiliations: South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia (L.E.X. Leong, S.L. Wesselingh, G.B. Rogers); Flinders University, Bedford Park, South Australia, Australia (L.E.X. Leong, G.B. Rogers); Royal Adelaide Hospital, Adelaide (D. Lagana, D. Shaw); University of Melbourne, Melbourne, Victoria, Australia (G.P. Carter, T.P. Stinear); The University of Sydney, Westmead, New South Wales, Australia (Q. Wang, V. Sintchenko); SA Pathology, Adelaide (K. Smith, I. Bastian)

DOI: https://doi.org/10.3201/eid2411.171929

Burkholderia lata was isolated from 8 intensive care patients at 2 tertiary hospitals in Australia. Whole-genome sequencing demonstrated that clinical and environmental isolates originated from a batch of contaminated commercial chlorhexidine mouthwash. Genomic analysis identified efflux pump–encoding genes as potential facilitators of bacterial persistence within this biocide.

bacterial contamination of chlorhexidine mouthwash (0.2% mg/mL)

blood and tracheal aspirates from 8 ICU patients in two hospitals

ICT noted discoloration of a commercial chlorhexidine mouthwash with all 5 bottles cultured positive

Also obtained from the surfaces of hand basins in separate ICU rooms, where bottles of mouthwash from the contaminated batch were in use

nationwide recall of the contaminated mouthwash batch with no more case reported

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 24, No. 11, November 2018
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6199994/pdf/17-1929.pdf

SUMMARY

Background: *Burkholderia cepacia* is intrinsically resistant to certain antiseptics. The authors noted a sudden increase in the frequency of isolation of *B. cepacia* from blood cultures in a neonatal intensive care unit (NICU) of a university-affiliated hospital.

Aim: To identify the source and intervene in the ongoing infections.

Methods: The cases were defined as patients with positive blood cultures for *B. cepacia* in an NICU between November 2014 and January 2015. Medical records were reviewed and NICU healthcare workers were interviewed. Samples of suspected antiseptics, blood culture bottles, cotton balls, gauze and a needle used in the NICU were analysed microbiologically.

Findings: During the outbreak period, *B. cepacia* was identified in 25 blood cultures obtained from 21 patients. The clinical features of the patients were suggestive of pseudobacteraemia. Regarding environmental samples, *B. cepacia* was cultured from 0.5% chlorhexidine gluconate (CHG) solution products that had been used as a skin antiseptic during blood drawing in the NICU. The clinical *B. cepacia* isolate and two strains obtained from 0.5% CHG exhibited identical pulsed-field gel electrophoresis patterns. After the CHG products were withdrawn, the outbreak was resolved.

Conclusions: The pseudobacteraemia cases were caused by contaminated 0.5% CHG produced by a single manufacturer. Stricter government regulation is needed to prevent contamination of disinfectants during manufacturing. In addition, microbial contamination of antiseptics and disinfectants should be suspected when a *B. cepacia* outbreak occurs in hospitalized patients.

Skin antiseptic (intrinsic) contamination resulting in pseudo-bacteremia in NICU in Korea

Outbreak of Burkholderia cepacia pseudobacteraemia caused by intrinsically contaminated commercial 0.5% chlorhexidine solution in neonatal intensive care units. J Hosp Infect. 2018 Mar;98(3):295-299. doi: 10.1016/j.jhin.2017.09.012. Epub 2017 Sep 19.

J Vet Diagn Invest. 2018 Sep;30(5):763-769. doi: 10.1177/1040638718782333. Epub 2018 Jun 7.

Cellulitis caused by the Burkholderia cepacia complex associated with contaminated chlorhexidine 2% scrub in five domestic cats.

Wong JK[1,2,3,4,5,6], Chambers LC[1,2,3,4,5,6], Elsmo EJ[1,2,3,4,5,6], Jenkins TL[1,2,3,4,5,6], Howerth EW[1,2,3,4,5,6], Sánchez S[1,2,3,4,5,6], Sakamoto K[1,2,3,4,5,6].

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6 Athens Veterinary Diagnostic Laboratory and Department of Infectious Diseases (Sánchez), College of Veterinary Medicine, University of Georgia, Athens, GA.

Abstract

Isolates of the Burkholderia cepacia complex (BCC) are known as plant and human pathogens. We describe herein BCC infections as the cause of subcutaneous abscesses and purulent cellulitis in 5 cats. All cats were presented with an open wound, and 4 received standard wound care and empiric antibiotic therapy. Despite treatment, clinical signs worsened in 4 cats. Isolates of the BCC were obtained from all 5 cases. Two cats were submitted for postmortem examination. Subcutaneous abscesses with draining fistulas were observed. Histopathology revealed severe, pyogranulomatous cellulitis with intralesional gram-negative bacilli. Based on susceptibility results, the other 3 cats were administered effective antibiotics and recovered without complications. The BCC was cultured from the 2% chlorhexidine surgical scrub solution used in the clinic, suggesting the source of infection for 4 of 5 cats. Given the ability to grow in antiseptic solutions, the extra steps required to culture from antiseptics, and innate multidrug resistance, the BCC poses a challenge to both detect and treat. Although the BCC causes disease almost exclusively in humans with cystic fibrosis or immunodeficiency, the bacteria should also be a differential for nosocomial infections in veterinary patients.

Perit Dial Int. 2019 Jan-Feb;39(1):92-95. doi: 10.3747/pdi.2018.00095.

Burkholderia cepacia: An Outbreak in the Peritoneal Dialysis Unit.

Gleeson S[1], Mulroy E[2], Bryce E[3], Fox S[4], Taylor SL[5], Talreja H[4].

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Abstract

Burkholderia cepacia is a ubiquitous, opportunistic, environmental gram-negative bacillus which most commonly affects cystic fibrosis and immunocompromised patients. Rarely, it can cause peritoneal dialysis (PD) exit-site infection (ESI). Information relating to predisposing factors, clinical course, and treatment options for *B. cepacia* ESIs is limited. Although reports of *B. cepacia* healthcare-associated infections exist, outbreaks in PD units have not previously been reported. A recent outbreak of *B. cepacia* ESI in our PD unit provided a unique opportunity to study *B. cepacia* ESIs and to outline an approach to investigating such an outbreak.After unexpectedly identifying *B. cepacia* as the cause of PD catheter ESIs in 3 patients over an 11-week period, we began systematically screening our PD population for *B. cepacia* exit-site colonization. A further 6 patients were found to be affected, 3 with asymptomatic colonization and 3 with symptomatic *B. cepacia* ESI. Four of the 6 developed tunnel infections requiring multiple courses of antibiotic treatment, and 3 patients required catheter removal; 2 patients with symptomatic ESIs without tunnel involvement responded to oral and topical antibiotics. Further investigation implicated 4% chlorhexidine aqueous bodywash used by all patients as the probable source of the outbreak.This is the first reported outbreak of *B. cepacia* ESIs. We noted an association between diabetes mellitus and refractory/more extensive infection. Our experience suggests that isolated ESIs can be treated successfully with oral antibiotics whereas tunnel infections generally require catheter removal.

SPARE SLIDES

Antiseptics	Gram-positive bacteria	Gram-negative bacteria	Viruses enveloped	Viruses non-enveloped	Myco-bacteria	Fungi	Spores
Alcohols	+++	+++	+++	++	+++	+++	-
Chloroxylenol	+++	+	+	±	+	+	-
Chlorhexidine	+++	++	++	+	+	+	-
Hexachlorophene[a]	+++	+	?	?	+	+	-
Iodophors	+++	+++	++	++	++	++	±[b]
Triclosan[d]	+++	++	?	?	±	±[e]	-
Quaternary ammonium compounds[c]	++	+	+	?	±	±	-

Antiseptics	Typical conc. in %	Speed of action	Residual activity	Use
Alcohols	60-70 %	Fast	No	HR
Chloroxylenol	0.5-4 %	Slow	Contradictory	HW
Chlorhexidine	0.5-4%	Intermediate	Yes	HR,HW
Hexachlorophene[a]	3%	Slow	Yes	HW, but not recommended
Iodophors	0.5-10 %)	Intermediate	Contradictory	HW
Triclosan[d]	(0.1-2%)	Intermediate	Yes	HW; seldom
Quaternary ammonium compounds[c]		Slow	No	HR,HW; Seldom; +alcohols

TABLE 4

Mechanisms of antimicrobial action of chlorhexidine

Antiseptics and Disinfectants: Activity, Action, and Resistance
Gerald McDonnell, A. Denver Russell
Clin Microbiol Rev. 1999 Jan; 12(1): 147–179.

Type of microorganism	Chlorhexidine action
Bacterial spores	Not sporicidal but prevents development of spores; inhibits spore outgrowth but not germination
Mycobacteria	Mycobacteristatic (mechanism unknown) but not mycobactericidal
Other nonsporulat-ing bacteria	Membrane-active agent, causing protoplast and spheroplast lysis; high concentrations cause precipitation of proteins and nucleic acids
Yeasts	Membrane-active agent, causing protoplast lysis and intracellular leakage; high concentrations cause intracellular coagulation
Viruses	Low activity against many viruses; lipid-enveloped viruses more sensitive than nonenveloped viruses; effect possibly on viral envelope, perhaps the lipid moieties
Protozoa	Recent studies against *A. castellanii* demonstrate membrane activity (leakage) toward trophozoites, less toward cysts

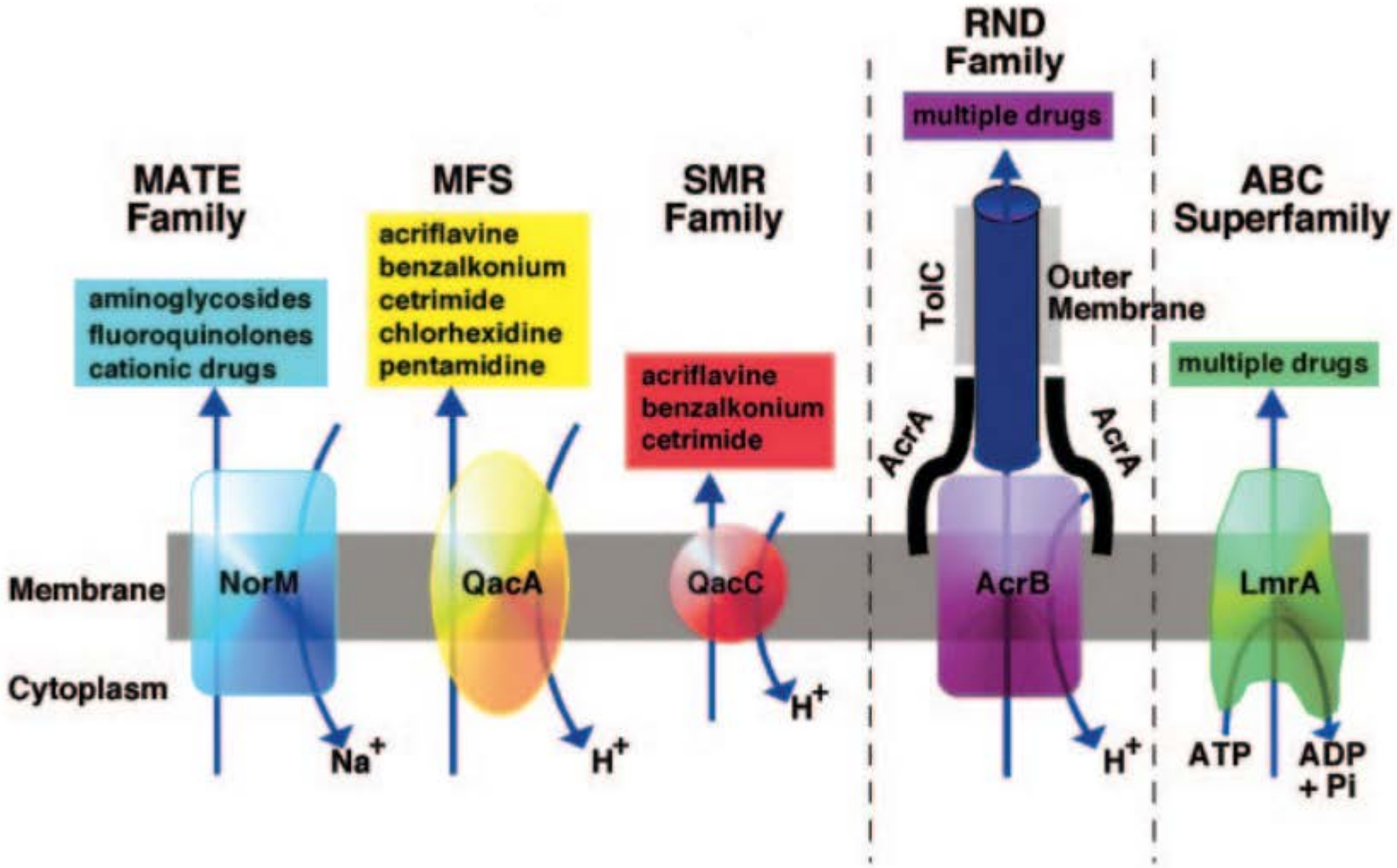
MIC of some antiseptics and disinfectants against gram-positive and gram-negative bacteria[a]

Chemical agent	MIC (µg/ml) for:		
	S. aureus[b]	*E. coli*	*P. aeruginosa*
Benzalkonium chloride	0.5	50	250
Benzethonium chloride	0.5	32	250
Cetrimide	4	16	64–128
Chlorhexidine	0.5–1	1	5–60
Hexachlorophene	0.5	12.5	250
Phenol	2,000	2,000	2,000
o-Phenylphenol	100	500	1,000
Propamine isethionate	2	64	256
Dibromopropamidine isethionate	1	4	32
Triclosan	0.1	5	>300

[a]Based on references 226 and 440.
[b]MICs of cationic agents for some MRSA strains may be higher (see Table 10).

Pseudomonas has efflux pump system in outer membrane resistant to biocide

Antiseptics and Disinfectants: Activity, Action, and Resistance
Gerald McDonnell, A. Denver Russell
Clin Microbiol Rev. 1999 Jan; 12(1): 147–179.



Diagrammatic comparison of the five families of efflux pumps. (Courtesy of Melissa Brown; reproduced by kind permission.)

Clinically Relevant Chromosomally Encoded Multidrug Resistance Efflux Pumps in Bacteria CLINICAL MICROBIOLOGY REVIEWS, Apr. 2006, p. 382–402

The effects of the different treatments on the reduction of total **biofilm** biomass showed that large reductions (>50%) were only obtained with Dettol, hot water (70 C; 30 and 60 min), H2O2 (3.0%; 30 min) and NaOCl. Treatments with low concentrations of H2O2 (0.3%; 30 min) or chlorhexidine (0.015%; 15 min) resulted in negligible reductions of the biofilm biomass compared to the untreated biofilms

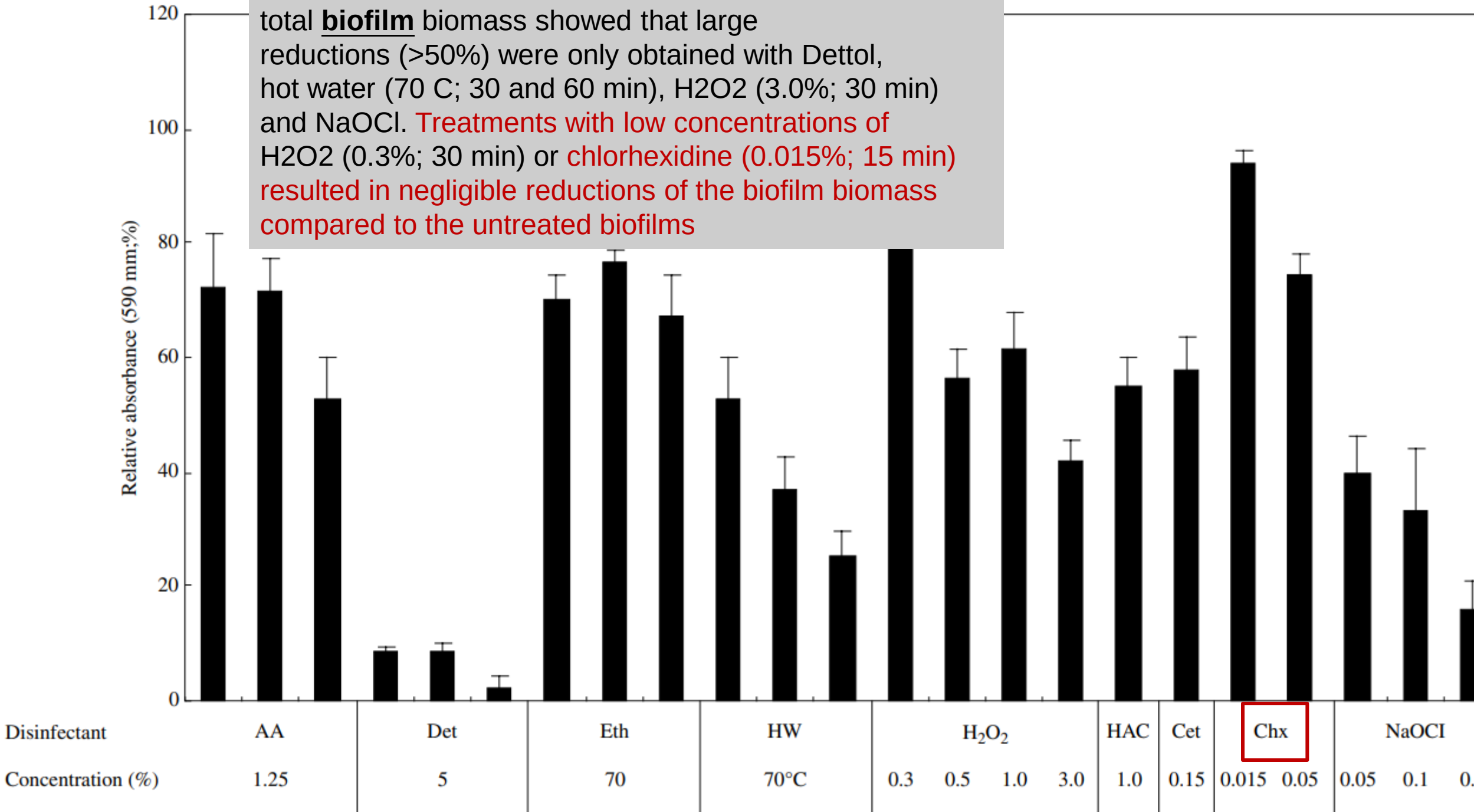


TABLE 3. Outbreaks and pseudo-outbreaks due to contaminated antiseptics

Antiseptic	Contaminant(s)	Site(s) of microbes	Mechanism of contamination/source	Author(s), yr (reference)
Alcohols	*Bacillus cereus*	Blood (pseudobacteremia), pleural fluid	Intrinsic contamination	Hsueh et al., 1999 (34)
Alcohols	*Burkholderia cepacia*	Blood (catheter related)	Contaminated tap water used to dilute alcohol for skin antisepsis	Nasser et al., 2004 (54)
Chlorhexidine	*Pseudomonas* spp.	Not stated	Refilling contaminated bottles; washing used bottles using cold tap water; contaminated washing apparatus; low concentration (0.05%)	Burdon and Whitby, 1967 (13)
Chlorhexidine	*Burkholderia cepacia*	Blood, urinary, wounds	Not determined	Speller et al., 1971 (84)
Chlorhexidine	*Flavobacterium meningosepticum*	Blood, CSF,[a] wounds, skin	Not determined but possibly due to contaminated water and/or topping off of stock solution or low concentration (1:1,000–1:5,000)	Coyle-Gilchrist et al., 1976 (17)
Chlorhexidine	*Pseudomonas* sp., *Serratia marcescens*, *Flavobacterium* sp.	Not stated	Not determined, but authors speculate due to overdilution or refilling of contaminated bottles	Marrie and Costerton, 1981 (47)
Chlorhexidine	*Pseudomonas aeruginosa*	Wounds	Tap water used to dilute stock solutions; low concentration (0.05%)	Anyiwo et al., 1982 (4)
Chlorhexidine	*Bulkholderia cepacia*	Blood, wounds, urine, mouth, vagina	Metal pipe and rubber tubing in pharmacy through which deionized water passed during dilution of chlorhexidine; low concentration	Sobel et al., 1982 (83)
Chlorhexidine	*Ralstonia pickettii*	Blood	Contaminated bidistilled water used to dilute chlorhexidine; low concentration (0.05%)	Kahan et al., 1983 (38)
Chlorhexidine	*Ralstonia pickettii*	Blood	Contaminated deionized water; low concentration (0.05%)	Poty et al., 1987 (63)
Chlorhexidine	*Ralstonia pickettii*	Blood (pseudobacteremia)	Distilled water used to dilute chlorhexidine; low concentration (0.05%)	Verschraegen et al., 1985 (89)
Chlorhexidine	*Ralstonia pickettii*	Blood (pseudobacteremia)	Distilled water used to dilute chlorhexidine; low concentration (0.05%)	Maroye et al., 2000 (46)
Chlorhexidine	*Achromobacter xylosoxidans*	Blood, wounds	Atomizer (low concentration, 600 mg/liter)	Vu-Thien et al., 1998 (91)

Outbreaks Associated with Contaminated Antiseptics and Disinfectants. Antimicrob Agents Chemother. 2007 Dec; 51(12): 4217–4224.

			concentration (0.05%)	
Chlorhexidine	*Achromobacter xylosoxidans*	Blood, wounds	Atomizer (low concentration, 600 mg/liter)	Vu-Thien et al., 1998 (91)
Chlorhexidine	*Achromobacter xylosoxidans*	Blood	Atomizer	Tena et al., 2005 (85)
Chlorhexidine	*Serratia marcescens*	Bood, urine, wounds, sputum, others	Not determined, but use of nonsterile water for dilution to 2% and distribution in reusable nonsterile containers	Vigeant et al., 1998 (90)
Chlorhexidine plus cetrimide	*Pseudomonas multivorans*	Wounds	Tap water used to prepare stock solutions; low concentrations (0.05% chlorhexidine and 0.5% cetrimide)	Bassett, 1970 (8)
Chlorhexidine plus cetrimide	*Stenotrophomonas maltophilia*	Urine, umbilical swabs, catheter tips, others	Deionized water used to prepare solutions; failure to disinfect contaminated bottles between use	Wishart and Riley, 1976 (93)
Chloroxylenol	*Serratia marcescens*	Multiple sites	Contaminated (extrinsic) 1% chloroxylenol soap; sink	Archibald et al., 1997 (5)
Benzalkonium chloride	*Pseudomonas* species	Blood	Storage of benzalkonium chloride (0.1%) with cotton/ gauze	Plotkin and Austrian, 1958 (61)
Benzalkonium chloride	*Pseudomonas-Achromobacteriaceae* group	Blood, urine	Storage of benzalkonium chloride (0.1%) with cotton/ gauze; dilution with nonsterile water	Lee and Fialkow, 1961 (43)
Benzalkonium chloride	*Enterobacter aerogenes*	Blood, sinus tract	Storage of benzalkonium chloride (0.13%) with cotton/ gauze	Malizia et al., 1960 (45)
Benzalkonium chloride	*Pseudomonas kingii*	Urine	Contamination (intrinsic) of antiseptic	CDC, 1969 (15)

Continued on following page

Outbreaks Associated with Contaminated Antiseptics and Disinfectants. Antimicrob Agents Chemother. 2007 Dec; 51(12): 4217–4224.

Table 1. Recommended acceptance criteria for microbiological quality of non-sterile dosage forms

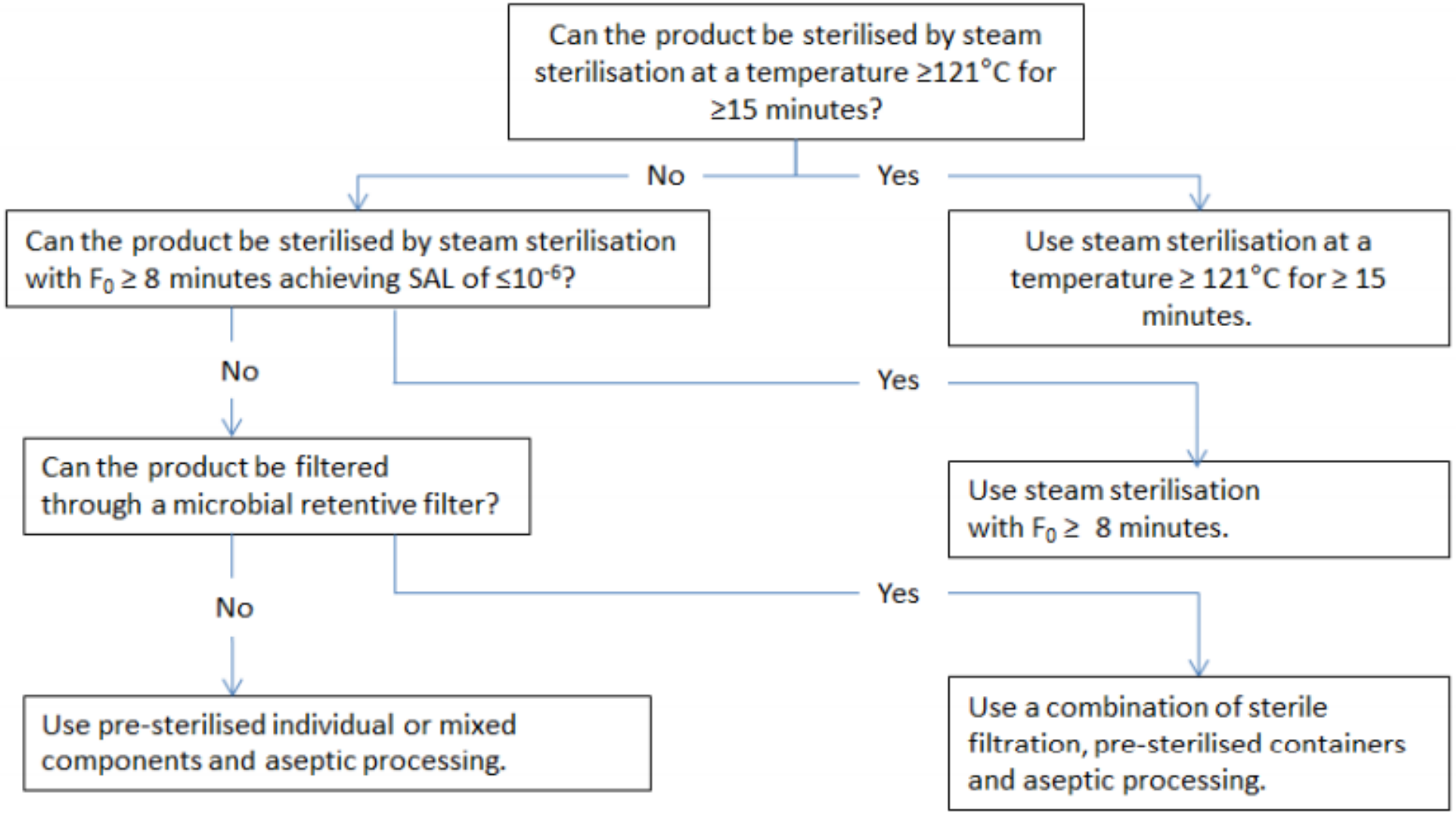
Route of administration	Total aerobic microbial count (CFU/g or CFU/ ml)	Total combined yeasts/moulds count (CFU/g or CFU/ ml)	Specified microorganism
Non-aqueous preparations for oral use	10^3	10^2	Absence of *Escherichia coli* (1 g or 1 ml)
Aqueous preparations for oral use	10^2	10^1	Absence of *Escherichia coli* (1 g or 1 ml)
Rectal use	10^3	10^2	-
Oromucosal use Gingival use Cutaneous use Nasal use Auricular use	10^2	10^1	Absence of *Staphylococcus aureus* (1 g or 1 ml) Absence of *Pseudomonas aeruginosa* (1 g or 1 ml)

In order to provide users with important information about contamination that may occur during the manufacturing process, we are also asking manufacturers to voluntarily revise the product labels for topical antiseptics to indicate whether the drug is manufactured as a sterile or nonsterile product. We believe this will assist health care professionals in making informed decisions about using these products. Topical antiseptics are not required to be manufactured as sterile and so may become contaminated with bacteria during manufacturing. Labeling stating a product is sterile means it was treated with a process during manufacturing to eliminate all potential microorganisms.

However, even topical antiseptics manufactured with a sterile process, can become contaminated if proper care is not taken when using them. Health care professionals and patients should follow all label directions to decrease the chances of infection. The term nonsterile on the product label means it was not sterilized during manufacturing; it does not mean the product contains harmful bacteria. All topical antiseptics are required to be manufactured under FDA's Current Good Manufacturing Practice (cGMP) regulations, which contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product.

FDA Drug Safety Communication: FDA requests label changes and single-use packaging for some over-the-counter topical antiseptic products to decrease risk of infection02/29/2016

Figure 1 Decision tree for sterilisation choices for aqueous products



Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container European Medicines Agency. 6 March 2019 https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-sterilisation-medicinal-product-active-substance-excipient-primary-container_en.pdf