BD ChloraPrep™ clinical evidence compendium

A summary of the key clinical studies supporting the use of BD ChloraPrep™ skin antiseptic for vascular access

Reducing the risk of healthcare-related complications with a 2% chlorhexidine gluconate and 70% isopropyl alcohol solution in a sterile single-use applicator

For use in the UK and Ireland only.

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BD

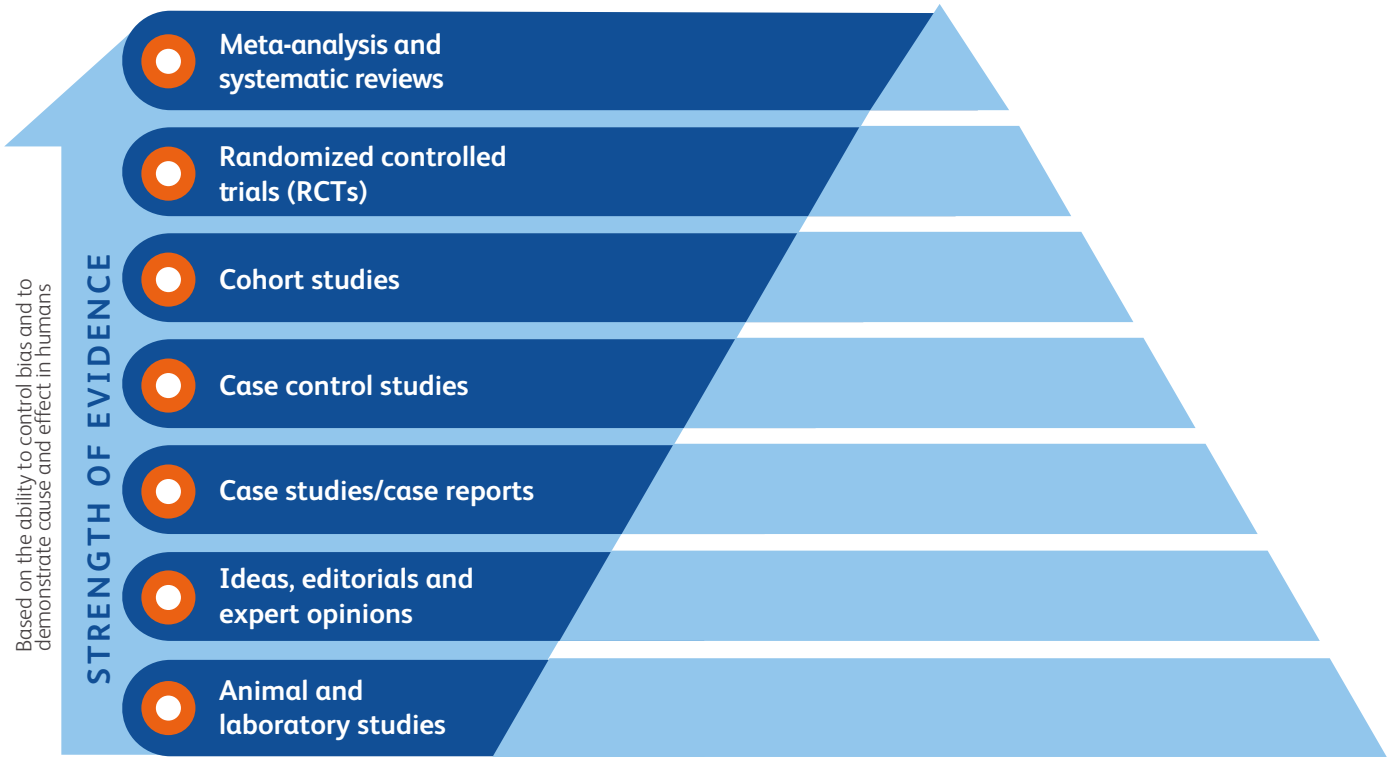
Introduction

Healthcare-associated infections (HAIs) have a significant impact on both patients and institutions worldwide. Impacts of HAIs can include prolonged hospital stay, long-term disability, increased resistance to antimicrobials and higher costs for patients and their families. HAIs represent a significant burden to public health globally, with financial losses estimated at €7 billion euros in Europe , over $6.5 billion USD in the United States[1] and over £1 billion GBP in the United Kingdom.[2] However, robust data indicate that HAIs, particularly surgical skin infections and bloodstream infections, are eminently preventable.[3-6] Since the patient's skin flora is considered to be a source of many infections, removing microbes from the skin prior to puncture or incision is key. Therefore, effective skin antisepsis is critical.

The evidence presented in the following studies illustrates the value of skin antisepsis with BD ChloraPrep™ in preventing infections related to vascular access procedures.

References: **1** World Health Organization. Health care-associated infections FACT SHEET. Accessed on June 7, 2019, at https://www.who.int/gpsc/country_work/gpsc_ccisc_fact_sheet_en.pdf. **2** National Clinical Guideline Centre (UK). Infection: Prevention and Control of Healthcare-Associated Infections in Primary and Community Care: Partial Update of NICE Clinical Guideline 2. London: Royal College of Physicians (UK); March 2012. **3** Connor R, ed. Guidelines for Perioperative Practice, 2015 ed. Denver, CO: Association of PeriOperative Registered Nurses (AORN); 2015. **4** World Health Organization. Global Guidelines for the Prevention of Surgical Site Infection. Published 2016. Accessed on June 7, 2019, at https://www.ncbi.nlm.nih.gov/books/NBK401132/pdf/Bookshelf_NBK401132.pdf. **5** Berríos-Torres SI, Umscheid CA, Bratzler DW, et al; Healthcare Infection Control Practices Advisory Committee. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA Surg.* 2017;152(8):784–791. **6** Ban KA, Minei JP, Laronga C, et al. American College of Surgeons and Surgical Infection Society: surgical site infection guidelines, 2016 update. *J Am Coll Surg.* 2017;224(1):59–174.

Pyramid of evidence



Adapted from:
Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence Working Group. The Oxford 2011 Levels of Evidence. Accessed May 2018 at https://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf.

Table of contents

Comparison of alcoholic chlorhexidine and povidone-iodine cutaneous antiseptics for the prevention of central venous catheter-related infection: a cohort and quasi-experimental multicenter study

Study authors
J Pages, P Hazera, B Mégarbane, et al.

Publication
Intensive Care Med 2016;42(9):1418–1426

Study design (level of evidence)
Prospective quasi-experimental

Study location
France

Study objective
Compare the effectiveness of different skin antiseptics in reducing risk of catheter-related infection (CRI) in intensive care unit patients

Study length
2 years and 7 months

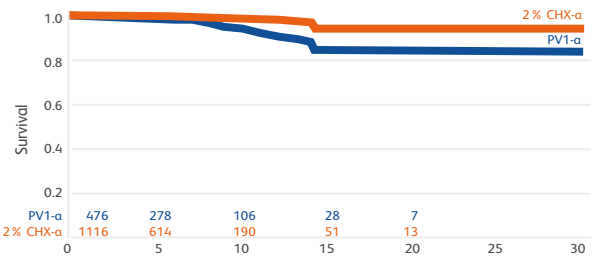
Study protocol
- A before-after comparison was conducted, evaluating 5% povidone-iodine (PVI-a) / 69% ethanol versus 2% chlorhexidine / 70% isopropyl alcohol (2% CHX-a, BD ChloraPrep™ with tint)
- A 1-step protocol was used for ChloraPrep™, whereas a 4-step protocol was used for other antiseptics that included scrub, rinse, dry and disinfect
- Leveraged Cox proportional-hazards modeling with multivariate (cohort analysis) and propensity scoring (quasi-experimental analysis)

Patient population
- Adults (ICU) – 3,027 patients (cohort analysis)
- Adults (ICU) – 1,368 patients (quasi-experimental analysis)

Key endpoint
Catheter-related infection (CRI)

Study limitations
- Under-reporting of side effects
- Compliance to antiseptic use not monitored
- Open label study

Catheter-related infection looking at inverse probability of treatment weighting (IPTW)



Hazard ratio (HR)	0.31
95 % confidence interval (CI)	0.14–0.70
P value	0.005

Study findings

70% From the quasi-experimental analysis, at any time point, skin preparation prior to central venous catheter (CVC) insertion with 2% CHX-a was up to 70% less likely to result in CRI than 5% PVI-a through both propensity score matching (HR, 0.35; 95% CI, 0.15–0.84; *P*=0.02) and IPTW (HR, 0.31; 95% CI, 0.14–0.70; *P*=0.005)

↓ From the cohort analysis, at any time point, skin preparation prior to CVC insertion with 2% CHX-a was 49% less likely to result in CRI than 5% PVI-a (HR, 0.51; 95% CI, 0.28–0.96; *P*=0.037)

0 No reports of skin irritation were associated with either group

Key point

Using 1-step ChloraPrep™ for cutaneous antisepsis of CVC site insertion and maintenance led to a greater reduction in CRI than 4-step alcoholic 5% povidone-iodine in ICU patients

Study conclusion

The use of 2% CHX-a prior to CVC insertion and maintenance care provided a reduced risk of infection

Skin antisepsis with chlorhexidine–alcohol versus povidone iodine–alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial

Study authors
O Mimoz, J Lucet, T Kerforne, et al.

Publication
The Lancet 2015; Nov 21;386(10008):2069–2077

Study design (level of evidence)
Prospective randomized clinical trial

Study location
France

Study objective
Determine if chlorhexidine-alcohol was more effective than povidone-iodine–ethanol in preventing short-term catheter-related infection (CRI). Additionally, evaluate whether scrubbing the skin with an antiseptic detergent prior to antiseptic application would reduce catheter colonization versus application of antiseptic alone

Study length
2 years and 4 months

Study protocol
- An open-label, multicenter, randomized, controlled, two-by-two factorial trial
- Patients were randomly assigned to receive intravascular catheters prepared with either 2% chlorhexidine and 70% isopropyl alcohol (chlorhexidine-alcohol) or 5% povidone-iodine and 69% ethanol (povidone-iodine–alcohol), with or without scrubbing of the skin with detergent before antiseptic application
- Microbiologists and outcome assessors were masked to group assignment

Patient population
Adults (medical ICU, surgical ICU) – 2,349 patients

Study limitations
- Open-label trial
- Adhesion to study protocol not regularly checked

Key endpoints
- Primary outcome: Catheter-related infection (CRI)
- Catheter-related bloodstream infection (CRBSI)
- Catheter colonization

Study findings

84% less incidence rates of CRIs in patients assigned to chlorhexidine–alcohol (0.28 per 1,000 catheter days) group compared to the Betadine scrub group (1.77 per 1,000 catheter days) (*P*=0.0002)

79% CRBSI incidence rates were lower in the chlorhexidine-alcohol group (0.28 per 1000 catheter days) compared to the Betadine scrub group (1.32 per 1000 catheter days) (*P*=0.003)

5x fewer colonized catheters seen in the chlorhexidine-alcohol group than in the Betadine scrub group (3.34 vs 18.74 per 1,000 catheter-days; *P*<0.0001)

The cost to prevent one episode of CRI with chlorhexidine-alcohol was estimated to be €227 (€74–€912),* which appears economically more efficient than povidone-iodine–alcohol when considering the cost associated with one CRI (€19,583)*

An additional step of scrubbing skin with either Hibiscrub (4% chlorhexidine gluconate) or Betadine scrub (povidone-iodine) prior to antiseptic application was not associated with a significant difference in catheter colonization (*P*=0.3877)

No adverse systemic reactions were reported, however as expected, skin reactions were more frequent with Chx-alcohol patients than with alcoholic povidone iodine.

*Currency in 2014 Euros (€)

Key point

Consideration should be given to include chlorhexidine–alcohol in all bundles for the prevention of intravascular CRIs

Study conclusion

Chlorhexidine-alcohol, compared to Betadine scrub, provides superior efficacy in decreasing catheter colonization, CRI and incidence of CRBSI. Skin cultures from catheter insertion sites also showed larger bacterial concentration decreases with chlorhexidine-alcohol than with Betadine scrub.

An intervention to decrease catheter-related bloodstream infections in the ICU

Study authors
P Pronovost, D Needham, S Berenholtz, et al.

Publication
N Engl J Med 2006;355(26):2725–2732

Study design (level of evidence)
Prospective, cohort

Study location
United States

Study objective
Evaluate the effect of an intervention in decreasing the rate of catheter-related bloodstream infection (CRBSI) up to 18 months after implementation

Study length
18 months (post-implementation)

Study protocol
Study intervention targeted the use of evidence-based procedures recommended by the CDC and identified as having the greatest effect on the rate of CRBSI and the lowest barriers to implementation, including:

- Washing hands
- Using full-barrier precautions during insertion of central venous catheters
- Cleaning the skin with chlorhexidine (2% preferred)
- Avoiding the femoral site and removing unnecessary catheters

The following was employed to support implementation of these evidence-based procedures:

- Education was provided about practices to control infection and harm resulting from CRBSIs
- A central-line cart with necessary supplies was created
- A checklist was used to ensure adherence to infection control practices
- Providers were stopped if breach in practice was observed
- Removal of catheters was discussed at daily rounds
- The number and rates of CRBSIs were reported at monthly and quarterly meetings

Patient population
103 ICUs across 67 hospitals

Key endpoint
Catheter-related bloodstream infection (CRBSI)

Study limitations
- Non-randomized
- Lack of baseline data from ICUs that immediately implemented the study intervention
- Compliance not evaluated
- Data on causal CRBSI organisms not collected

Incidence-rate ratios for catheter-related bloodstream infections

Variable study period	Incidence-rate ratio (IRR) (95% CI)	*P* value
Baseline	1.00	
During implementation	0.76 (0.57–1.01)	0.063
After implementation		
0–3 months	0.62 (0.47–0.81)	0.001
4–6 months	0.56 (0.38–0.84)	0.005
7–9 months	0.47 (0.34–0.65)	<0.001
10–12 months	0.42 (0.28–0.63)	<0.001
13–15 months	0.37 (0.20–0.68)	0.001
16–18 months	0.34 (0.23–0.50)	<0.001
Teaching hospital	1.34 (0.73–2.46)	0.35
Bed size (per 100 beds)	1.03 (0.97–1.09)	0.33

Study findings

66% There was a 66% decrease in the incidence rate of CRBSIs 18 months post-implementation compared to baseline (IRR, 0.34; 95%CI, 0.23–0.50; *P*<0.001)

0 Within 3 months of intervention implementation, the median rate of CRBSIs per 1000 catheter-days decreased from 2.7 to 0 compared to baseline (*P*<0.002)

Key point

Within 3 months after implementation of the simple and inexpensive intervention practices, the median rate of infection was 0, a rate sustained throughout the remaining 15 months of follow-up

Study conclusion

The ICUs experienced large and sustained reduction in rates of CRBSIs that were maintained throughout the 18-month study period

Horizontal infection control strategy decreases methicillin-resistant *Staphylococcus aureus* infection and eliminates bacteremia in a surgical ICU without active surveillance

Study authors
M Traa, L Barboza, S Doron, et al.

Publication
Crit Care Med 2014;42(10):2151–2157

Study design (level of evidence)
Retrospective, observational

Study location
United States

Study objective
Evaluate whether horizontal infection control strategies could reduce the occurrence of methicillin-resistant *Staphylococcus aureus* (MRSA) infection in the ICU, without the need for active surveillance

Study length
7 years

Study protocol
Evidence-based infection prevention strategies were implemented in an interactive fashion, including:

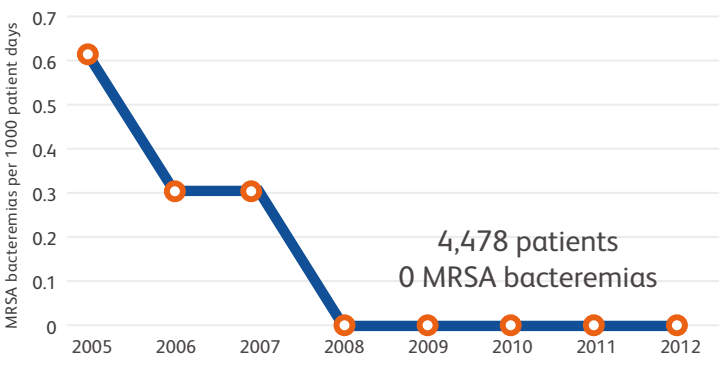
- Hand hygiene program using 63% isopropyl alcohol with refresher education campaign
- Chlorhexidine oral hygiene program
- Bathing using 2% chlorhexidine impregnated towels 1–3 times per day
- Catheter-associated bloodstream infection program involves a nurse-led time-out at the beginning of each catheter placement procedure, use of full sterile technique with complete patient draping and ChloraPrep™ (2% chlorhexidine with 70% isopropyl alcohol) skin preparation, use of antimicrobial-coated catheters and chlorhexidine-impregnated central-catheter dressings changed every 7 days and removal as soon as no longer medically necessary
- Daily goals sheets to remind staff to access catheters daily

Patient population
Adults (surgical ICU) – 6,697 patients

Key endpoint
MRSA infection

Study limitations
- Lack of internal control due to hospital units implementing only some of the infection control interventions
- Individual intervention effects could not be clearly distinguished

Reduction in rate of MRSA bacteremias to zero



Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremias fell to zero during the last 5 years of the study period

Study findings

21% average decrease of MRSA infections from 2005 to 2012 (2.66 vs 0.69 per 1000 patient days)

Compliance was achieved in the hand hygiene program for 92% of the months

Not a single case of methicillin-resistant *Staphylococcus aureus* bacteremia was detected among 4,478 surgical ICU admissions over the last 5 years

Key point

The use of ChloraPrep™ as part of infection prevention strategy has resulted in a significant decrease in methicillin-resistant *Staphylococcus aureus*

Study conclusion

Aggressive multifaceted horizontal infection control can successfully and significantly reduce MRSA infection and bacteremia in an ICU while avoiding the additional staff and patient costs of vertical control

Evaluation of two chlorhexidine-alcohol-based skin disinfectants in blood donation setting

Study authors
BKL So, CCY Chu, PL Ho, et al.

Publication
Vox Sang 2014;106(4):316–321

Study design (level of evidence)
Prospective observational

Study location
China

Study objective
Assess limitations and effectiveness of two chlorhexidine-alcohol–based disinfectants in a blood donation setting to 2-step sequential method of 10% povidone-iodine and 70% isopropyl alcohol

Study length
Undisclosed

Study protocol
Skin disinfectants were evaluated in a 2-stage observational study.

Disinfectant methods included:

- Povidone-iodine/isopropyl alcohol (PI/IPA): 10% povidone-iodine swab stick for 30 seconds followed by 70% isopropyl alcohol swab for 30 seconds with 60-second dry time (PDI®)
- Chlorhexidine gluconate/isopropyl alcohol-1 (CHX/IPA-1): a single-applicator brush of 2% chlorhexidine and 70% isopropyl alcohol applied for 60 seconds with 60-second dry time (BD ChloraPrep™)
- Chlorhexidine gluconate/isopropyl alcohol-2 (CHX/IPA-2): a swab stick of 2% chlorhexidine and 70% isopropyl alcohol applied for 60 seconds with 60-second dry time (3M™ SoluPrep™)

The disinfectant assignments were blinded to the researcher who carried out the plate counting.

- In part 1 of the study, a baseline bacterial count was taken by applying a commercial TSA standard contact plate for 10 seconds to the 4x4-cm area of the antecubital fossa. The selected arm was then disinfected with either PI/IPA or CHX/IPA-1, air-dried and followed by the application of a culture plate to determine residual bacteria
- In part 2, the contact plate was further prepared with neutralizers reported to have better neutralization effect on chlorhexidine but non-toxic to bacteria. Both arms were disinfected by CHX/IPA-1 or CHX/IPA-2 with the same steps to specify bacterial counts before and after procedure

Patient population
Adults (blood donation) – 326 patients

Study limitation
Unable to directly compare povidone-iodine and CHX disinfectants at the same time

Key endpoint
Bacterial growth

Study findings

Part 1 of the study:

10x less residual bacterial colonies (approximately) occurred post-disinfection in the ChloraPrep™ arm compared to the povidone-iodine/isopropyl alcohol arm (5.9% vs. 61.7%; *P*<0.001)

Part 2 of the study:
Residual bacterial growth was equivalent between the CHX/IPA groups (*P*=0.26)

Key point

Single-application ChloraPrep™ is more convenient, simpler to handle and may be more efficient in reducing bacterial counts than a 2-step process

Study conclusion

Skin disinfection is a critical step in reducing bacterial contamination during blood donation. The 1-step application of using ChloraPrep™ has been proven efficacious, and it could replace the sequential 2-step method of 10% povidone-iodine and 70% isopropyl alcohol in pre-donation skin disinfection.

A novel rapid and effective donor arm disinfection method

Study authors
C McDonald, S McGuane, J Thomas et al.

Publication
Transfusion 2010;50(1):53–58

Study design (level of evidence)
Prospective observational

Study location
United Kingdom

Study objective
Identify a donor arm disinfection technique that is faster but comparable or superior to previous "best practice" using a 1-minute process of 70% isopropyl alcohol followed by application of 2% tincture of iodine (IATI)

Study length
Undisclosed

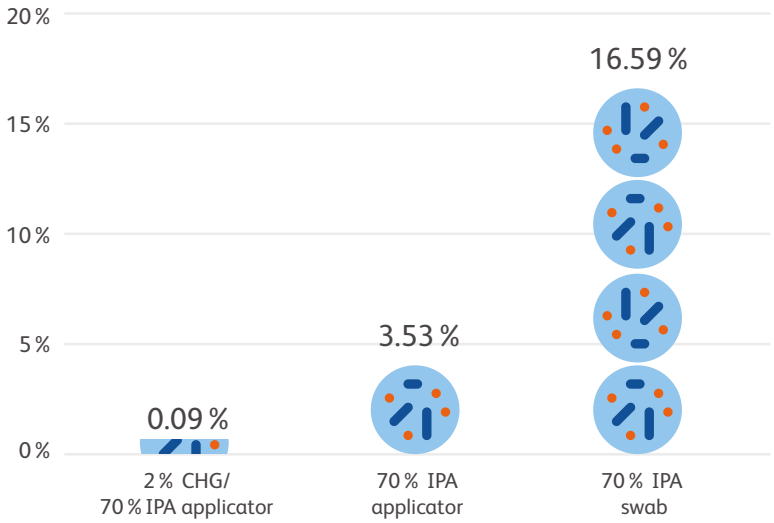
Study protocol
- 2-stage design evaluating the hospital skin preparation and catheter site maintenance of routine blood donors
- To determine efficacy, a direct swabbing and plating technique was used to calculate bacterial counts before and after each disinfection
- Stage 1 evaluated the onset and efficacy of five disinfection methods using a 30-second application time
- The chlorhexidine-alcohol applicator (CAA) was evaluated as both a single and double application
- Stage 2 evaluated if a reduction in solution volume could reduce dry time to approximately 30 seconds, while maintaining efficacy
- CAA was applied using specifically designed 1.5-mL and 1-mL devices

Patient population
Adults (blood donation) – 908 patient arms

Key endpoint
Bacterial growth

Study limitation
Single-center

Percentage of bacteria remaining after skin disinfection



CHG, chlorhexidine gluconate; IPA, isopropyl alcohol

Study findings

In stage 1, single (*P*=0.25) and double (*P*=0.67) application of CAA was equivalent to isopropyl alcohol plus tincture of iodine (IATI). Both isopropyl alcohol swab stick and applicator methods were inferior to CAA and IATI (*P*<0.001)

50% In stage 2, with reduced dry time and single-step applicator, procedural time was reduced with the 1.5-mL ChloraPrep™ method compared with application of 70% isopropyl alcohol and 2% tincture of iodine

Key points

- Chlorhexidine gluconate maintains persistent antimicrobial activity by disrupting the cell membrane and precipitating cell contents
- Applicator method yielded superior bacteria disinfection compared to swab method

Study conclusion

A single application of the combined formulation of 2% chlorhexidine and 70% isopropyl alcohol is a rapid and effective donor arm disinfection method. The data, along with negligible patient skin reactions to CAA, supported full implementation of the CAA (1.5 mL) as the sole disinfection method throughout the entire English blood service program for all donations.

Efficacy of adding 2% (w/v) chlorhexidine gluconate to 70% (v/v) isopropyl alcohol for skin disinfection prior to peripheral venous cannulation

Study authors
H Small, D Adams, AL Casey, et al.

Publication
Infect Control Hosp Epidemiol 2008;29(10):963–965

Study design (level of evidence)
Prospective randomized clinical trial

Study location
United Kingdom

Study objective
Evaluate the number of peripheral venous catheter (PVC) tips that had microorganisms present following skin decolonization with 2% chlorhexidine gluconate (CHG) in 70% isopropyl alcohol (IPA) (ChloraPrep™ Sepp™) or with 70% IPA alone.

Study length
Undisclosed

Study protocol
- Patients were randomly assigned to skin preparations prior to PVC insertion
- Both ChloraPrep™ Sepp™ and the 70% IPA wipe were applied for 30 seconds
- Each antiseptic was then allowed to dry for 2 minutes

Patient population
Adults (cardiology) – 170 patients

Key endpoint
PVC colonization

Study limitation
Application method of skin disinfection may have resulted in differences in the removal of epithelial cells and bacterial commensals and may have influenced the penetration of antiseptic into the skin

Study finding

~2.5x more microbes were present on PVC tips in the 70% IPA group (49.4%) compared to the 2% CHG in IPA group (19.8%) (*P*<0.001)

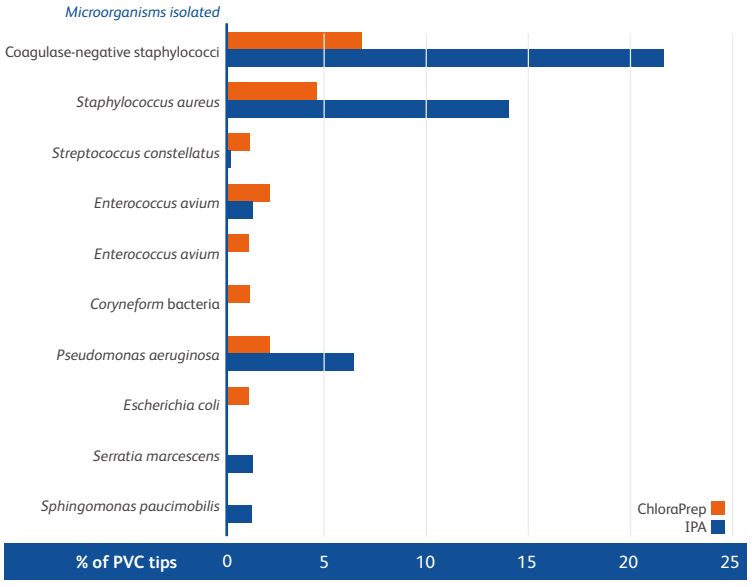
Key point

ChloraPrep™ Sepp™ demonstrates dual action that both reduces the number of microorganisms on the skin and provides microbial activity up to 24 hours

Study conclusion

Skin disinfection with 2% CHG in IPA prior to PVC insertion resulted in a significant reduction in the number of PVC tips that had microorganisms present on their surface, compared with skin disinfection with 70% IPA alone

Comparison of microorganisms isolated on PVC tips of patients who received skin insertions



Effectiveness of ChloraPrep™ in reduction of blood culture contamination rates in emergency department

Study authors
D Tepus, E Fleming, S Cox, et al.

Publication
J Nurs Care Qual 2008;23(3):272–276

Study design (level of evidence)
Prospective observational study

Study location
United States

Study objective
Compare blood culture contamination rates using a tincture of iodine skin preparation process versus the ChloraPrep™ skin preparation process in the emergency department at a 963-bed community teaching hospital

Study length
Undisclosed

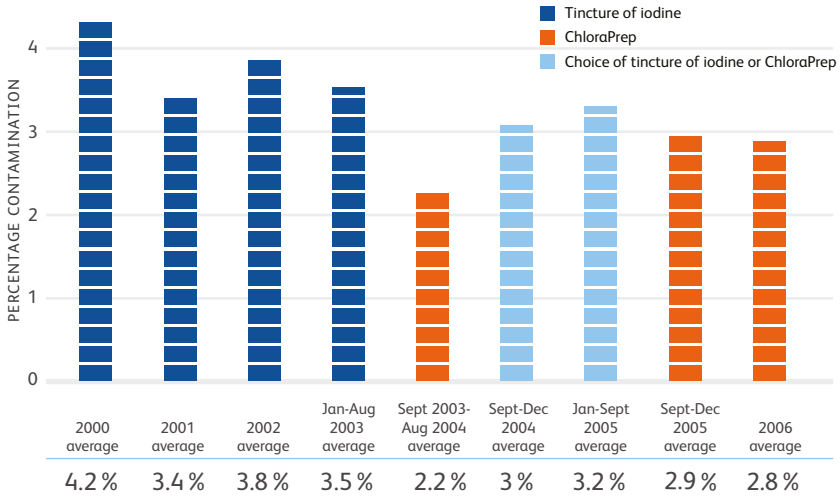
Study protocol
- Used a pre-implementation/post-implementation design
- Contamination rates were collected and obtained from the hospital database for a full year review
- Pre-implementation, the skin-preparation policy was to apply a tincture of iodine to the skin in an outward circular motion, allow 2 minutes to dry and then draw the culture
- During the implementation, ChloraPrep™ was used for all blood cultures drawn in the emergency department, applied by trained personnel using a back-and-forth scrubbing action to exfoliate the top layers of the skin
- Dry time (15–30 seconds) was significantly faster than the iodine preparation
- Following the 1-year study period, both skin preparation methods were available and used based on personnel preference

Patient population
Adults (ED) – 14,764 blood cultures

Key endpoint
Blood culture contamination (BCC)

Study limitations
- Non-randomized
- Unable to blind
- Single-center

Emergency department blood cultures contamination rate



Study findings

37% drop in the blood culture contamination rate after the implementation of ChloraPrep™ (3.5% vs. 2.2%; *P*<0.0001)

$875,000 projected annual savings when the ChloraPrep™ method was implemented, through reduction in in BCCs

<3% contamination rate has been maintained at the facility since adoption of the ChloraPrep™ method

~2 minutes less dry time with ChloraPrepTM vs iodine tincture led to comparable costs when accounting for extra nursing time spent ($0.68 vs $0.66, respectively)

Skin preparation	Cost	Cost w/ nursing time*
ChloraPrep™	$0.68	$0.68
Iodine tincture	$0.20	$0.66

*2 minutes of extra dry time with iodine tincture

Key point

A significant decrease in contamination rates and cost was achieved using ChloraPrep™ versus tincture of iodine

Study conclusion

ChloraPrep™ demonstrated a statistically significant decrease in blood culture contamination rates compared to a tincture of iodine method in a clinical environment where skin preparation technique and dry times are critical steps in achieving clinical efficacy. The cost savings achieved through the reduction in contamination rates when the ChloraPrep™ method was implemented resulted in a significant cost savings

Combined education and skin antisepsis intervention for persistently high blood-culture contamination rates in neonatal intensive care

Study authors
C O'Connor, R Philip, J Powell, et al.

Publication
J Hosp Infect 2016;93(1):105–107

Study design (level of evidence)
Prospective, observational

Study location
Ireland

Study objective
Study intervention with premature and very low-birth-weight (<1500 g) newborn babies, a population with a consistently high blood culture contamination rate (3-year range of 3.1%–3.4%)

Study length
1 year (6 months pre-intervention and 6 months for the post-intervention)

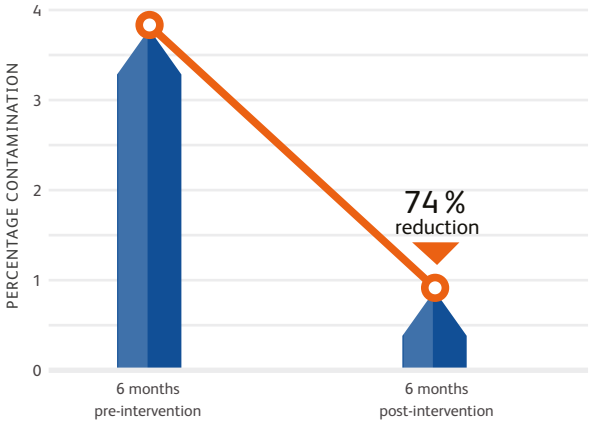
Study protocol
- Contamination rates were measured pre-intervention and post-intervention
- The intervention included:
  - Replacement of 70% isopropyl alcohol swabs with 2% chlorhexidine in 70% alcohol for skin antisepsis prior to phlebotomy for all neonates
  - 30-minute staff education detailing hand hygiene, the intervention procedures and use of the sterile applicators
- ChloraPrep™ was introduced following staff training
- No other changes were introduced during either period
- Adverse events potentially associated with chlorhexidine use were carefully monitored by doctors for 3 to 5 months following the kit's introduction to evaluate its use

Patient population
Neonates (NICU) – 678 patients

Key endpoint
Blood culture contamination (BCC) rates

Study limitations
- Single-center
- Unable to determine which intervention had the most effect

Blood culture contamination rates pre- and post-intervention



Study findings

74.4% reduction in contaminated blood cultures between pre- and post-intervention

Clinicians found the ChloraPrep™ sterile applicator to be user-friendly and have dry times similar to 70% alcohol swabs previously employed

No dermatological adverse events were observed

Key points

- The use of ChloraPrep™ demonstrated significant and sustained contamination reduction
- ChloraPrep™ caused no adverse skin reactions in neonatal patients with fragile skin
- ChloraPrep™ is to be used with caution in neonates

Study conclusion

The intervention that included staff education and use of ChloraPrep™ for neonatal skin antisepsis significantly reduced blood culture contamination. Although it was not possible to identify the dominant element of the intervention, ChloraPrep™ was adopted as the skin antiseptic throughout the University of Limerick Group of Hospitals for medical, surgical and obstetric patients

Chlorhexidine-based antiseptic solutions effectively reduce catheter-related bacteremia

Study authors
AM Onder, J Chandar, A Billings, et al.

Publication
Pediatr Nephrol 2009;24(9):1741–1747

Study design (level of evidence)
Retrospective chart review

Study location
United States

Study objective
Investigate whether using chlorhexidine-based solutions (ChloraPrep™) as a catheter-cleansing method could prevent catheter-related bacteremia (CRB) and prolong overall and infection-free catheter survival times for tunneled cuffed hemodialysis catheters when compared to povidone-iodine (PVI) solutions

Study length
Undisclosed

Study protocol
- Retrospective study conducted on 59 children on long-term hemodialysis with a total of 116 catheters and 20,784 catheter days included
- In both treatment groups, 22 patients overlapped
- During the baseline period, patients had exit sites and hubs cleansed with 10% PVI with each hemodialysis session
- In the intervention period, patients had exit sites and hubs cleansed with ChloraPrep™ with each hemodialysis session

Patient population
Pediatric (dialysis) – 59 patients

Key endpoint
Catheter-related bacteremia (CRB)

Study limitation
Limited surveillance data from lab reports

Comparison on outcomes for the two different treatment groups. Twenty-two patients overlapped in both treatment groups

Study period No. of ICUs No. of bloodstream infections per 1000 catheter-days

Parameter	Betadine(R)[10] era (n=39)	ChloraPrep[10] era (n=35)	*P* value
Total number of catheter days	10,960 days	9,824 days	NS 0.9866
Total number of CRB episodes	24	10	0.0041
CRB/1000 catheter days	2.2	1.0	0.0415
Exit site infection	3 infections/ 2 patients infected	2 infections/2 patients infected	NS 0.9129
ESI/1000 catheter days	0.3	0 (0–2.7)	NS 0.7393
Hospitalization for CRB/ 1000 catheter days	4.1 days/7 patients admitted	1.8 days/3 patients admitted	0.0416
Overall catheter survival times (days ± 50)	161.1 ± 107.2	207.6 ± 136.0	NS 0.0535
Infection-free catheter survival times (days ± 50)	106.9 ± 56.7	122.0 ± 54.3	NS 0.1100
Number of catheters lost to malfunction/breakage	21/64 (33%)	20/52 (38%)	NS 0.5309

ESI, exit site infection; NS, not significant

Study findings

56% fewer hospitalizations due to CRB when ChloraPrep™ was used (1.8 days vs. 4.1 days per 1000 catheter days; *P*=0.0416)

Incidence of CRB was approximately 50% lower in the ChloraPrep™ group compared to the povidone-iodine group (1.0 vs. 2.2 per 1000 catheter days; *P*=0.0415)

Key point

The residual antimicrobial effect of chlorhexidine coupled with the immediate activity of alcohol has shown to be effective against pathogens known to be responsible for catheter infections in long-term catheter usage

Study conclusion

Chlorhexidine-based solutions are more effective for the prevention of CRB than povidone-iodine solutions. The overall CRB rate in this study was lower than that reported in the literature and the lowest from this study institution. Authors note that if chlorhexidine can decrease the CRB rate for a population with an already low CRB incidence, it potentially may have more significant impact in hemodialysis units with higher CRB rates

Reducing blood culture contamination in community hospital emergency departments: a multicenter evaluation of a quality improvement intervention

Study authors
WH Self, J Mickanin, CG Grijalva, et al.

Publication
Acad Emerg Med 2014;21(3):274–282

Study design (level of evidence)
Interrupted time series (quasi-experimental)

Study location
United States

Study objective
The objective of the current study was to evaluate the effectiveness of this sterile blood culture collection process for reducing blood culture contamination in two community hospital EDs

Study length
2 years 3 months

Study protocol
- Hospital A, which historically had a contamination rate of approximately 5%, and Hospital B, with a 2.5% historical contamination rate, were evaluated
- With an interrupted times-series design and segmented regression analysis to adjust for secular trends and autocorrelation, the monthly percentages of cultures contaminated at each hospital during an intervention period (sterile technique) were compared to that of a 10-month baseline period immediately preceding implementation (clean technique)
- Hospital A implemented the full sterile blood culture collection process throughout the 16-month intervention period. Hospital B, due to poor adherence to the process due and difficulty implementing the fenestrated drape component, simplified the process. The new process included emphasis on sterile gloves and large-volume skin antisepsis, but omitted the fenestrated drape component
- Therefore, Hospital B had two intervention periods that were compared to the baseline period: the 8-month intervention period 1 (full sterile process) and the subsequent 8-month intervention period 2 (modified sterile process)

Patient population
Adults (ED) – 8,655 blood cultures

Key endpoints
Blood culture contamination (BCC)

Study limitations
- Unable to separate out individual components of the bundle
- Direct observation of adherence of blood culture collection not feasible
- Series definition of culture contamination could reflect overestimation or underestimation of true BCC rate

Study findings

In Hospital A:

43% less BCCs during the intervention period compared to the baseline period (4.83% vs. 2.71%; *P*<0.01)

In Hospital B:
With a modified sterile process, there was a significant reduction in BCCs between the intervention period and the baseline period (*P*<0.01)

The segmented regression model showed that the modified sterile process for blood culture collection was associated with an immediate absolute reduction of 1.53% (95% confidence interval [CI], 1.00–1.88) and significant sustained reductions

In the segmented regression model, the full sterile blood culture collection process was associated with an immediate **2.68%** (95% CI, 1.43–3.52) absolute reduction in contamination with sustained reductions during the entire intervention period

Key point

The use of ChloraPrep™ demonstrated significant and sustained BCC reduction

Study conclusion

A fully sterile or modified sterile process is feasible for community hospital EDs to reduce BCCs. Feedback and surveillance are essential to successfully implement standardized sterile processes for blood culture collection.

Cost-effectiveness analysis of chlorhexidine-alcohol versus povidone iodine-alcohol solution in the prevention of intravascular-catheter-related bloodstream infections in France

Study authors
F Maunoury, C Farinetto, S Ruckly, et al.

Publication
PLoS One 2018;13(5):e0197747

Study design (level of evidence)
Economic evaluation

Study location
France

Study objective
Perform a cost-effectiveness analysis (CEA) comparing chlorhexidine-alcohol (CHG) and povidone-iodine–alcohol (API) solutions for the prevention of catheter-related bloodstream infections (CRBSIs) based on results from an open-label, multicenter, randomized controlled (CLEAN)

Study length
N/A

Study protocol
- 100-day time semi-Markovian model fitted to longitudinal patient data from the CLEAN database
- Model includes eight health states
- Sensitivity analyses on cost and effectiveness
- Costs based on ICU stay from multicenter study

Patient population
Adults (medical ICU, surgical ICU) – 2,349 patients

Key endpoints
Cost-effectiveness

Study limitations
- Based on single clinical study
- Specific cost-effectiveness criterion to French ICUs, which cannot be transposed to other countries with varying CRBSI rates

Study findings

- Compared with 1-step API, 1-time application of ChloraPrep™ significantly prevents 22.55 CRBSIs per 1000 patients
  - 1-step application ChloraPrep™: 3.49 (95% confidence interval [CI], 0.42–12.57) vs. 1-step API: 26.04 (95%CI, 14.64–42.58)
- Mean cost per patient was comparable between 1-time application of ChloraPrep™ and 1-step API
- In comparison to the 1-time PVI solution, the 1-time CHG solution avoids 22.55 CRBSIs per 1000 patients, and saves €1,076 per patient

Skin preparation	Mean cost per patient	95% Confidence interval
1-step ChloraPrep™	€23,798	€20,584–€34,331
1-step API	€24,874	€21,011–€31,678

Key point

With greater CRBSI prevention, 1-time application of ChloraPrep™ yields greater effectiveness at no additional cost for the ICU

Study conclusion

One-time application of ChloraPrep™ is more effective than 1-step API at the same cost. It is recommended that the antiseptic be used routinely for patient care in the ICU.

Three years experience in implementing HICPAC recommendations for the reduction of central venous catheter-related bloodstream infections

Study authors
R Garcia, L Jendresky, S Landesman, et al.

Publication
Manag Infect Control. 2003;10:42-49

Study design (level of evidence)
Prospective, observational

Study location
United States

Study objective
To determine the effectiveness of implementing various scientifically supported interventions to reduce the incidence of Central Venous Catheter (CVC)-Related Bloodstream Infections (CR-BSI)

Study length
Jan 1999–Mar 2003

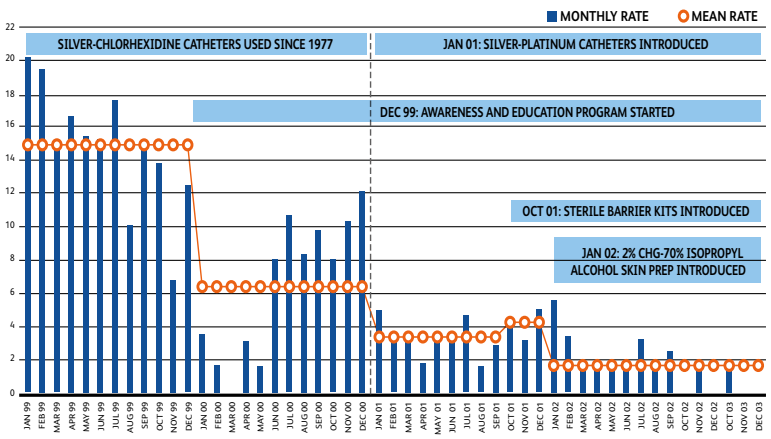
Study protocol
- Infection Control Professionals (ICPs) conducted surveillance for CR-BSI between Jan 1999–Dec 2002 using definitions published by the Centers for Disease Control and Prevention (CDC)
- Jan–Dec 1999 served as the "control" pre-intervention period, during which time silver-CHG catheters were used, no standard barrier kit was in place, and 10% tincture of iodine solution was the default antiseptic
- In concert with a multi-disciplinary working group, the center's Infection Control Committee devised this to study examine the impact on CR-BSI of 4 different strategic interventions:
    1. Establishment of an education and awareness program for targeted hospital-based HCPs (Implementation: Jan 2000)
    2. Conversion of silver-chlorhexidine (CHG) CVCs to silver-platinum catheters (Implementation: Jan 2001)
    3. Consistent use of a custom barrier kit containing sterile gloves, gown and mask (Implementation: Sept 2001)
    4. Utilization of 2% CHG-70% alcohol (ChloraPrep™) as the standard skin antiseptic (Implementation: Jan 2002)

Patient population
3,079 patients (31,445 catheter days)

Key endpoints
- Actual number of CR-BSIs
- Mean CR-BSI rate per 1000 catheter days

Study limitations
Single institution
- Not a randomized, controlled trial
- Based on single clinical study

CVC-relayed bloodstream infections, 1999-2003
Brookdale University Medical Center



Study findings

57.3% reduction in mean CR-BSI rate (6.4) vs the pre-intervention rate (15)—as a result of focused education to targeted physicians and nurses (Intervention #1)

48.4% reduction in mean CR-BSI rate (3.3) vs the prior year's baseline rate (6.4)—following conversion from silver-chlorhexidine (CHG) CVCs to silver-platinum catheters (Intervention #2)

A slight increase to 4.2 in mean CR-BSI rate—an anomaly most likely due to a short or compromised transition when shifting from old to new barrier products (Intervention #3)

61.9% reduction in mean CR-BSI rate (1.6) vs the previous baseline rate (4.2)—after implementing ChloraPrep™ as the standard skin antiseptic (Intervention #4)

89.3% reduction in overall CR-BSI rate—the result of all 4 key strategic interventions

237 cases of CR-BSI avoided during the 39-month intervention period

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Key point

HICPAC-recommended interventions, including the use of ChloraPrep™, have been proven to reduce the incidence of CR-BSI and may save millions of dollars annually in health-related costs.

Study conclusion

Implementing 4 key interventions, including the standard use of ChloraPrep™, recommended by HICPAC and subsequently addressed in the 2002 HICPAC guidelines, resulted in the avoidance of 237 cases of CR-BSI over 39 months. The annual cost savings of these interventions was estimated to be between $2,519,084 and $4,088,000.

DHSC

UK Department of Health and Social Care: CVC and PIVC Related Infection Prevention Care Bundle

Year
2011

Country
United Kingdom

Key recommendations

- Insertion site should be cleaned with 2% chlorhexidine gluconate in 70% isopropyl alcohol prior to if dressing changed.
- Ports or hubs are cleaned with 2% chlorhexidine gluconate in 70% isopropyl alcohol prior to catheter access.

epic3

National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England

Year
2014

Key recommendations

- Decontaminate the skin at the insertion site with a single-use application of 2% chlorhexidine gluconate in 70% isopropyl alcohol (or povidone-iodine in alcohol for patients with sensitivity to chlorhexidine) and allow to dry prior to the insertion of a central venous access device.
- Decontaminate the skin at the insertion site with a single-use application of 2% chlorhexidine gluconate in 70% isopropyl alcohol (or povidone-iodine in alcohol for patients with sensitivity to chlorhexidine) and allow to dry before inserting a peripheral vascular access device.
- A single-use application of 2% chlorhexidine gluconate in 70% isopropyl alcohol (or povidone-iodine in alcohol for patients with sensitivity to chlorhexidine) should be used to decontaminate the access port or catheter hub.The hub should be cleaned for a minimum of 15 seconds and allowed to dry before accessing the system.

NICE

National Institute for Health and Clinical Excellence: Prevention and Control of Healthcare-Associated Infections in Primary and Community Care

Year
2012

Key recommendations

- Decontaminate the skin at the insertion site with chlorhexidine gluconate in 70% alcohol before inserting a peripheral vascular access device or a peripherally inserted central catheter.
- Decontaminate the central venous catheter insertion site and surrounding skin during dressing changes using chlorhexidine gluconate in 70% alcohol, and allow to air dry.
- Consider using an aqueous solution of chlorhexidine gluconate if the manufacturer's recommendations prohibit the use of alcohol with their catheter.

GAVeCeLT

Long-term Central Venous Access (Gli Accessi Venosi Centrali a Lungo Termine)

Year 2008

Country Italy

Key recommendation

- 2% chlorhexidine solution

IHI

Institute for Healthcare Improvement: Central Line Bundle

Year 2011

Country Global

Key recommendations

- Implement the central line bundle (evidence-based interventions): hand hygiene maximal barrier precautions upon insertion; chlorhexidine skin antisepsis; optimal catheter site selection, with avoidance of the femoral vein for central venous access in adult patients; daily review of line necessity, with prompt removal of unnecessary lines.

WHO

World Health Organization Guidelines on Drawing Blood: Best Practices in Phlebotomy

Year 2010

Key recommendations

- Unless drawing blood cultures or prepping for a blood collection:
    1. Clean the site with a 70% alcohol swab for 30 seconds and allow to dry completely.
    2. Alcohol is preferable to povidone-iodine (PI) because blood contaminated with PI may falsely increase levels of potassium, phosphorus or uric acid in laboratory test results.
- Skin preparation for venipuncture for blood donation:
    1. Clean the skin with a combination of 2% chlorhexidine gluconate (CHG) in 70% isopropyl alcohol (IPA).
    2. Cover the whole area and ensure that the skin area is in contact with the disinfectant for at least 30s; allow the area to dry completely (about 30 seconds).
- If 2% CHG in 70% IPA is not available use 2-step procedure:
    Step 1—Use 70% IPA and cover the whole area and ensure that the skin area is in contact with the disinfectant for at least 30s; allow the area to dry completely (about 30 seconds).
    Step 2 —Use tincture of iodine (more effective than PI) or 2% CHG and cover the whole area and ensure that the skin area is in contact with the disinfectant for at least 30 seconds; allow the area to dry completely (about 30 seconds).
- Skin preparation for arterial blood sampling: Disinfect the sampling site on the patient with 70% alcohol and allow it to dry.
- Skin preparation for pediatric and neonatal blood sampling:
    1. Disinfect the sampling site and allow it to dry.
    2. Do not use CHG on children under 2 months of age.
- Skin preparation for capillary blood sampling:
    1. Apply alcohol to entry site and allow to air dry.
    2. Do not use PI for a capillary skin puncture in pediatric and neonatal patients.

Prescribing Information: ChloraPrep™ & ChloraPrep with Tint 2% chlorhexidine gluconate w/v / 70% isopropyl alcohol v/v cutaneous solution. Refer to the Summary of Product Characteristics before prescribing. **Presentation:** ChloraPrep – each applicator contains 0.67ml, 1ml, 1.5ml, 3ml, 10.5ml or 26ml of 20 mg/ml chlorhexidine & 0.70 ml/ml isopropyl alcohol; ChloraPrep with Tint – each applicator contains 3ml, 10.5ml or 26ml of 20 mg/ml chlorhexidine & 0.70 ml/ml isopropyl alcohol. **Indication:** Disinfection of skin prior to invasive medical procedures. **Dosage & administration:** Applicator volume dependent on invasive procedure being undertaken. May be used for all age groups and patient populations. Use with care in newborn babies and those born prematurely. Applicator squeezed to break ampoule and release antiseptic solution onto sponge. Solution applied by gently pressing sponge against skin and moving back and forth for 30 seconds. The area covered should be allowed to air dry. **Contra-indications:** Patients with known hypersensitivity to ChloraPrep or ChloraPrep with Tint or any of its components, especially those with a history of possible Chlorhexidine-related allergic reactions. **Warnings and precautions:** Solution is flammable. Do not use electrocautery procedures or other ignition sources until dry. Remove any soaked materials before proceeding with the intervention. Do not use in excessive quantities, allow to pool in patient skin folds or drip on materials in contact with patient skin. Ensure no excess product is present prior to application of occlusive dressing. For external use only on intact skin, do not use on open skin wounds or broken or damaged skin. Over-vigorous use on fragile or sensitive skin or repeated use may lead to local skin reactions. Avoid prolonged skin contact. Avoid contact with eyes, mucous membranes, middle ear and neural tissue. Chlorhexidine may induce hypersensitivity, including generalised allergic reactions and anaphylactic shock. Chlorhexidine-containing products are known causes of anaphylactic reactions during anaesthesia. The symptoms of anaphylactic reactions might be masked in an anesthetized patient. If symptoms of an anaphylactic reaction are detected during anaesthesia, chlorhexidine related allergic reaction should be considered. When chlorhexidine-related allergic reaction during anaesthesia is suspected, other products containing chlorhexidine used during anaesthesia (e.g. IV lines) should be removed. Special precaution should be taken to avoid patient exposure to any other product containing chlorhexidine during the course of the treatment. May cause chemical burns in neonates, with a higher risk in preterm infants and within the first 2 weeks of life. **Pregnancy & lactation:** Although no studies have been conducted, no effects are anticipated as systemic exposure is negligible. **Undesirable effects:** Very rare; allergic or irritation skin reactions to chlorhexidine, isopropyl alcohol or sunset yellow (E110, present in ChloraPrep with Tint only), including erythema, rash, pruritus and blisters or application site vesicles, other local symptoms have included skin burning sensation, pain and inflammation. Frequency not known; hypersensitivity including anaphylactic shock, dermatitis, eczema, urticaria, chemical burns in neonates, eyes irritation, hyperaemia, impaired vision, chemical burn and eye injury. Discontinue use at the first sign of local skin reaction. Cases of anaphylactic reactions have been reported during anaesthesia. Description of selected adverse reactions: There have been isolated spontaneous reports of generalised allergic reactions potentially associated with ChloraPrep solution and have been reported during anaesthesia. In some cases, the patient may have had a pre-existing sensitivity to chlorhexidine. This product may cause a severe allergic reaction. Symptoms may include wheezing/difficulty breathing, shock, facial swelling, hives, or rash. Use of ChloraPrep is contra-indicated where patients have shown previous hypersensitivity to chlorhexidine or isopropyl alcohol (see Section Contra-indications). If hypersensitivity or an allergic reaction occurs, stop use and seek medical help right away. **Per applicator costs** (ex VAT) ChloraPrep: 0.67ml (SEPP) - UK £0.30, Ireland €0.39; 1.5ml (FREPP) - UK £0.55, Ireland €0.64; 1.5ml – UK £0.78, Ireland €0.94; 3ml; 3ml – UK £0.85, Ireland €1.06; 10.5ml - UK £2.92, Ireland €3.79; 26ml - – UK £6.50, Ireland €7.96. ChloraPrep with Tint: 3ml – UK £0.89, Ireland €1.09; 10.5ml – UK £3.07, Ireland €3.88; 26ml - UK £6.83, Ireland €8.19 **Legal category:** UK: GSL. Ireland: Not subject to medical prescription. **Marketing Authorisation Numbers:** ChloraPrep, (UK: PL05920/0002-001; Ireland: PA2287/001/002) & ChloraPrep with Tint, (UK: PL05920/0003-0001; Ireland: PA2287/001/001) **Marketing Authorisation Holder:** UK : Becton Dickinson UK Ltd, 1030 Eskdale Road, Winnersh, Wokingham RG41 5TS, United Kingdom. Ireland : Becton Dickinson France, 11 Rue Aristide Bergès, 38800 Le Pont de Claix, France **Date of Revision:** May 2020.

Reporting suspected adverse reactions is important to monitor the benefit/risk balance of the medicinal product. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard (for UK) and www.hpra.ie (for Ireland). Adverse events should also be reported to BD Freephone number: **For UK** 0800 0437 546 or email: CareFusionGB@professionalinformation.co.uk. **For Ireland**: +353 01 4287895/7896 or email: CareFusionIE@professionalinformation.co.uk

1030 Eskdale Road, Winnersh Triangle, Wokingham, RG41 5TS

bd.com/en-uk