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Dear Health Care Professional,

Re: Safety Guideline: skin antisepsis for central neuraxial blockade, Anaesthesia 2014, 69, 1279-1286.

The purpose of this letter is to outline CareFusion's position following publication of the guideline above, by the Working Party established by the Association of Anaesthetists of Great Britain and Ireland (AAGBI). This is in response to an increasing number of clinical enquiries CareFusion has received from hospitals which have standardised to ChloraPrep®, (a sterile, single patient use applicator containing a sterile solution of 2% chlorhexidine gluconate in 70% isopropyl alcohol), for skin disinfection prior to neuraxial procedures.

CareFusion supports recommendations 1, 2, 3 and 5 in the safety guideline, however we believe current evidence does not support Recommendation 4 and its rationale. Further by excluding the use of the only sterile single patient use applicator containing chlorhexidine in alcohol, recommendation 4 compromises the ability of clinicians to comply with recommendations 1, 3 and 5.

CareFusion wishes to maintain an open dialogue with the AAGBI and at the request of the AAGBI senior members of our clinical team have been invited to meet with members of the Working Party in the coming weeks.

Recommendation 4 states:
'Given the lack of convincing evidence of the antimicrobial superiority of a 2% solution of chlorhexidine in alcohol over a 0.5% solution, but the presence of clear evidence of the neurotoxicity of chlorhexidine, the Working Party has concluded that the use of a 0.5% solution be preferred over a 2% solution for skin antisepsis before CNB' (central neuraxial blockade).

1. There is evidence that 2% chlorhexidine in alcohol is superior to 0.5% chlorhexidine in alcohol in decontaminating the skin prior to invasive procedures (Adams, *et al*., 2005, Hibbard 2005, MacDonald CR, *et al*, 2006 & 2011, Crowley L *et al*, 2008, Madeo M, Barlow G, 2008; Casey, AL *et al*, 2008, NishiharaY *et al*, 2012,). Conversely, there is no evidence demonstrating superiority of 0.5% over 2% chlorhexidine in alcohol. So the phrase '…lack of convincing evidence…' is subjective. Other guidelines do recommend 2% over 0.5%. (Loveday, H.P. *et al*, Epic 3 2013, HPS & NHS National Services Scotland, 2012, Department of Health High Impact Interventions, 2011, SARI,2010 & RCSI&RCPI 2012).

2. The phrase '…clear evidence of the neurotoxicity of chlorhexidine…' aside from animal studies where chlorhexidine has been injected directly into the cerebrospinal fluid (Weston-Hurst, E. 1955), the evidence of neurotoxicity associated with skin disinfection which has been reviewed is broadly anecdotal. Whilst supported by some additional evidence, the risk is practice based, not concentration dependent. The Working Party did not refer to a large retrospective cohort study, analysing 11,095 adult patients from the Mayo Clinic, in which 2% chlorhexidine in 70% isopropyl

alcohol (ChloraPrep) is exclusively used for skin antisepsis for this procedure (Sviggum, *at al,* 2012). The authors concluded: 'These results support the hypothesis that CHG (chlorhexidine gluconate) can be used for skin antisepsis before spinal placement without increasing the risk of neurologic complications attributed to the spinal anaesthetic'. The theoretical risk that a higher concentration of chlorhexidine, used correctly, is more likely to result in a clinically relevant volume of molecules passing into the neuraxial space via the epidural needle has been refuted in a study of neuronal and schwann cells (Doan, L *et al* 2012)

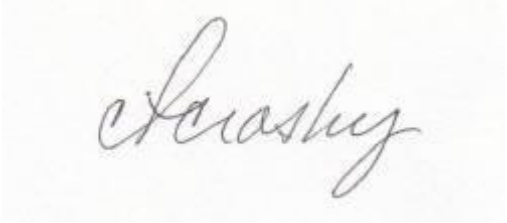
3. The method of application for skin antisepsis is reviewed in the guidelines; Recommendation 1 – optimum aseptic technique, Recommendation 3 – meticulous measures to prevent chlorhexidine reaching the cerebrospinal fluid. However only a sterile, single use applicator, containing chlorhexidine in alcohol, controlling the flow of solution will help clinicians comply with the guideline and specific recommendations. In addition, use of sprays or gallipots increase the risk of potential contamination of the sterile field and equipment. The Working Party do acknowledge the benefits of sterile single-patient use applicators and have asked CareFusion to consider producing an applicator containing 0.5% chlorhexidine in alcohol. Since we believe there is no clinical rationale and hence no commercial rationale to do this, we have no plans to invest the significant R&D resources and the years it would take to develop and secure a new MHRA license (Marketing Authorisation) to market such a product for the UK. The risk of infection following neuraxial procedures is greater than that of Chronic Adhesive Arachnoiditis in clinical practice (Killeen 2012, Wang et al 1999, Royal College of Anaesthetists 2009).

CareFusion believes the evidence supports a sterile single use applicator containing a sterile solution of 2% chlorhexidine gluconate in 70% isopropyl alcohol as currently the most effective way to minimise infection and contamination risks associated with neuraxial procedures. To date there have been no reported neurotoxic adverse events associated with ChloraPrep (Data on file) Similarly, ChloraPrep is not contraindicated for neuraxial procedures. The Summary of Product Characteristics (SmPC), (in keeping with other chlorhexidine based skin preparations) does state that direct contact with neural tissue should be avoided. It is recommended that before all invasive procedures, including neuraxial, ChloraPrep is allowed to air dry fully.

There is a comprehensive package of information and clinical training support available from CareFusion designed to support the appropriate and effective use of ChloraPrep. If you would like further information please contact your local CareFusion representative or call our Customer Service team on 0800 917 8776

Thank you.

Yours sincerely,



Dr. Cynthia T Crosby, PhD
VP Clinical Strategy
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References in order of appearance:

- Adams D *et al*. J Hosp Infect 2005; 61: 287-90.
- Hibbard J. J Infus Nurs 2005; 28: 194–207.
- McDonald CP et al. Vox Sanguinis 2006; 91 (Suppl. 3): P–150. Or
- McDonald CP, Biggs C, Lees B *et al.*Transfus Med Hemother 2011; 38 (4): 255-258
- Crowley L, Preston R, Wong A *et al*. *Anesthesia and Analgesia*, 2008; 106: A1-A221 (Abstract A3)
- Madeo M, Barlow G. J Hosp Infect 2008; 69: 307–9
- Casey AL *et al*. Poster presented at ECCMID, Barcelona, Spain, April 2008.
- Nishihara Y, Kajiura T, Yokota K *et al*. *J Infus Nursing*. 2012; 35(1): 44-50
- Loveday H.P. *et al.* J Hosp Infect 2014; 85 (Suppl 1): S1-70.
- Department of Health High Impact Interventions, 2011 http://webarchive.nationalarchives.gov.uk/20120118164404/hcai.dh.gov.uk/whatdoido/high-impact-interventions (Last accessed 27/10/2014)
- Health Protection Scotland: What are the key infection prevention and control recommendations to inform a surgical site infection (SSI) prevention quality improvement tool? http://www.documents.hps.scot.nhs.uk/hai/infection-control/evidence-for-care-bundles/literature-reviews/ssi-review.pdf (Last accessed 27/10/2014)
- A Strategy for the control of Antimicrobial Resistance in Ireland (SARI) 2010, updated 2014 http://www.hpsc.ie/A-Z/Hepatitis/GuidanceforRenalUnits/File,4115,en.pdf (Last accessed 27/10/2014)
- Royal College of Surgeons in Ireland & Royal College of Physicians of Ireland SSI Guidelines 2012
- http://www.rcpi.ie/content/docs/000001/1005_5_media.pdf (Last accessed 27/10/2014)
- Weston-Hurst, E. Journal of Path and Bact 1955; 38: 167-78
- Sviggum HP et al. Reg Anesth Pain Med 2012; 37: 139–44.
- Doan L et al. Reg Anesth Pain Med 2012; 37: 131–8.
- Killeen, T et al. Anaesthesia 2012, 67, 1386–1394
- Wang LP, Hauerberg J, Schmidt JF.. Anesthesiology. 1999; 91: 1928Y1936.
- 3rd National Audit Project of the Royal College of Anaesthetists Report, 2009. www.rcoa.ac.uk/node/4207 Last accessed on 27/10/14
- Data on File, CareFusion.
- ChloraPrep Summary of Product Characteristics, UK PL 31760/0001

Prescribing Information: ChloraPrep® (PL31760/0004) & ChloraPrep with Tint (PL31760-0001) 2% chlorhexidine gluconate w/v / 70% isopropyl alcohol v/v cutaneous solution. **Indication**: Disinfection of skin prior to invasive medical procedures **Dosage & administration**: ChloraPrep - 0.67ml, 1.5ml, 3ml, 10.5ml, 26ml ; ChloraPrep with Tint – 3ml, 10.5ml, 26ml. Volume dependent on invasive procedure being undertaken. 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. **Side effects, precautions & contra-indications**: Very rarely allergic or skin reactions reported with chlorhexidine, isopropyl alcohol and Sunset Yellow. Contra-indicated for patients with known hypersensitivity to these constituents. For external use only on intact skin. Avoid contact with eyes, mucous membranes, middle ear and neural tissue. Should not be used in children under 2 months of age. Solution is flammable. Do not use with ignition sources until dry, do not allow to pool, and remove soaked materials before use. Over-vigorous use on fragile or sensitive skin or repeated use may lead to local skin reactions. At the first sign of local skin reaction, application should be stopped. **Per applicator costs** (ex VAT) ChloraPrep: 0.67ml (SEPP) - 30p; 1.5ml (FREPP) - 55p; 1.5ml – 78p; 3ml – 85p; 10.5ml - £2.92; 26ml - £6.50 ChloraPrep with Tint: 3ml – 89p; 10.5ml – £3.07; 26ml - £6.83 **Legal category**: GSL **Marketing Authorisation Holder**: CareFusion UK 244 Ltd, The Crescent, Jays Close, Basingstoke, Hampshire, RG22 4BS. **Date of Preparation:** May 2014

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard. mhra.gov.uk. Adverse events should also be reported to CareFusion Freephone number: 0800 0437 546 or email: CareFusionGB@professionalinformation.co.uk