



## Clinical trial results:

### Chlorhexidine Versus Povidone-Iodine For Skin Antisepsis Prior To Central Venous Catheter Insertion In Preterm Infants: Protocol For A Randomised Trial (The SKA Trial)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2011-002962-19   |
| Trial protocol           | IE               |
| Global end of trial date | 19 December 2014 |

#### Results information

|                                   |                                                                                                                                                                                                                                                                                                                                                                  |
|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number             | v1 (current)                                                                                                                                                                                                                                                                                                                                                     |
| This version publication date     | 22 February 2019                                                                                                                                                                                                                                                                                                                                                 |
| First version publication date    | 22 February 2019                                                                                                                                                                                                                                                                                                                                                 |
| Summary attachment (see zip file) | 2% chlorhexidine-70% isopropyl alcohol versus 10% povidone-iodine for insertion site cleaning before central line insertion in preterm infants: a randomised trial (Kieran et al - 2016 - 2% chlorhexidine-70% isopropyl alcohol versus 10% povidone-iodine for insertion site cleaning before central line insertion in preterm infants a randomised trial.pdf) |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | SKA 001 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |   |
|------------------------------------|---|
| ISRCTN number                      | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN)   | - |

Notes:

#### Sponsors

|                              |                                                                                                 |
|------------------------------|-------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | University College Dublin                                                                       |
| Sponsor organisation address | Belfield, Dublin, Ireland,                                                                      |
| Public contact               | UCD Clinical Research Centre, UCD Clinical Research Centre, 00353 017164597, peter.doran@ucd.ie |
| Scientific contact           | UCD Clinical Research Centre, UCD Clinical Research Centre, 00353 017164597, peter.doran@ucd.ie |

Notes:

#### Paediatric regulatory details

|                                                                      |    |
|----------------------------------------------------------------------|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 19 December 2014 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 19 December 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 19 December 2014 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To determine whether the use of 2% chlorhexidine in 70% isopropyl alcohol compared to 10% povidone-iodine for skin antisepsis prior to central venous catheter insertion results in fewer catheter related blood stream infections in infants <31 weeks gestation

Protection of trial subjects:

The decision to insert a central venous catheter and the type of central venous catheter to be inserted were made by the attending clinicians.

Central venous catheters were inserted under maximum sterile barrier precautions (sterile gown, sterile gloves, hat and mask and using full-body drape) following local clinical guidelines that were common to both neonatal intensive care units.

Central venous catheters could remain in place when sepsis was suspected. However, if a blood culture was positive, the central venous catheter was removed, the tip (5 cm length, cut using sterile blade) was sent for culture and a further blood culture was taken from a different peripheral site.

Infants at both centres suspected of having late onset sepsis were empirically treated with flucloxacillin and gentamicin as a first line. Vancomycin could subsequently be used if catheter-related bloodstream infection was confirmed, and treatment was considered appropriate. Antibiotics for catheter-related bloodstream infection were not given through a central venous catheter that was suspected to be infected.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 05 September 2011 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Ireland: 310 |
| Worldwide total number of subjects   | 310          |
| EEA total number of subjects         | 310          |

Notes:

### Subjects enrolled per age group

|                                           |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 310 |
| Newborns (0-27 days)                      | 0   |

|                                          |   |
|------------------------------------------|---|
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years)                    | 0 |
| Adolescents (12-17 years)                | 0 |
| Adults (18-64 years)                     | 0 |
| From 65 to 84 years                      | 0 |
| 85 years and over                        | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited from two stand-alone university maternity hospital: the National Maternity Hospital, Holles Street, Dublin and the Coombe Women and Infants University Hospital, Dublin.

### Pre-assignment

Screening details:

Infants born at less than 31 weeks of gestational age were eligible for enrolment if they were undergoing CVC insertion for the first time in the neonatal ICU. Infants with congenital anomalies and infants who had previously undergone CVC insertion before the agent used to clean the insertion site could be randomly assigned were excluded.

### Pre-assignment period milestones

|                              |                    |
|------------------------------|--------------------|
| Number of subjects started   | 434 <sup>[1]</sup> |
| Number of subjects completed | 304                |

### Pre-assignment subject non-completion reasons

|                            |                                                      |
|----------------------------|------------------------------------------------------|
| Reason: Number of subjects | Adverse event, non-fatal: 14                         |
| Reason: Number of subjects | Consent withdrawn by subject: 32                     |
| Reason: Number of subjects | Physician decision: 2                                |
| Reason: Number of subjects | Outborn central venous catheter in situ: 30          |
| Reason: Number of subjects | Inborn umbilical venous catheter in delivery room: 2 |
| Reason: Number of subjects | No-one to consent: 9                                 |
| Reason: Number of subjects | not approached: 40                                   |
| Reason: Number of subjects | Gestational age was 31 weeks: 1                      |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 6 subjects excluded after baseline due to meeting exclusion criteria. These were not included in baseline results.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Baseline Period         |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| Arm title                    | POV IOD |

Arm description:

Subjects in the PI arm were randomised to be treated with povidone-iodine.

|                                        |                                    |
|----------------------------------------|------------------------------------|
| Arm type                               | Experimental                       |
| Investigational medicinal product name | 10% w/w povidone-iodine            |
| Investigational medicinal product code |                                    |
| Other name                             | Videne 10% w/w antiseptic Solution |
| Pharmaceutical forms                   | Cutaneous liquid                   |
| Routes of administration               | Cutaneous use, Local use           |

Dosage and administration details:

Approximately 3 ml of brown 10% w/w povidone-iodine was poured directly into a sterile dish, and a

sterile cotton swab was dipped into it for 1–2 seconds. The swab was squeezed to remove excess solution and used to clean the site for 30 seconds. The area was allowed to dry naturally before CVC insertion.

|                                                                                                                                             |                                                          |
|---------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| <b>Arm title</b>                                                                                                                            | CHX-IA                                                   |
| Arm description:<br>Subjects in the CHX-IA arm were randomised to be treated with chlorhexidine gluconate/isopropyl alcohol/water solution. |                                                          |
| Arm type                                                                                                                                    | Experimental                                             |
| Investigational medicinal product name                                                                                                      | 2% w/v chlorhexidine in 70% v/v isopropyl alcohol        |
| Investigational medicinal product code                                                                                                      |                                                          |
| Other name                                                                                                                                  | ChoraPrep 2% chlorhexidine w/v/isopropyl alcohol 70% v/v |
| Pharmaceutical forms                                                                                                                        | Cutaneous solution                                       |
| Routes of administration                                                                                                                    | Cutaneous use, Local use                                 |

**Dosage and administration details:**

The CVC insertion site was cleaned with 1 0.67 ml ampoule of 2% w/v chlorhexidine in 70% v/v isopropyl alcohol using a single applicator for 30 seconds and then allowed to dry naturally before CVC insertion. If a second ampoule was used, the reason for use was documented on the CVC checklist.

| <b>Number of subjects in period 1<sup>[2]</sup></b> | POV IOD | CHX-IA |
|-----------------------------------------------------|---------|--------|
| Started                                             | 156     | 148    |
| Completed                                           | 156     | 148    |

**Notes:**

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 6 subjects excluded after baseline due to meeting exclusion criteria. These were not included in baseline results.

|                              |                         |
|------------------------------|-------------------------|
| <b>Period 2</b>              |                         |
| Period 2 title               | Period 2                |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

**Arms**

|                              |        |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes    |
| <b>Arm title</b>             | CHX-IA |

**Arm description:**

Infants randomised to CHX-IA group had the CVC insertion site cleaned with chlorhexidine gluconate/isopropyl alcohol/water solution.

|                                        |                                                          |
|----------------------------------------|----------------------------------------------------------|
| Arm type                               | Experimental                                             |
| Investigational medicinal product name | 2% w/v chlorhexidine in 70% v/v isopropyl alcohol        |
| Investigational medicinal product code |                                                          |
| Other name                             | ChoraPrep 2% chlorhexidine w/v/isopropyl alcohol 70% v/v |
| Pharmaceutical forms                   | Cutaneous solution                                       |
| Routes of administration               | Cutaneous use, Local use                                 |

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**Dosage and administration details:**

The CVC insertion site was cleaned with 1 0.67 ml ampoule of 2% w/v chlorhexidine in 70% v/v isopropyl alcohol using a single applicator for 30 seconds and then allowed to dry naturally before CVC insertion. If a second ampoule was used, the reason for use was documented on the CVC checklist.

|                                                                               |                                    |
|-------------------------------------------------------------------------------|------------------------------------|
| <b>Arm title</b>                                                              | POV IOD                            |
| Arm description:<br>Subjects in the PI arm were treated with povidone-iodine. |                                    |
| Arm type                                                                      | Experimental                       |
| Investigational medicinal product name                                        | 10% w/w povidone-iodine            |
| Investigational medicinal product code                                        |                                    |
| Other name                                                                    | Videne 10% w/w antiseptic Solution |
| Pharmaceutical forms                                                          | Cutaneous liquid                   |
| Routes of administration                                                      | Cutaneous use, Local use           |

**Dosage and administration details:**

Approximately 3 ml of brown 10% w/w povidone-iodine was poured directly into a sterile dish, and a sterile cotton swab was dipped into it for 1–2 seconds. The swab was squeezed to remove excess solution and used to clean the site for 30 seconds. The area was allowed to dry naturally before CVC insertion.

| <b>Number of subjects in period 2</b> | CHX-IA | POV IOD |
|---------------------------------------|--------|---------|
| Started                               | 148    | 156     |
| Completed                             | 148    | 156     |

## Baseline characteristics

### Reporting groups

|                                                                                                                         |         |
|-------------------------------------------------------------------------------------------------------------------------|---------|
| Reporting group title                                                                                                   | POV IOD |
| Reporting group description:                                                                                            |         |
| Subjects in the PI arm were randomised to be treated with povidone-iodine.                                              |         |
| Reporting group title                                                                                                   | CHX-IA  |
| Reporting group description:                                                                                            |         |
| Subjects in the CHX-IA arm were randomised to be treated with chlorhexidine gluconate/isopropyl alcohol/water solution. |         |

| Reporting group values                             | POV IOD | CHX-IA | Total |
|----------------------------------------------------|---------|--------|-------|
| Number of subjects                                 | 156     | 148    | 304   |
| Age categorical                                    |         |        |       |
| Units: Subjects                                    |         |        |       |
| In utero                                           |         |        | 0     |
| Preterm newborn infants (gestational age < 37 wks) |         |        | 0     |
| Newborns (0-27 days)                               |         |        | 0     |
| Infants and toddlers (28 days-23 months)           |         |        | 0     |
| Children (2-11 years)                              |         |        | 0     |
| Adolescents (12-17 years)                          |         |        | 0     |
| Adults (18-64 years)                               |         |        | 0     |
| From 65-84 years                                   |         |        | 0     |
| 85 years and over                                  |         |        | 0     |
| Age continuous                                     |         |        |       |
| Gestational age                                    |         |        |       |
| Units: weeks                                       |         |        |       |
| arithmetic mean                                    | 27      | 27     |       |
| standard deviation                                 | ± 2     | ± 2    | -     |
| Gender categorical                                 |         |        |       |
| Units: Subjects                                    |         |        |       |
| Female                                             | 87      | 67     | 154   |
| Male                                               | 69      | 81     | 150   |
| Antenatal steroid exposure                         |         |        |       |
| Subjects treated with antenatal steroids           |         |        |       |
| Units: Subjects                                    |         |        |       |
| Exposed                                            | 155     | 144    | 299   |
| Not exposed                                        | 1       | 4      | 5     |
| Caesarean section                                  |         |        |       |
| Subjects born by caesarean section                 |         |        |       |
| Units: Subjects                                    |         |        |       |
| Born by caesarean section                          | 100     | 91     | 191   |
| Not born by caesarean section                      | 56      | 57     | 113   |
| Clinical chorioamnionitis                          |         |        |       |
| Subjects with clinical chorioamnionitis            |         |        |       |
| Units: Subjects                                    |         |        |       |
| Clinical chorioamnionitis                          | 24      | 14     | 38    |
| No clinical chorioamnionitis                       | 132     | 134    | 266   |

|                                                                                                                    |         |         |     |
|--------------------------------------------------------------------------------------------------------------------|---------|---------|-----|
| Multiple birth                                                                                                     |         |         |     |
| Subjects who were part of a multiple birth                                                                         |         |         |     |
| Units: Subjects                                                                                                    |         |         |     |
| Multiple birth                                                                                                     | 54      | 62      | 116 |
| No multiple birth                                                                                                  | 102     | 86      | 188 |
| Ventilation prerandomisation                                                                                       |         |         |     |
| Subjects who were ventilated before randomisation                                                                  |         |         |     |
| Units: Subjects                                                                                                    |         |         |     |
| Ventilated before randomisation                                                                                    | 78      | 64      | 142 |
| Not ventilated before randomisation                                                                                | 78      | 84      | 162 |
| CPAP prerandomisation                                                                                              |         |         |     |
| Subjects who were administered continuous positive airway pressure before randomisation.                           |         |         |     |
| Units: Subjects                                                                                                    |         |         |     |
| CPAP before randomisation                                                                                          | 100     | 102     | 202 |
| No CPAP before randomisation                                                                                       | 56      | 46      | 102 |
| UVC as first CVC                                                                                                   |         |         |     |
| Subjects who received an umbilical venous catheter or a peripherally inserted central catheter as there first CVC. |         |         |     |
| Units: Subjects                                                                                                    |         |         |     |
| UVC                                                                                                                | 104     | 96      | 200 |
| PICC                                                                                                               | 52      | 52      | 104 |
| Birth weight                                                                                                       |         |         |     |
| Units: gram(s)                                                                                                     |         |         |     |
| arithmetic mean                                                                                                    | 1014    | 1017    |     |
| standard deviation                                                                                                 | ± 326   | ± 289   | -   |
| Apgar score at 1 min                                                                                               |         |         |     |
| The Apgar score at 1 minute post-delivery                                                                          |         |         |     |
| Units: arbitrary                                                                                                   |         |         |     |
| arithmetic mean                                                                                                    | 6       | 6       |     |
| standard deviation                                                                                                 | ± 2     | ± 2     | -   |
| Apgar score at 5 min                                                                                               |         |         |     |
| The Apgar score at 1 minute post-delivery                                                                          |         |         |     |
| Units: arbitrary                                                                                                   |         |         |     |
| arithmetic mean                                                                                                    | 8       | 8       |     |
| standard deviation                                                                                                 | ± 2     | ± 2     | -   |
| Day of life randomised                                                                                             |         |         |     |
| Day of life on which subjects were randomised.                                                                     |         |         |     |
| Units: day                                                                                                         |         |         |     |
| median                                                                                                             | 0       | 0       |     |
| inter-quartile range (Q1-Q3)                                                                                       | 0 to 0  | 0 to 1  | -   |
| Number of CVCs per patient                                                                                         |         |         |     |
| Number of central venous catheters per subject.                                                                    |         |         |     |
| Units: CVCs                                                                                                        |         |         |     |
| arithmetic mean                                                                                                    | 3       | 3       |     |
| standard deviation                                                                                                 | ± 1     | ± 1     | -   |
| Duration CVC in situ per patient                                                                                   |         |         |     |
| Duration of central venous catheter left in situ per subject.                                                      |         |         |     |
| Units: days                                                                                                        |         |         |     |
| median                                                                                                             | 9       | 9       |     |
| inter-quartile range (Q1-Q3)                                                                                       | 6 to 13 | 6 to 12 | -   |



## End points

### End points reporting groups

|                                                                                                                                                                      |         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Reporting group title                                                                                                                                                | POV IOD |
| Reporting group description:<br>Subjects in the PI arm were randomised to be treated with povidone-iodine.                                                           |         |
| Reporting group title                                                                                                                                                | CHX-IA  |
| Reporting group description:<br>Subjects in the CHX-IA arm were randomised to be treated with chlorhexidine gluconate/isopropyl alcohol/water solution.              |         |
| Reporting group title                                                                                                                                                | CHX-IA  |
| Reporting group description:<br>Infants randomised to CHX-IA group had the CVC insertion site cleaned with chlorhexidine gluconate/isopropyl alcohol/water solution. |         |
| Reporting group title                                                                                                                                                | POV IOD |
| Reporting group description:<br>Subjects in the PI arm were treated with povidone-iodine.                                                                            |         |

### Primary: Incidence of catheter-related bloodstream infection per infant

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Incidence of catheter-related bloodstream infection per infant |
| End point description:<br>The primary outcome for our study was the number of infants with a CR-BSI. Infants were diagnosed with a CR-BSI if they were >72 hours of age and had a CVC in situ or removed within the previous 48 hours and met at least one of the following three criteria:<br>a recognised pathogen (eg, Staphylococcus aureus and Candida species) in one peripheral blood culture (ie, not taken through CVC) that was not related to an infection at another site (eg, meningitis or skin abscess),<br>a common skin commensal (eg, coagulase-negative Staphylococcus (CONS)) cultured from two or more peripheral blood cultures drawn on separate occasions,<br>a common skin commensal (eg, CONS) isolated from one peripheral blood culture with a CVC tip culture growing >15 colony-forming units of a pure growth of the same organism. |                                                                |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                                        |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                |

| End point values                               | CHX-IA          | POV IOD         |  |  |
|------------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                             | Reporting group | Reporting group |  |  |
| Number of subjects analysed                    | 148             | 156             |  |  |
| Units: catheter-related bloodstream infections | 10              | 8               |  |  |

### Statistical analyses

|                            |                                       |
|----------------------------|---------------------------------------|
| Statistical analysis title | Difference in proportion between arms |
| Comparison groups          | CHX-IA v POV IOD                      |

|                                         |               |
|-----------------------------------------|---------------|
| Number of subjects included in analysis | 304           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | = 0.631       |
| Method                                  | Fisher exact  |

### Primary: Incidence of catheter-related bloodstream infection per catheter

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Incidence of catheter-related bloodstream infection per catheter |
|-----------------|------------------------------------------------------------------|

End point description:

The primary outcome for our study was the number of infants with a CR-BSI. Infants were diagnosed with a CR-BSI if they were >72 hours of age and had a CVC in situ or removed within the previous 48 hours and met at least one of the following three criteria:

a recognised pathogen (eg, Staphylococcus aureus and Candida species) in one peripheral blood culture (ie, not taken through CVC) that was not related to an infection at another site (eg, meningitis or skin abscess),

a common skin commensal (eg, coagulase-negative Staphylococcus (CONS)) cultured from two or more peripheral blood cultures drawn on separate occasions,

a common skin commensal (eg, CONS) isolated from one peripheral blood culture with a CVC tip culture growing >15 colony-forming units of a pure growth of the same organism.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.

| End point values                               | CHX-IA          | POV IOD         |  |  |
|------------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                             | Reporting group | Reporting group |  |  |
| Number of subjects analysed                    | 148             | 156             |  |  |
| Units: catheter-related bloodstream infections | 10              | 10              |  |  |

### Statistical analyses

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | Difference in proportion between arms |
| Comparison groups                       | CHX-IA v POV IOD                      |
| Number of subjects included in analysis | 304                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.824                               |
| Method                                  | Fisher exact                          |

### Primary: Catheter-related bloodstream infection per 1000 catheter days

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Catheter-related bloodstream infection per 1000 catheter |
|-----------------|----------------------------------------------------------|

**End point description:**

The primary outcome for our study was the number of infants with a CR-BSI. Infants were diagnosed with a CR-BSI if they were >72 hours of age and had a CVC in situ or removed within the previous 48 hours and met at least one of the following three criteria:

a recognised pathogen (eg, *Staphylococcus aureus* and *Candida* species) in one peripheral blood culture (ie, not taken through CVC) that was not related to an infection at another site (eg, meningitis or skin abscess),

a common skin commensal (eg, coagulase-negative *Staphylococcus* (CONS)) cultured from two or more peripheral blood cultures drawn on separate occasions,

a common skin commensal (eg, CONS) isolated from one peripheral blood culture with a CVC tip culture growing >15 colony-forming units of a pure growth of the same organism.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

**End point timeframe:**

>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.

**Notes:**

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis used is unknown

| End point values                 | CHX-IA          | POV IOD         |  |  |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type               | Reporting group | Reporting group |  |  |
| Number of subjects analysed      | 148             | 156             |  |  |
| Units: CR-BSI/1000 catheter days |                 |                 |  |  |
| number (not applicable)          | 6.8             | 6.2             |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects with skin damage from IMP**

|                 |                                              |
|-----------------|----------------------------------------------|
| End point title | Number of subjects with skin damage from IMP |
|-----------------|----------------------------------------------|

**End point description:**

Any area of skin irritation, erythema, excoriation or breakdown that was in the distribution of contact with the investigational medicinal product, and brought to the attention of the research team, was reported as an adverse skin reaction caused by a study solution.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

**End point timeframe:**

>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.

| End point values            | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             | 3               | 2               |  |  |

**Statistical analyses**

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | Difference in proportion between arms |
| Comparison groups                       | CHX-IA v POV IOD                      |
| Number of subjects included in analysis | 304                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.677                               |
| Method                                  | Fisher exact                          |

### Secondary: Incidence of raised thyroid-stimulating hormone on screening

|                                                                                                                                                                                                                                                                                                                |                                                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                | Incidence of raised thyroid-stimulating hormone on screening |
| End point description:<br>Thyroid-stimulating hormone (TSH) values from 8 to 15 mU/L trigger a request for a repeat sample, and if persistently >15 mU/L prompt a request for formal serum thyroid function tests. Any abnormal TSH levels on newborn screening card or subsequent serum sample were recorded. |                                                              |
| End point type                                                                                                                                                                                                                                                                                                 | Secondary                                                    |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.                                                                                                                                                               |                                                              |

|                                |                 |                 |  |  |
|--------------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>        | CHX-IA          | POV IOD         |  |  |
| Subject group type             | Reporting group | Reporting group |  |  |
| Number of subjects analysed    | 148             | 156             |  |  |
| Units: incidence of raised TSH | 0               | 12              |  |  |

### Statistical analyses

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | Difference in proportion between arms |
| Comparison groups                       | CHX-IA v POV IOD                      |
| Number of subjects included in analysis | 304                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | < 0.001                               |
| Method                                  | Fisher exact                          |

### Secondary: Incidence of raised thyroid-stimulating hormone

|                                                                                                                                                                                                                                                                                                                |                                                 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                | Incidence of raised thyroid-stimulating hormone |
| End point description:<br>Thyroid-stimulating hormone (TSH) values from 8 to 15 mU/L trigger a request for a repeat sample, and if persistently >15 mU/L prompt a request for formal serum thyroid function tests. Any abnormal TSH levels on newborn screening card or subsequent serum sample were recorded. |                                                 |

|                                                                                                                          |           |
|--------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                           | Secondary |
| End point timeframe:                                                                                                     |           |
| >72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |           |

| End point values               | CHX-IA          | POV IOD         |  |  |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type             | Reporting group | Reporting group |  |  |
| Number of subjects analysed    | 148             | 156             |  |  |
| Units: incidence of raised TSH | 0               | 10              |  |  |

### Statistical analyses

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | Difference in proportion between arms |
| Comparison groups                       | CHX-IA v POV IOD                      |
| Number of subjects included in analysis | 304                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.002                               |
| Method                                  | Fisher exact                          |

### Secondary: Number of subjects requiring thyroxine replacement therapy

|                                                                                                                          |                                                            |
|--------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| End point title                                                                                                          | Number of subjects requiring thyroxine replacement therapy |
| End point description:                                                                                                   |                                                            |
| Number of subjects treated with thyroxine replacement therapy on the advice of paediatric endocrinologists.              |                                                            |
| End point type                                                                                                           | Secondary                                                  |
| End point timeframe:                                                                                                     |                                                            |
| >72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |                                                            |

| End point values            | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             | 0               | 8               |  |  |

### Statistical analyses

|                                   |                                                   |
|-----------------------------------|---------------------------------------------------|
| <b>Statistical analysis title</b> | Difference number of subjects requiring thyroxine |
| Comparison groups                 | CHX-IA v POV IOD                                  |

|                                         |               |
|-----------------------------------------|---------------|
| Number of subjects included in analysis | 304           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | = 0.003       |
| Method                                  | Fisher exact  |

### Secondary: Number of subjects with confirmed LOS (non-CR-BSI)

|                                                                                                                                                                                                                                                                |                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| End point title                                                                                                                                                                                                                                                | Number of subjects with confirmed LOS (non-CR-BSI) |
| End point description:<br>Number of subjects with confirmed late-onset sepsis (non-CR-BSI). Defined as laboratory confirmed sepsis (positive blood or cerebral spinal fluid culture for a recognised pathogen) after 72 hours of age and not related to a CVC. |                                                    |
| End point type                                                                                                                                                                                                                                                 | Secondary                                          |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.                                                                                                               |                                                    |

| End point values            | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             |                 |                 |  |  |
| Confirmed LOS               | 17              | 26              |  |  |
| No confirmed LOS            | 131             | 130             |  |  |

### Statistical analyses

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Statistical analysis title              | Differen in incidence of confirmed LOS |
| Comparison groups                       | POV IOD v CHX-IA                       |
| Number of subjects included in analysis | 304                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | = 0.249                                |
| Method                                  | Fisher exact                           |

### Secondary: Number of subjects with suspected sepsis

|                                                                                                                                                                                                                       |                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| End point title                                                                                                                                                                                                       | Number of subjects with suspected sepsis |
| End point description:<br>Defined as clinical signs of sepsis, for example, increased frequency of apnoea, tachycardia or temperature instability, with negative blood culture, and treated with ≥5 days antibiotics. |                                          |
| End point type                                                                                                                                                                                                        | Secondary                                |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or                                                                                            |                                          |

discharge of subject.

| End point values            | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             |                 |                 |  |  |
| Suspected sepsis            | 13              | 12              |  |  |
| No suspected sepsis         | 135             | 144             |  |  |

### Statistical analyses

|                                         |                                              |
|-----------------------------------------|----------------------------------------------|
| Statistical analysis title              | Difference in subjects with suspected sepsis |
| Comparison groups                       | CHX-IA v POV IOD                             |
| Number of subjects included in analysis | 304                                          |
| Analysis specification                  | Pre-specified                                |
| Analysis type                           | superiority                                  |
| P-value                                 | = 0.835                                      |
| Method                                  | Fisher exact                                 |

### Secondary: Courses of antibiotics per subject

|                                                                                                                          |                                    |
|--------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| End point title                                                                                                          | Courses of antibiotics per subject |
| End point description:                                                                                                   |                                    |
| End point type                                                                                                           | Secondary                          |
| End point timeframe:                                                                                                     |                                    |
| >72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |                                    |

| End point values                          | CHX-IA          | POV IOD         |  |  |
|-------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                        | Reporting group | Reporting group |  |  |
| Number of subjects analysed               | 148             | 156             |  |  |
| Units: Courses of antibiotics per subject |                 |                 |  |  |
| median (inter-quartile range (Q1-Q3))     | 2 (2 to 4)      | 3 (2 to 4)      |  |  |

### Statistical analyses

|                            |                                                  |
|----------------------------|--------------------------------------------------|
| Statistical analysis title | Difference in mean courses of antibiotic/patient |
| Comparison groups          | CHX-IA v POV IOD                                 |

|                                         |                 |
|-----------------------------------------|-----------------|
| Number of subjects included in analysis | 304             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.588         |
| Method                                  | t-test, 2-sided |

### Secondary: Total days of antibiotics per subject

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Total days of antibiotics per subject |
|-----------------|---------------------------------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.

| End point values                      | CHX-IA          | POV IOD         |  |  |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type                    | Reporting group | Reporting group |  |  |
| Number of subjects analysed           | 148             | 156             |  |  |
| Units: days                           |                 |                 |  |  |
| median (inter-quartile range (Q1-Q3)) | 5 (2 to 12)     | 5 (2 to 12)     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of blood cultures performed per subject

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Number of blood cultures performed per subject |
|-----------------|------------------------------------------------|

End point description:

Number of blood cultures performed per subject. Decisions to remove CVCs and to perform blood cultures were at the discretion of treating clinicians to determine the presence of sepsis. If the blood culture was positive a further blood culture was taken from a different peripheral site. A second blood culture was not taken if the first was negative.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.



| End point values                               | CHX-IA          | POV IOD         |  |  |
|------------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                             | Reporting group | Reporting group |  |  |
| Number of subjects analysed                    | 148             | 156             |  |  |
| Units: blood cultures                          |                 |                 |  |  |
| arithmetic mean (inter-quartile range (Q1-Q3)) | 3 (2 to 5)      | 3 (2 to 5)      |  |  |

### Statistical analyses

| Statistical analysis title              | Difference in blood cultures/subject |
|-----------------------------------------|--------------------------------------|
| Comparison groups                       | POV IOD v CHX-IA                     |
| Number of subjects included in analysis | 304                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | superiority                          |
| P-value                                 | = 0.319                              |
| Method                                  | t-test, 2-sided                      |

### Secondary: Number of subjects with any respiratory support on day 28

|                        |                                                                                                                          |
|------------------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title        | Number of subjects with any respiratory support on day 28                                                                |
| End point description: | The number of subjects who were receiving any respiratory support on day 28                                              |
| End point type         | Secondary                                                                                                                |
| End point timeframe:   | >72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |

| End point values                 | CHX-IA          | POV IOD         |  |  |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type               | Reporting group | Reporting group |  |  |
| Number of subjects analysed      | 148             | 156             |  |  |
| Units: subjects                  |                 |                 |  |  |
| Respiratory support on day 28    | 77              | 89              |  |  |
| No respiratory support on day 28 | 71              | 67              |  |  |

### Statistical analyses

| Statistical analysis title | Difference subjects on respiratory support day 28 |
|----------------------------|---------------------------------------------------|
| Comparison groups          | CHX-IA v POV IOD                                  |

|                                         |               |
|-----------------------------------------|---------------|
| Number of subjects included in analysis | 304           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | = 0.42        |
| Method                                  | Fisher exact  |

### Secondary: Number of subjects with oxygen at 36 weeks CGA

|                                                                                                                                                  |                                                |
|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|
| End point title                                                                                                                                  | Number of subjects with oxygen at 36 weeks CGA |
| End point description:<br>The number of subjects who were being treated with supplemental oxygen at a corrected gestational age of 36 weeks      |                                                |
| End point type                                                                                                                                   | Secondary                                      |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |                                                |

| End point values            | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             |                 |                 |  |  |
| Oxygen at 36 weeks CGA      | 27              | 47              |  |  |
| No oxygen at 36 weeks CGA   | 141             | 109             |  |  |

### Statistical analyses

|                                         |                                                    |
|-----------------------------------------|----------------------------------------------------|
| Statistical analysis title              | Difference in subjects with oxygen at 36 weeks CGA |
| Comparison groups                       | CHX-IA v POV IOD                                   |
| Number of subjects included in analysis | 304                                                |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | superiority                                        |
| P-value                                 | = 0.017                                            |
| Method                                  | Fisher exact                                       |

### Secondary: Number of subjects with NEC ≥ Bell stage 2

|                                                                                                                                                  |                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                  | Number of subjects with NEC ≥ Bell stage 2 |
| End point description:<br>The number of subjects with necrotising enterocolitis ≥ Bell stage 2.                                                  |                                            |
| End point type                                                                                                                                   | Secondary                                  |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |                                            |

| <b>End point values</b>     | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             |                 |                 |  |  |
| NEC $\geq$ Bell stage 2     | 14              | 15              |  |  |
| No NEC $\geq$ Bell stage 2  | 134             | 141             |  |  |

### Statistical analyses

|                                         |                                                     |
|-----------------------------------------|-----------------------------------------------------|
| <b>Statistical analysis title</b>       | Difference in subjects with NEC $\geq$ Bell stage 2 |
| Comparison groups                       | CHX-IA v POV IOD                                    |
| Number of subjects included in analysis | 304                                                 |
| Analysis specification                  | Pre-specified                                       |
| Analysis type                           | superiority                                         |
| P-value                                 | = 1                                                 |
| Method                                  | Fisher exact                                        |

### Secondary: Number of subjects with any ROP

|                        |                                                                                                                          |
|------------------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title        | Number of subjects with any ROP                                                                                          |
| End point description: | The number of subjects with any retinopathy of prematurity.                                                              |
| End point type         | Secondary                                                                                                                |
| End point timeframe:   | >72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |

| <b>End point values</b>     | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             |                 |                 |  |  |
| ROP                         | 31              | 15              |  |  |
| No ROP                      | 117             | 141             |  |  |

### Statistical analyses

|                                   |                                     |
|-----------------------------------|-------------------------------------|
| <b>Statistical analysis title</b> | Difference in subjects with any ROP |
| Comparison groups                 | CHX-IA v POV IOD                    |

|                                         |               |
|-----------------------------------------|---------------|
| Number of subjects included in analysis | 304           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | = 0.845       |
| Method                                  | Fisher exact  |

### Secondary: Number of subjects with CRUSS IVH III/IV or PVL

|                                                                                                                                                                           |                                                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| End point title                                                                                                                                                           | Number of subjects with CRUSS IVH III/IV or PVL |
| End point description:<br>The number of subjects with intraventricular haemorrhage grade III/IV or periventricular leukomalacia as determined by cranial ultrasound scan. |                                                 |
| End point type                                                                                                                                                            | Secondary                                       |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject.                          |                                                 |

| End point values            | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: subjects             |                 |                 |  |  |
| CRUSS IVH III/IV or PVL     | 16              | 22              |  |  |
| No CRUSS IVH III/IV or PVL  | 132             | 134             |  |  |

### Statistical analyses

|                                         |                                                  |
|-----------------------------------------|--------------------------------------------------|
| Statistical analysis title              | Difference subjects with CRUSS IVH III/IV or PVL |
| Comparison groups                       | CHX-IA v POV IOD                                 |
| Number of subjects included in analysis | 304                                              |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | superiority                                      |
| P-value                                 | = 0.488                                          |
| Method                                  | Fisher exact                                     |

### Secondary: Number of deaths prior to hospital discharge

|                                                                                                                                                  |                                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| End point title                                                                                                                                  | Number of deaths prior to hospital discharge |
| End point description:                                                                                                                           |                                              |
| End point type                                                                                                                                   | Secondary                                    |
| End point timeframe:<br>>72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |                                              |

| End point values            | CHX-IA          | POV IOD         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 148             | 156             |  |  |
| Units: deaths               |                 |                 |  |  |
| Dead                        | 15              | 18              |  |  |
| Alive                       | 133             | 138             |  |  |

### Statistical analyses

|                                         |                      |
|-----------------------------------------|----------------------|
| <b>Statistical analysis title</b>       | Difference in deaths |
| Comparison groups                       | CHX-IA v POV IOD     |
| Number of subjects included in analysis | 304                  |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | superiority          |
| P-value                                 | = 0.716              |
| Method                                  | Fisher exact         |

### Secondary: Duration of hospital stay

|                                                                                                                          |                           |
|--------------------------------------------------------------------------------------------------------------------------|---------------------------|
| End point title                                                                                                          | Duration of hospital stay |
| End point description:                                                                                                   |                           |
| End point type                                                                                                           | Secondary                 |
| End point timeframe:                                                                                                     |                           |
| >72 hours after birth and had a CVC in situ or removed within the previous 48 hours until death or discharge of subject. |                           |

| End point values                      | CHX-IA          | POV IOD         |  |  |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type                    | Reporting group | Reporting group |  |  |
| Number of subjects analysed           | 148             | 156             |  |  |
| Units: days                           |                 |                 |  |  |
| median (inter-quartile range (Q1-Q3)) | 59 (49 to 85)   | 67 (46 to 90)   |  |  |

### Statistical analyses

|                                   |                                         |
|-----------------------------------|-----------------------------------------|
| <b>Statistical analysis title</b> | Difference in duration of hospital stay |
| Comparison groups                 | CHX-IA v POV IOD                        |

|                                         |                 |
|-----------------------------------------|-----------------|
| Number of subjects included in analysis | 304             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.199         |
| Method                                  | t-test, 2-sided |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded over 39 months with non-serious adverse events reported every 3 months and serious adverse events reported within 24 hours.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |    |
|-----------------|----|
| Dictionary name | NA |
|-----------------|----|

|                    |    |
|--------------------|----|
| Dictionary version | NA |
|--------------------|----|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | POV IOD |
|-----------------------|---------|

Reporting group description:

Subjects in the PI arm were randomised to be treated with povidone-iodine.

|                       |        |
|-----------------------|--------|
| Reporting group title | CHX-IA |
|-----------------------|--------|

Reporting group description:

Subjects in the CHX-IA arm were randomised to be treated with chlorhexidine gluconate/isopropyl alcohol/water solution.

| Serious adverse events                               | POV IOD           | CHX-IA            |  |
|------------------------------------------------------|-------------------|-------------------|--|
| Total subjects affected by serious adverse events    |                   |                   |  |
| subjects affected / exposed                          | 18 / 156 (11.54%) | 15 / 148 (10.14%) |  |
| number of deaths (all causes)                        | 18                | 15                |  |
| number of deaths resulting from adverse events       |                   |                   |  |
| General disorders and administration site conditions |                   |                   |  |
| Death before hospital discharge                      |                   |                   |  |
| subjects affected / exposed                          | 18 / 156 (11.54%) | 15 / 148 (10.14%) |  |
| occurrences causally related to treatment / all      | 0 / 18            | 0 / 15            |  |
| deaths causally related to treatment / all           | 0 / 18            | 0 / 15            |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | POV IOD         | CHX-IA          |  |
|-------------------------------------------------------|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                 |                 |  |
| subjects affected / exposed                           | 2 / 156 (1.28%) | 3 / 148 (2.03%) |  |
| Skin and subcutaneous tissue disorders                |                 |                 |  |
| Skin reaction                                         |                 |                 |  |
| subjects affected / exposed                           | 2 / 156 (1.28%) | 3 / 148 (2.03%) |  |
| occurrences (all)                                     | 2               | 3               |  |





## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29074717>