Health Policy Advisory Committee on Technology

Technology Brief

AIGISRx® Antibacterial Envelope for preventing infection in implanted cardiac devices

August 2013

HealthPACT
emerging health technology
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This brief was prepared by Dr Meegan Vandepeer from the Australian Safety and Efficacy Register of New Interventionsal Procedures – Surgical (ASERNIP-S).
Technology, Company and Licensing

Register ID  WP165

Technology name  AIGISrx® Antibacterial Envelope

Patient indication  For use in patients who are being implanted with either a pacemaker or implantable cardioverter-defibrillator (ICD)

Description of the technology

The AIGISrx® Antibacterial Envelope is intended to securely enclose a cardiac implantable electronic device (CIED), that is a pacemaker or implantable cardioverter defibrillator (ICD), in order to create a stable environment around the device and reduce the risk of post-surgery infections associated with the implanted pulse generator (Figure 1). The envelope is made from a non-resorbable mesh comprising a knitted polypropylene substrate that is coated with a bioresorbable polymer containing two antimicrobial agents (minocycline and rifampicin). The envelopes come in two sizes—one for pacemakers (medium, 6.3 cm x 6.9 cm) and one for defibrillators (large, 7.4 cm x 8.5 cm)—and may be used for a patient’s first implant or when the pacemaker or ICD needs to be replaced. The envelopes are not reusable.1

![The AIGISrx® Antibacterial Envelope](image)

Figure 1  The AIGISrx® Antibacterial Envelope

The two antibiotics are released continuously over a 7- to 10-day period by the antibacterial envelope (locally, at the surgical site), following implantation of the pacemaker or ICD. According to the manufacturers of AIGISrx®, minocycline has been shown to be effective against Staphylococcus aureus, Streptococcus pneumonia, Escherichia coli, Enterobacter aerogenes, Haemophilus influenzae and Acinetobacter baumannii, whilst rifampicin has been shown to be effective against Staphylococcus aureus, Staphylococcus epidermidis and Haemophilus influenzae. The mesh contains 86 µg/cm² of each antibiotic.2

Within the first 24 hours of device implantation, the amount of antibiotics is approximately 5,000 times the minimum lethal concentration of antibiotics that would kill Staphylococcus
aureus (including methicillin-resistant Staphylococcus aureus), Staphylococcus epidermis, Escherichia coli, Acinetobacter baumannii and Staphylococcus capitis. The resorbable polymer that contains the two antibiotics takes approximately 140 days to be absorbed by the body, leaving the non-resorbable mesh behind to hold and stabilise the device.

Prior to implantation, the skin at the site where the CIED is to be placed is shaved/clipped and cleaned and the patient is given a local anaesthetic and sedative. An incision is made in the chest where the leads and device are to be inserted. The initial surgical incision needs to be somewhat larger than what is needed for placing the same pacemaker or ICD without an antibiotic envelope, especially for subpectoral implantations. After the generator is attached to the leads, the AIGISRx® is activated by briefly immersing it in saline solution. Next the pacemaker or ICD generator is placed in the AIGISRx® Envelope. This may require expanding the opening of the envelope by tearing or cutting it. The generator, and as much of the looped leads as possible, are placed inside. The AIGISRx® Envelope, containing either the pacemaker or ICD, is placed into the pocket underneath the skin, which is then closed following normal procedure. Removal of the AIGISRx® Envelope during a pulse generator replacement is not required except in the case of an infection. In this situation, it is common practice to perform a capsulectomy, a procedure in which the entire ‘capsule’ of scar tissue surrounding the implant is removed, and/or a debridement.

Company or developer
TYRX, Inc., New Jersey, United States of America (USA).

Reason for assessment
The AIGISRx® Antibacterial Envelope may reduce infections that can occur when implanting pacemakers and ICDs, particularly in high-risk patients, with potential cost benefits to the healthcare system.

Stage of development in Australia
☐ Yet to emerge  ☑ Established
☐ Experimental  ☐ Established but changed indication or modification of technique
☐ Investigational  ☐ Should be taken out of use
☐ Nearly established

Licensing, reimbursement and other approval
TYRX, Inc.’s AIGISRx® Antibacterial Envelope was granted United States Food and Drug Administration (FDA) 510 (k) clearance in January 2008 (application number: K063091). In June 2012, TYRX, Inc. received a licence from Health Canada to market the AIGISRx® Antibacterial Envelope with implantable electronic devices. The AIGISRx® Antibacterial
Envelope does not appear to have received a CE mark, nor is it listed on the Australian Register of Therapeutic Goods (ARTG).

**Australian Therapeutic Goods Administration approval**

☐ Yes  ARTG number (s) Not applicable
☒ No
☐ Not applicable

**Technology type**  Device

**Technology use**  Preventative

**Patient Indication and Setting**

**Disease description and associated mortality and morbidity**

Surgical site infections (SSI) can develop in anyone who receives an implantable pacemaker or ICD. However, there are a number of patient-specific and procedure-based factors that increase the risk of developing a SSI. Patient-related risk factors include the use of oral anticoagulants and steroids, the presence of a fever within the previous 24 hours and the presence of comorbidities such as diabetes and chronic renal disease. Procedure-related factors that can increase the risk of infection include not using antibiotic prophylaxis, the number of leads implanted, the procedure type, the operator’s experience, the performance of a device revision or replacement versus a new implant and the need for early re-intervention.\

There are two main types of CIED infections.

A. Local SSIs at the generator pocket and the subcutaneous segment of the leads. Symptoms of local infections include erythema, warmth, wound dehiscence, tenderness, purulent drainage, erosion of the generator or leads through the skin. These typically occur within the first several months after implantation or revision, although late-onset infections can occur years after device manipulation.

B. Trans-venous lead infections or lead-related endocarditis. These infections are less common and are deeper than SSIs. These patients commonly present with systemic symptoms, such as fever or sepsis, and often produce positive blood cultures. Trans-oesophageal echocardiography may be useful in detecting CIED-related endocarditis.\

Complications resulting from a CIED infection may occur at the site of implantation or at an anatomically remote site. Complications that can occur at the site of implantation include chest wall abscess, septic thrombophlebitis and right-sided endocarditis. Complications that occur more remotely include skeletal complications, both local (clavicular osteomyelitis and
sternoclavicular arthritis) and remote (metastatic osteomyelitis, discitis and septic arthritis); cardiopulmonary complications (septic pulmonary emboli, mycotic pulmonary artery aneurysm and left-sided endocarditis); and metastatic complications, including soft tissue and organ or muscle abscess formation and sepsis.\textsuperscript{7}

Evidence-based recommendations for the management of CIED infections have been provided by the American Heart Association.\textsuperscript{7} It recommends that all infections should be treated with antibiotic therapy, and in cases of severe infection, the device should be removed.

**Number of patients**

According to public hospital reports from the Australian Institute of Health and Welfare (AIHW), between 2009 and 2010 there were:

- 12,842 procedures for insertion of cardiac pacemaker generators
- 5,083 procedures for adjustment, replacement or removal of cardiac pacemaker generators
- 3,198 procedures for insertion of cardiac defibrillator generators
- 1,644 procedures for adjustment, replacement or removal of cardiac defibrillator generators.\textsuperscript{8}

Medical Benefits Schedule (MBS) statistics for similar procedures within the private hospital system revealed that in 2012 there were:

- 8,342 services for permanent cardiac pacemaker insertion, removal or replacement (MBS item 38353)
- 742 services for automatic defibrillator generator insertion or replacement (MBS item 38387)
- 1,065 services for automatic defibrillator generator insertion or replacement—not for patients with heart failure or as primary prevention for tachycardia arrhythmias (MBS item 38393).\textsuperscript{9}

CIED infection rates vary between medical centres but tend to occur in one to two per cent of patients receiving an implantable pacemaker or ICD.\textsuperscript{10,11} One Australian study investigating cases of pacemaker and ICD-related CIED infections in three hospitals in Geelong between June 1994 and December 2004 was identified. In this study, a total of 24 infections were recorded at the primary centre, where 1,481 operations were performed (infection rate of 1.6%).\textsuperscript{12} All patients had received perioperative prophylactic antibiotics.

There were no New Zealand data identified for the number of patients undergoing pacemaker or ICD implantation/removal, or for the incidence of CIED infection in this population.
Speciality: Cardiovascular disease and vascular surgery

Technology setting: General hospital

**Impact**

**Alternative and/or complementary technology**

As the AIGISrx® Antibacterial Envelope works locally, at the site where the device is implanted, it is designed to complement, not replace, the current conventional treatment of prophylactic intravenous or oral systemic antibiotics for patients receiving an ICD or pacemaker implant.

**Current technology**

The current recommendation by the American Heart Association to prevent CIED infection is to use prophylactic antibiotics which have in vitro activity against *Staphylococcus*. Cefazolin is the recommended antibiotic and should be administered intravenously one hour prior to surgery. In patients who are allergic to cephalosporins and in centres where oxacillin resistance among *staphylococci* is high, vancomycin is used as an alternative to cefazolin. It should be administered two hours prior to surgery.

The AIGISrx® Antibacterial Envelope is the first antibacterial device for preventing infections associated with the implantation of cardiac devices. The purported advantages of using local antibacterial prophylaxis are as follows:

- higher local concentration of antibiotics than with systemic administration, thus reducing the potential for antibacterial resistance;
- ability to manipulate the duration of antibacterial activity; and
- more effective inhibition of bacterial colonisation of the implanted device.

**Diffusion of technology in Australia**

The AIGISrx® Antibacterial Envelope is yet to emerge in Australia.

**International utilisation**

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trials underway or completed</td>
</tr>
<tr>
<td>Canada</td>
<td>√</td>
</tr>
<tr>
<td>USA</td>
<td>√</td>
</tr>
</tbody>
</table>

*A representative from TYRX Inc. has indicated that the AIGISrx® Antibacterial Envelope is widely diffused in the USA however, as no evidence could be found to support this in the literature its level of use is marked as ‘trials underway or completed’.*
Cost infrastructure and economic consequences

The AIGISrx® Antibacterial Envelope costs US $895 (A$980.03\textsuperscript{1}) for either the medium pacemaker size (6.3 cm x 6.9 cm) or large (ICD) sizes (7.4 cm x 8.5 cm). No additional costs are anticipated for use of this device.\textsuperscript{13}

Ethical, cultural or religious considerations

No ethical, cultural or religious considerations were identified in the published literature.

Evidence and Policy

Safety and effectiveness

One non-randomised comparative study with a historical control (level III-3 Intervention evidence) and one retrospective case series study (level IV Intervention evidence) were included in this Technology Brief. The historical control group in the comparative study was a cohort of patients with matched risk factors and a CIED implanted prior to the use of the antibacterial envelope. The safety and effectiveness of the AIGISrx® was assessed in a total of 884 patients across the two studies. Relevant details regarding the studies are presented in Table 1.

Table 1  Details of the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Kolek et al, 2013\textsuperscript{14}</th>
<th>Bloom et al, 2011\textsuperscript{15}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of evidence</td>
<td>III-3</td>
<td>IV</td>
</tr>
<tr>
<td>Number of patients</td>
<td>AIGISrx n = 260, Control n = 639</td>
<td>624</td>
</tr>
<tr>
<td>Patient details</td>
<td>Patients with ≥ 2 risk factors for CIED infection who had a CIED implanted (types of CIED not stated)</td>
<td>Patients with a first-time PM, ICD or CRT-D or revision/replacement implantation utilizing the AIGISrx</td>
</tr>
<tr>
<td>Intervention</td>
<td>Implantation with AIGISrx plus systemic prophylactic antibiotics</td>
<td>AIGISrx</td>
</tr>
<tr>
<td>Comparative treatment</td>
<td>Implantation with systemic prophylactic antibiotics</td>
<td>NA</td>
</tr>
<tr>
<td>Outcomes</td>
<td>CIED infection, deaths</td>
<td>Implantation success, CIED infection</td>
</tr>
<tr>
<td>Randomisation</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Mean follow-up (SD)</td>
<td>19 months (SD 7.7) (intervention group) 42 months (SD 5.2) (control group)</td>
<td>2 months (SD 2.4)</td>
</tr>
<tr>
<td>Conflict of Interest</td>
<td>One author received honorarium/speakers fees from TYRX, Inc.</td>
<td>Authors received research grant to conduct study from TYRX, Inc., who defined the budget and scope of the research. One author is the Chief Medical Officer at TYRX, Inc.</td>
</tr>
</tbody>
</table>

CRT-D: cardiac resynchronisation therapy device with defibrillator; ICD: implantable cardioverter-defibrillator; PM: pacemaker; NA: not applicable; SD: standard deviation.

\textsuperscript{1} 1 US = 1.095 AUD (source: currency-converter.com, 16\textsuperscript{th} July 2013)
Kolek et al, 2013

A non-randomised comparative study with a historical control (Level III-3 Intervention Evidence) was conducted in the USA by Kolek et al. (2013). The intervention group included 260 consecutive adults who had a CIED implanted with an AIGISrx® Envelope between November 1, 2009 and April 30, 2012. The patients had at least two of the following risk factors present within two weeks of original implantation: diabetes, renal insufficiency (creatinine ≥1.5 mg/dL 24 hours prior to implantation), systemic anticoagulation (treatment-dose heparin or warfarin), chronic daily corticosteroid use, fever (temperature ≥ 38.1 °C) or leucocytosis (≥ 11,000 white blood cells/µL 24 hours prior to implantation), prior documented CIED infection, or at least three trans-venous leads (3-lead cardiac resynchronisation therapy system or at least one abandoned lead, pacemaker dependence, or early pocket re-entry). The historical control group (n = 639) was derived from a patient database. The database is a de-identified, time-shifted and previously validated clone of the electronic medical record. Adult patients who had a CIED implanted between August 2007 and February 2009 (18 months prior to the institutional use of the AIGISrx® envelope) and who had at least two risk factors for CIED infection (as defined above) were included. Selection was not consecutive. The types of CIED devices implanted were not described. All patients in the intervention and control cohorts received peri-procedural antibiotic prophylaxis infused from 0 to 15 minutes prior to skin incision. Outpatients received 1 g of intravenous cefazolin unless they were allergic to penicillin, in which case they received 1 g of vancomycin. The mean duration of follow-up was 19 months (standard deviation [SD] 7.7 months) for the intervention group and 42 months (SD 5.2) for the control group. No losses to follow-up were reported.

The mean age of the intervention group was 67 years (SD 12.5) and 30 per cent were women. The mean age of the control group was 68 years (SD 13.0) and 37 per cent were female. The number of risk factors did not differ between the two groups, with both having a mean of 3 (SD 1.2) (p > 0.05), however, significant differences were noted between the intervention and control groups with respect to the type of risk factors. Significantly more patients in the intervention group had at least three leads (62.7% versus 26.5%), experienced early pocket re-entry (15% versus 3%) or were undergoing either a generator change, device upgrade, or lead or other revision (47.3% versus 34%). In comparison, significantly more patients in the control group had diabetes (54.1% versus 40.8%; p <0.001).

Safety

Death was only reported for patients who developed an infection. In the control group (n = 639), four of the 19 patients who developed an infection died (21%). CIED infection was a cause of, or major contributing factor to, mortality in three of the four patients. The cause of death in the other control patient was not mentioned. No deaths occurred in the
intervention group. No mention was made in the study as to whether any deaths occurred in patients without infections. Major and minor complications were not reported.

**Effectiveness**

The study’s primary outcome was CIED infection after a minimum of 90 days’ follow-up. CIED infection was defined as local or systemic infection (e.g., sepsis, bacteremia or endocarditis) requiring systemic antibiotics and/or explantation of the CIED system. The incidence of infection was significantly lower in the intervention, with 0.4 per cent (1/260 patients) of the patients developing an infection compared with three per cent (19/639 patients) in the control group ($p = 0.04$).

The one patient who developed an infection in the intervention group was a 77-year old man with a history of atrial fibrillation, chronic anticoagulation, heart failure and left bundle branch block. He had previously undergone relocation of a left-sided cardiac resynchronisation therapy device with defibrillator (CRT-D) to his right chest to facilitate local radiation therapy for lung cancer. Forty-five days after this procedure, he presented with poor wound healing, which necessitated relocation of the device to the left chest. Two months later he developed a skin erosion that required pocket revision. During this procedure an AIGISrx® Antibacterial Envelope was used. One week after treatment he presented with fever, pneumonia, purulent discharge from the incision and a positive blood culture (*Pseudomonas aeruginosa*). He was treated with systemic antibiotics and the CIED was explanted. Later, he underwent implantation of a new CRT-D with the AIGISrx® Envelope. No further infection was observed during nine months of follow-up.

Of the 19 patients in the control group who developed infections, 13 were considered systemic infections whilst the other six appeared to be localised to the device. The mean time from CIED implantation until diagnosis of infection was 5.1 months (SD 4.1). Treatment included complete system removal in addition to parenteral antibiotics (13 patients) or antibiotics alone (6 patients).

In order to account for the effect of significant differences in individual CIED infection risk factors on CIED infection incidence between the intervention and control groups, the authors re-evaluated the data using multivariate logistic regression, after adjustment for the variable of having an antibacterial envelope, using a propensity score. In addition, they further analysed the data by univariate logistic regression on propensity score matched data. The significant difference in CIED infection rate between the intervention and control groups persisted, even after adjustment using the propensity score (odds ratio 0.09, 95% CI [0.01, 0.73], $p = 0.024$) and propensity score matching (odds ratio 0.11, 95% CI [0.01, 0.85], $p = 0.04$).
Bloom et al, 2011\textsuperscript{15}

A case series (level IV Intervention evidence) was conducted at 10 medical centres (academic, community and Veterans Affairs) in the USA by Bloom et al. (2011) with data reported retrospectively.\textsuperscript{15} A total of 642 consecutive CIED patients who had undergone initial implantation or revision/replacement procedures utilising the AIGIS\textsuperscript{Rx} Antibacterial Envelope between June 2008 and June 2009 were enrolled. Of the included patients, 35 per cent received pacemakers, 29 per cent received an ICD and 36 per cent received CRT-Ds. Revision/replacement procedures accounted for 62 per cent of the pacemaker procedures, 73 per cent of the ICD procedures and 69 per cent of the CRT-D procedures. The patients had an average of three (SD 1.4) predefined risk factors for infection based on nine predefined risk factors the authors identified from published literature. Forty-nine per cent had three or more predefined risk factors. At least one method of antimicrobial prophylaxis (oral, intravenous, or generator pocket irrigation), in addition to the antibacterial envelope, was administered in 99.5 per cent of the procedures. Antibiotics were administered systemically prior to or during the procedure (88%), locally to the generator pocket during the procedure (87%) and/or systemically after the procedure (70%). Of the 642 patients, 17 were excluded from analyses following device removal for a prior CIED infection and one was excluded from analysis because the antibacterial envelope had been used for an off-label indication. Seven of the patients died, although the authors did not state when the deaths occurred; these patients were included in the analyses of implantation success rate and incidence of infection. The mean duration of follow-up was two months (SD 2.4). Of the included patients, 32 per cent were women. The mean age of the entire cohort was 70 years (SD 13.0).

\textit{Safety}

There were seven deaths. The authors stated that none of these were attributable to the antibacterial envelope or the CIED procedure. Major and minor complications were not reported.

\textit{Effectiveness}

The primary effectiveness endpoints of the study included successful CIED implantation (defined as implantation without removal in the subsequent 24 hours) and the occurrence of major and minor CIED infections. Minor infection was regarded as superficial incisional SSI, while major infection was defined as deep incisional or organ/space (generator pocket) SSI or endocarditis. A replacement/revision procedure was defined as any CIED procedure performed between the time of implantation and hospital discharge.

A CIED implantation success rate of 99.5 per cent was reported (621 out of 624 procedures). The three unsuccessful implantations were all CRT-Ds. One of these was attributed to the antibacterial envelope, the distal end of which folded upon itself and made it difficult to
implant the CRT-D. The other two unsuccessful implantations were caused by a stenosed innominate vein and the need for lead repositioning.

Overall, the incidence of infection was 0.48 per cent (0% for initial procedures and 0.7% for replacement/revision procedures). The highest rate of infection occurred for CRT-Ds (0.89%), followed by ICDS (0.56%). There were no CIED infections in patients receiving pacemakers. All three infections which occurred during the study were considered major (one in the ICD group and two in the CRT-D group) and resulted in the CIEDS being explanted. In two of the three patients, the diagnosis was made within 12 days of the procedure. In the third patient, a chronic, non-healing incision at the implantation site was monitored until the CIED was finally removed 146 days after the procedure. No minor infections were reported.

**Economic evaluation**

The potential cost effectiveness of an AIGISrx® ICD Antibacterial Envelope has been estimated in a USA setting. The estimated absolute risk reduction associated with the use of the device was 2.5 per cent, with a corresponding 40 patients needed to treat to prevent one infection. Using data from Sohail et al, Ellis and Kolek estimate that USA hospitals could expect to recoup US$17,549 (A$19,151.22) for each ICD-related infection that could be prevented.

**Ongoing research**

Two clinical trials that are currently underway were identified from searches of www.ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Register (Table 2).

<table>
<thead>
<tr>
<th>Trial Identifier</th>
<th>Trial Status</th>
<th>N</th>
<th>Study location</th>
<th>Study Design</th>
<th>Interventions</th>
<th>Outcome measures</th>
<th>Estimated completion date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01043861</td>
<td>Recruitment suspended. Safety data collection in progress</td>
<td>465</td>
<td>United States (multicentre)</td>
<td>Non-randomised comparative study</td>
<td>AIGISRx vs no AIGISRx</td>
<td>CRMD mechanical complication</td>
<td>July 2013</td>
</tr>
<tr>
<td>NCT01043705</td>
<td>Recruitment suspended. Safety data analysis continues</td>
<td>4000</td>
<td>United States (multicentre)</td>
<td>Non-randomised comparative study</td>
<td>AIGISRx vs no AIGISRx</td>
<td>Major CRMD infection</td>
<td>July 2013</td>
</tr>
</tbody>
</table>

*Estimated enrolment; CRMD: cardiac rhythm management device

Both trials are sponsored by TYRX, Inc., the company that manufactures the AIGISrx® Antibacterial Envelope. The study population in one of the trials is patients who have undergone cardiac rhythm management device (CRMD) replacement with an ICD (NCT01043861), whilst the study population in the other trial is patients who have undergone CRMD replacement with a CRT (NCT01043705).

Other issues

Bloom et al. (2011)\textsuperscript{15} acknowledged several limitations to their study, including the retrospective design and its associated biases, the short follow-up, the lack of a control group, and the small study sample size. They suggested that a prospective randomised controlled trial is required to further evaluate the antibacterial envelope. The study reported that data were analysed on an intent-to-treat basis; however, the authors stated that 18 of the enrolled patients were excluded. These patients were not included in the analyses. No mention was made in the methods regarding pre-defined exclusion criteria. The manufacturers of the AIGISrx® Antibacterial Envelope state that it is indicated for holding a pacemaker or ICD. In the study by Bloom et al. (2011)\textsuperscript{15}, patients with a CRT-D were included as well, so the results may not reflect the population for which the device is intended. The authors stated that, in addition to the antibacterial envelope, at least one method of antimicrobial prophylaxis (oral, intravenous or generator pocket irrigation) was administered in 99.5 per cent of procedures. They were administered systemically prior to or during the procedure, locally to the generator pocket during the procedure and/or systemically after the procedure. It is possible that the method and timing of antimicrobial prophylaxis may affect the results achieved with the AIGISrx® Antibacterial Envelope. Ideally, it should be assessed in patients who have all received the same prophylactic antibiotic treatment with respect to method and timing of administration and type of antibiotic used. Conflicts of interest associated with this study are that it was funded by the manufacturer of the AIGISrx® Antibacterial Envelope, which prospectively defined the budget and scope of the research. In addition, one of the authors is the Chief Medical Officer at TYRX, Inc.

Kolek et al. (2013)\textsuperscript{14} also reported several limitations to their study, including that it was a single-centre study and, therefore, the results may not be generalisable to a broader clinician or patient population. Furthermore, it was retrospective in design and used a historical control group. They stated that differences in clinical practice between the intervention and control groups may have resulted in the observed differences in CIED infection incidence. Another potentially confounding variable was the difference in prevalence of various CIED infection risk factors between the treatment groups. They further stated that women were under-represented in the study and that there might be differences between men and women in their risk of CIED infection. The types of CIED devices that were implanted in the study were not stated, so it is unknown whether the
patient population was representative of those for whom the device is indicated. A conflict of interest associated with this study is that one of the authors is a recipient of honorarium/speakers fees from TYRX, Inc.

It should be noted that a newer generation fully-resorbable AIGISrx® Antibacterial Envelope has been developed. The fully resorbable AIGISrx® Antibacterial Envelope is constructed from a bioresorbable multifilament knitted mesh substrate (polymer made of glycolide, caprolactone, and trimethylene carbonate) that is coated with a bioresorbable polyarylate polymer. It comes in the same sizes as the non-resorbable envelope. This newer device was given FDA 510 (k) approval in May 2013 (K130943) and in January 2013 TYRX received a licence from Health Canada to market the fully resorbable antibacterial envelope with implantable electronic devices. At a cost of US $995.00 (A$1,089.53) for both the medium and large sizes it is slightly more expensive than the non-resorbable antibacterial envelope. Currently no peer reviewed studies have been published on this newer fully resorbable version of the antibacterial envelope and thus its benefits, if any, over the non-resorbable envelope are unknown.

Summary of findings

Two studies were eligible for inclusion in this Technology Brief: one retrospective case series study and one non-randomised comparative study with a historical control cohort. In total, the AIGISrx® Antibacterial Envelope was evaluated in 884 patients who were implanted with CIEDs for either primary or replacement/revision procedures and who had two or more risk factors for CIED infection. Only the case series study reported the type of devices that were implanted, which included pacemakers, ICDs and CRT-Ds. Neither study reported on complications related to the implant procedure. No deaths were associated with the use of the antibacterial envelope. The incidence of infection was low in both studies (<0.5%) considering that the selected patients had a high risk for CIED infection. In addition, the patients implanted with the AIGISrx® Antibacterial Envelope in the comparative study had a significantly lower incidence of infection compared with the historical control group. Only the case series reported on CIED implantation success rate, which was very high (99.5%). Only one of the three unsuccessful implants was attributed to the AIGISrx® Antibacterial Envelope.

Several limitations/issues were identified with both studies, many of them highlighted by the authors, which compromised the validity of their results. The comparative study was limited by its retrospective design, used an historical control and had significant differences in the prevalence of various CIED infection risk factors between the treatment groups that may have affected treatment outcomes. With respect to the case series, it was retrospective in design, had a very short follow-up period and the patients varied in the timing, type and

3 1 US = 1.095 AUD (source: currency-converter.com, 16th July 2013)
method of administration of the prophylactic antibiotic treatment they received. The study reported that data were analysed on an intention-to-treat basis; however, 18 of the enrolled patients were excluded from analysis. Both studies had conflicts of interest in that they had connections to the company that manufactures the AIGISRx® Antibacterial Envelope. It was not clear whether the patient population in either study was entirely representative of that for which the device is indicated by the manufacturers.

HealthPACT assessment

Positive results have been reported for the AIGISRx® Antibacterial Envelope with respect to CIED implantation success and incidence of infection. However, this has come from two low-quality studies and data from randomised trials demonstrating a clear reduction in device pocket infections are required to reliably inform its clinical use. It is, therefore, recommended that the AIGISRx® Antibacterial Envelope be monitored for a period of 24 months. During this time, results from two non-randomised comparative trials that are currently underway should become available in the peer-reviewed literature and will add to the current evidence base for the technology.

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

| Total number of studies | 2 |
| Total number of Level III-3 studies | 1 |
| Total number of Level IV studies | 1 |

References


**Search criteria to be used (MeSH terms)**

Text words were:
AIGISRx, antibacterial envelope, cardiovascular implantable electronic device* AND antimicrobial, cardiovascular implantable electronic device* AND antibiotic*, CIED and antimicrobial*, CIED and antibiotic*, CIED and antibacterial, cardiac pacemaker and antibiotic*, cardiac pacemaker and antimicrobial*, cardiac pacemaker and antibacterial, defibrillator AND antimicrobial*, defibrillator AND antibiotic*, defibrillator AND antibacterial.