

# Bactiguard® Technology

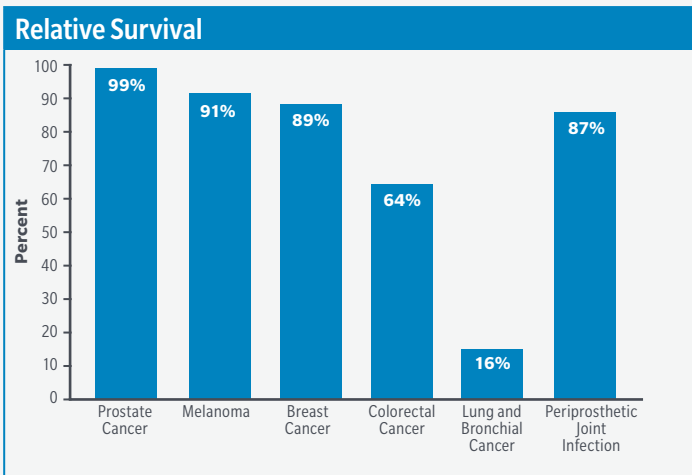
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## Background and Clinical Need

Healthcare-associated infections (HAI) are one of the major challenges in medicine: 3.2 million people are estimated to receive an infection diagnosis every year in Europe, of whom approximately 37,000 become fatal [1]. This leads to 16 million extra-days of hospital stay, and an annual cost of approximately € 7 billion across Europe [2]. The frequency of periprosthetic infections after arthroplasty can vary broadly depending on site and type of reconstruction, ranging from 1-2 % for a primary arthroplasty [3] to as high as 36 % in the case of megaprosthesis [4]. It has been calculated that affected patients have a lower chance of survival at 5 years than people affected by three of the most common types of cancer [5], as illustrated in Figure 1.

In orthopaedic trauma, it has been estimated that up to 30 % of cases may result in infection [6]. Almost 80 % of all open fractures present



**Figure 1.** Five-year survival rate of patients affected by the most common forms of cancer, compared to patients affected by periprosthetic joint infection [5].

some bacterial contamination [7], many of which may develop into early, delayed and/or late established infections. The risk of infection can also differ widely depending on the classification of open fracture, varying between 0-2 % for Type I fractures, between 2-10 % for Type II fractures, and between 10-50 % for Type III fractures [8, 9]. A recent linear regression analysis of the available literature published since 2000 in peer-reviewed journals and conducted by Zimmer Biomet estimated that infections following intramedullary nailing (IMN) are diagnosed, on average, in the 1.6 % of cases for closed fractures and 11.9 % of cases for open fractures, with 0.1 % and 7.5 % of deep infections in closed and open fractures, respectively [10]. A breakdown of overall and deep infection rates per surgical site is presented in Table 1.

Site	Overall Infection Rate (%)	Deep Infection Rate (%)
Tibia	6.46	1.27
Distal Femur	3.92	0.94
Proximal Femur	1.53	0.09
Humerus	1.26	0.79
Ankle	7.9	5.01

**Table 1.** Rate of infection following IMN [10].

## Socioeconomic Impact

Implant associated infections not only have a devastating impact on the quality of life of patients, but also have significant socioeconomic consequences.

These infections place a significant personal burden on healthcare professionals [11] and an economic burden on healthcare systems. It has been estimated that, in Belgium, treatment costs for deep infections following tibial fractures are approximately 6.5 times higher than uninfected cases [12]. In the UK, infections following proximal femoral fractures present a median cost of £ 24,410 with length of stay of 132.5 days, compared to uninfected cases that present a median cost of £ 7,210 and require a length of stay of 30 days [13]. In Italy, an average additional cost of € 9,560 was estimated in case of orthopaedic surgical site infections [14].

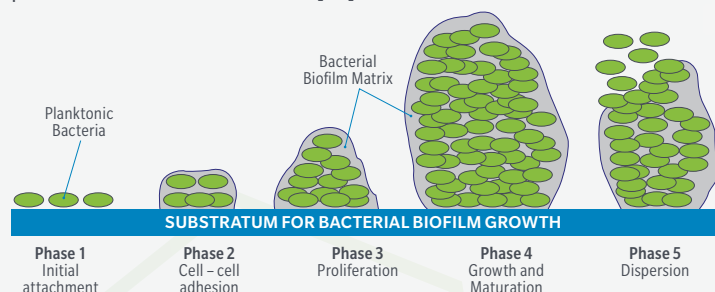
Families and wider society are also hugely impacted [15], as patients affected by implant associated infections require additional care and assistance, and their mental health is negatively affected [16]; younger patients are significantly less likely to return to work within a year from fracture [17, 18], and elderly patients have a significantly increased risk of mortality and of not returning to their own home when they require further surgery following complications after fixation of proximal femoral fractures [19].

## The Role of the Biofilm

The primary challenge with treating or eradicating implant-associated infections is the ability of certain bacteria to create a protected community called a biofilm. As represented in Figure 2, shortly after planktonic or 'free floating' bacteria have come into contact with a surface, they start to proliferate and embed themselves in an organic matrix known as the extracellular polymeric substance (EPS). Inside the biofilm, aggregates of bacterial microcolonies are shielded from the surrounding environment, making them less susceptible to the attacks of the immune system or to regular dosage of antibiotics [20].

As the biofilm matures, it can release new planktonic bacteria into the environment, resulting in a new cycle of biofilm formation and spread of the infection. The entire process from the colonisation of a surface by planktonic bacteria to the creation of a mature biofilm can take place in a few days [21].

In 2001, the U.S. Centers for Disease Control (CDC) estimated that biofilms cause 65 % of infections in the developed world [22,23], and the National Institutes of Health (NIH) later referenced 80 % in a public announcement in 2007 [24].



**Figure 2.** Biofilm formation on an implant surface.

### Antibiotic Resistance

Current strategies for the control of implant associated infections rely primarily on the administration of local and systemic antibiotics. However, it is well known that bacteria develop resistance to antibiotics, even more so in healthcare facilities rather than in the community [25]. Without alternative treatments to antibiotics, it has been predicted that, by the year 2050, 10 million people worldwide will die every year due to multi-resistant microbial infections, overtaking the number of deaths caused by cancer [26].

The decreased susceptibility of bacteria grown in biofilms to antibiotics highly reduces the chances of eradicating these infections, thus further increasing the risk of triggering antibiotic resistance. Every year, more than 670,000 infections occur in the EU/EEA due to antibiotic-resistant bacteria, with the death of 33,000 people and with a cost for healthcare systems of € 1.1 billion as a direct consequence [27].

To address the growing concerns over antibiotic resistance and to ensure responsible antibiotic stewardship, Bactiguard Technology provides an alternative non antibiotic-releasing approach to tackle biofilms.

### History of Bactiguard Technology [28]

The Bactiguard Technology has its origins in the work of Nobel Prize laureate Gustaf Dahlén. His apprentice Axel Bergström developed the technique of applying a thin layer of metals to non-conductive materials; Bergström's apprentice, Billy Södervall, started to apply the noble metal coating to medical devices in the 70's, filing numerous patents for the technology in the U.S.

The coating was first applied to urinary catheters through a partnership with BD (Becton, Dickinson & Company, previously C.R. Bard), with the first FDA clearance in 1994.

The Bactiguard Infection Protection (BIP) technology was then developed in the early 2000s, and in 2005 Bactiguard was founded as a standalone company, in Sweden. The first BIP urinary catheters were introduced to the European market in 2008, and the BIP central venous catheters (CVC) and BIP endotracheal tubes (ETT) in 2013.

In 2013, the technology was also licensed to Vigilenz Medical Devices to apply the noble metal coating to orthopaedic trauma products, including IM nails, which obtained the CE mark in 2018. Vigilenz was acquired by Bactiguard in 2020.

In 2019, Bactiguard and Zimmer Biomet entered into a global, exclusive licensing agreement for orthopaedic trauma implants, which led to the CE marking of the ZNN™ Bactiguard and ANN™ Bactiguard at the beginning of 2021.

The Bactiguard Technology has been applied to medical devices outside of orthopaedics for over 25 years, and to date over 200 million Bactiguard coated products have been sold worldwide (including Europe, U.S., Japan, China, Brazil, India and Mexico) [29].

**1912 – Gustav Dahlén**, Swedish Nobel Prize laureate in Physics. The man behind the AGA lighthouse system, from which Bactiguard Technology originates

**1978 – Billy Södervall** starts developing the Bactiguard Technology

**1990 – Partnership with C.R. Bard**

**1994 – FDA 510k**

**1995 – Patent in the US**

**2005 – Bactiguard AB founded**

**2008 – Launch of BIP Foley**

**2013 – Launch of BIP CVC & BIP ETT**  
License agreement with **Vigilenz**

**2016 – Launch of BIP ETT Evac**

**2018 – Launch of BIP Foley Tiemann & Female**  
Launch of **BIP CVC** with **Raulerson Syringe**  
CE mark of orthopaedic trauma implants with Bactiguard

**2019 – Partnership with Zimmer Biomet**

**2020 – Acquisition of Malaysian Vigilenz**

**2021 – CE mark of ZNN Bactiguard and ANN Bactiguard**

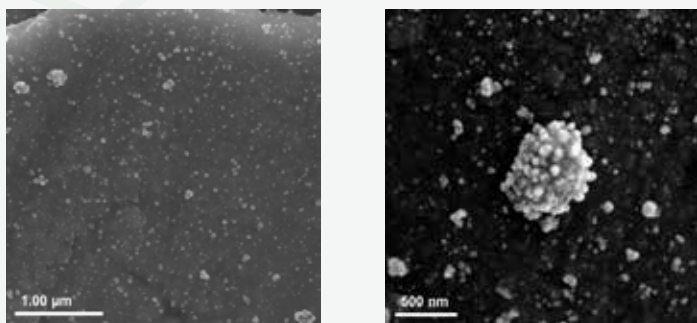
## The Bactiguard Technology

### Coating Characterization

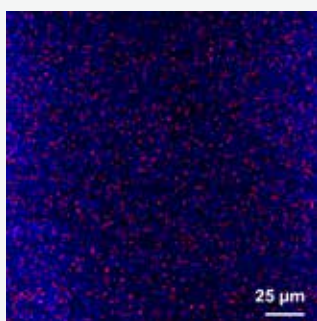
The Bactiguard Technology is a stable and durable metallic coating that is firmly bound to the implant surface through strong covalent bonds [30,31].

More specifically, the Bactiguard coating is a noble metal alloy coating containing silver, gold and palladium that is applied to substrates via a wet chemistry process. The coating consists of a thin, non-continuous layer of discrete clusters, as shown by the Scanning Electron Microscope (SEM) and Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) images in Figure 3 and Figure 4, respectively [32].

The amount of noble metals released by the coating has been shown to be well below the applicable tolerable intake or permitted daily exposure, thus demonstrating the toxicological safety of the Bactiguard coating [33,34]. In addition, since the coating is covalently bonded to the substrate, it does not meet the definition of a 'nanomaterial' according to the definition stated in the 2017/745/EU Medical Device Regulation [35].



**Figure 3.** SEM micrographs of a titanium substrate with the Bactiguard Technology at lower (left) and higher (right) magnification. (SEM images taken internally at Zimmer Biomet)



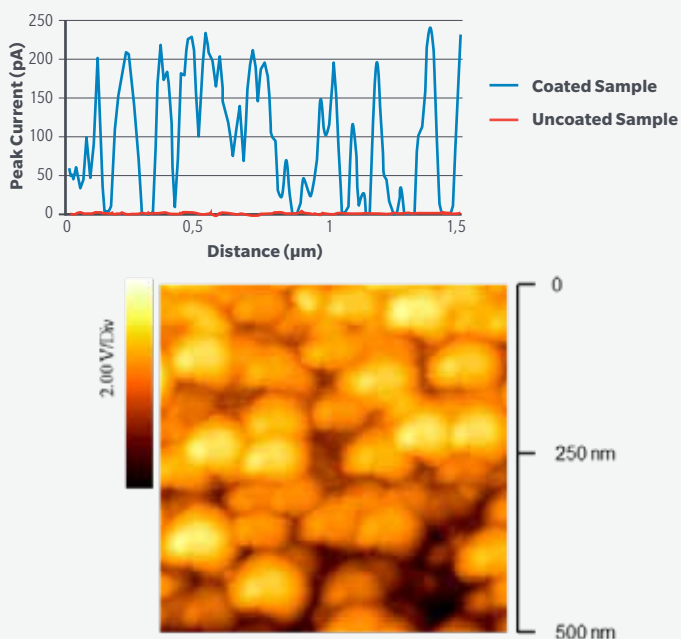
**Figure 4.** ToF-SIMS image showing the distribution of palladium (red) and silver (blue) on a silicone substrate [32].

### Mechanism of Action

The noble metals in the Bactiguard coating have different electro-potentials and so, in combination, this results in a 'galvanic effect' that generates pico-currents (trillionth of an Ampere,  $10^{-12}$  A) on the implant surface. These pico-currents lead to reduced adhesion of microorganisms to coated surfaces and, consequently, decreased possibility of biofilm formation, as discussed later. [36,37,38].

The electric potentials and currents that produce this galvanic effect in the coating have been measured via Electrostatic Force Microscopy (EFM) [39] and PeakForce TUNA Atomic Force Microscopy (AFM) [40], respectively (Figure 5). The current was found to vary between 0 to almost 250 pA, with an average of 71 pA compared to 0.17 pA in the uncoated control [40]. The magnitude of these currents is very small, and only detectable *in vitro* with these highly sensitive instruments.

The measured currents affect microbial adhesion by interfering with the respiratory chain, which in bacteria is located in the inter-membrane space, thus close to the surrounding environment. On the contrary, in eukaryotic (human) cells, which are about ten times larger than bacteria, the mitochondria (the respiratory organelles) are situated inside the cell membrane and are therefore more protected and less affected by electrical currents of such a small magnitude [41].



**Figure 5.** Top: Current distribution over a line on coated and uncoated stainless steel, measured using PeakForce TUNA AFM [40]. Bottom: EFM image showing the electric potential distribution on Bactiguard-coated glass slide [39].

While the galvanic effect requires the release of a very small amount of silver, the amount released during elution studies was found to be below the minimum inhibitory concentrations (MIC) reported in the literature for ionic silver [42]. The absence of inherent antibacterial properties due to this release of silver from the coating has also been confirmed with zone of inhibition tests, where none of the coated samples prevented or inhibited bacterial growth [42]. This is further evidence that the primary mechanism of action of the Bactiguard Technology is the galvanic effect.

## Experimental and Clinical Evidence

### In Vitro Evidence

The anti-adhesive nature of the Bactiguard coating has been demonstrated through *in vitro* microbial tests based on methods adapted from the work of Ahearn and co-workers at Georgia State University [43,44]. Numerous substrates, representing different Bactiguard-coated devices, have been tested against different microbial species; relevant results are summarised in Table 2.

	<i>S. aureus</i>	<i>P. aeruginosa</i>
Ti6Al4V rods	84%	99.997%
BIP Foley catheter (latex)	N.T.	85%
BIP Foley catheter (silicone)	97% (98% MRSA)	81%
BIP ETT (PVC)	91% (81% MRSA)	97%
BIP CVC (Polyurethane)	75% (79% coagulase negative <i>S. aureus</i> )	77%

**Table 2.** Reduction in adhesion of *Staphylococcus aureus* and *Pseudomonas aeruginosa* when the Bactiguard coating was applied to different substrates, compared to uncoated controls [45]. The Ti6Al4V rods were supplied by Zimmer Biomet. MRSA: methicillin-resistant *Staphylococcus aureus*; N.T.: Not tested.

### Clinical Evidence

The reduction in bacterial adhesion observed *in vitro* has been shown to translate into reduction in infection rates in the clinical setting as well, for all Bactiguard-coated devices. Since urinary catheters were the first coated devices to enter the market, numerous studies have been published over the years reporting positive outcomes [46,47,48,49,50,51], the most recent being a randomised, prospective, multicentre study on 1,000 patients that showed a reduction in infections of 69 % compared to uncoated catheters over a mean duration of catheterization of 11 days [52]. A 52 % reduction in infection rate (median catheterization time 13 days) [53] and significantly fewer adverse events (mean catheterization time 9.2 days, range 4 to 16 days) [54] were also observed for Bactiguard coated CVC devices, whilst ETT devices showed reduced high-grade biofilm formation (median intubation time 3.6 days) [55] and a 67 % reduction in infection rates at 5 days [56].

A recent single-centre, prospective study on 148 trauma patients showed an 80 % reduction at 24 months (odds ratio 0.2, 95% confidence interval [0.07-0.55],  $p=0.002$ ) in infection rates between the study group, who received Bactiguard-coated titanium alloy Orthosyn tibial and femoral IM nails (Vigilenz), and the uncoated control group, as well as some reduction in revision rates [57]. In addition, the same study also observed a 100 % rate of bony union in the study group, compared to 84 % in the control group [57]. This is in agreement with what was previously observed with Bactiguard-coated, commercially pure titanium screws, which presented comparable bone integration to that of uncoated screws in an *in vivo* animal model [58].

### Durability

The durability of the coating after implantation has been observed in a retrieval study including qualitative and quantitative analysis of a nail retrieved from a patient after 8 months: all the metal elements of the coating were still detected, and were still within the coating specification [31], which suggests that the coating was still effective. This is also supported by clinical studies related to Bactiguard-coated devices, which have shown that the use of these products reduces the number of antibiotic days [47], as well as the prevalence of antibiotic resistance in the treated population [48].

Notably, no adverse event related to the Bactiguard coating has ever been recorded over more than 25 years that products have been on the market [59]. This includes CVCs, where the Bactiguard coating is in direct contact with the blood stream, and Foley urinary catheters periodically changed throughout the lifetime of some patients, thus subjecting them to the repeated exposure to the coating every time the catheter is exchanged.

### Conclusion

The Bactiguard Technology consists of a thin, non-continuous layer of clusters of a silver, gold and palladium alloy, which generates galvanic currents that reduce microbial adhesion to implant surfaces, and thus decrease the possibility of biofilm formation.

The coating is non-eluting, durable, and does not contain antibiotics. This avoids challenges associated with handling of products or their shipping and storage, as it does not require controlled temperatures and conditions as seen with alternative solutions using antibiotics.

The Bactiguard Technology is well-established, with proven clinical safety and efficacy in reducing infection rates from urinary catheters, endotracheal tubes and central venous catheters.

The use of the Bactiguard Technology on titanium alloys for trauma applications has also shown effectiveness, and is expected to aid in reducing the burden of orthopaedic implant associated infections, while also supporting fracture repair.

Although the use of Bactiguard-coated intramedullary nails does not substitute for standard preventive antibiotic protocols, the availability of a non-antibiotic prophylactic solution provides an alternative approach to infection management. This is particularly timely given that the current infection control scenario is ever more challenged by antibiotic resistance.

## Disclaimers

ZNN and ANN Bactiguard are intended to reduce the risk of implant related infections, but are not indicated for the treatment of established infections.

Use of this product does not replace existing standard practice for infection control such as the use of prophylactic antibiotics.

## References

1. European Centre for Disease Prevention and Control, Economic evaluations of interventions to prevent healthcare-associated infections – Literature review. Stockholm: ECDC, 2017.
2. World Health Organization, Report on the Burden of Endemic Health Care-Associated Infection Worldwide - Clean Care is Safer Care. WHO 2011.
3. Izakovicova *et al.*, Periprosthetic joint infection: current concepts and outlook. *EFORT Open Reviews* 4: 482-494, 2019.
4. Savvidou *et al.* Efficacy of antimicrobial coated orthopaedic implants on the prevention of periprosthetic infections: a systematic review and meta-analysis. *The Journal of Bone and Joint Infection* 5(4): 212-222, 2020.
5. Zmistowski, A quarter of patients treated for PJI dead within 5 years. *Orthopedics Today*, 2012. <https://www.healio.com/news/orthopedics/20130104/a-quarter-of-patients-treated-for-pji-dead-within-5-years> (Accessed on 12th March 2021).
6. Schwarz *et al.*, 2018 International Consensus Meeting on Musculoskeletal Infection: Research Priorities from the General Assembly Questions. *Journal of Orthopaedic Research* 37(5): 997-1006, 2019.
7. Seekamp *et al.*, Bacterial Cultures and Bacterial Infections in Open Fractures. *European Journal of Trauma and Emergency Surgery* 26(3): 131-138, 2000.
8. Neubauer *et al.*, Open fractures and infection. *Acta Chirurgiae Orthopaedicae et Traumatologiae Čechoslovaca* 73(5): 301-312, 2006.
9. Kim *et al.*, Gustilo-Anderson classification. *Clinical Orthopaedics and Related Research* 470(11): 3270-3274, 2012.
10. Data on file at Zimmer Biomet (Kaufmann, Infections after IMN of Long Bones Synthesis. 2020. (DK Consulting review)).
11. Mallon *et al.*, Surgeons are deeply affected when patients are diagnosed with prosthetic joint infection. *PLoS ONE* 13(11): e0207260, 2018.
12. Metsemakers *et al.*, Infection after fracture fixation of the tibia: Analysis of healthcare utilization and related costs. *Injury* 48(6): 1204-1210, 2017.
13. Pollard *et al.*, Deep wound infection after proximal femoral fracture: consequences and costs. *Journal of Hospital Infection* 63(2): 133-139, 2006.
14. Nobile *et al.*, Developing a model for analysis the extra costs associated with surgical site infections (SSIs): an orthopaedic and traumatological study run by the Gaetano Pini Orthopaedic Institute. *Antimicrobial Resistance and Infection Control* 4(Suppl 1): 68, 2015.
15. Golics *et al.*, The impact of disease on family members: a critical aspect of medical care. *Journal of the Royal Society of Medicine* 106(10) 399-407, 2013.
16. Brinker *et al.*, The Devastating Effects of Tibial Nonunion on Health-Related Quality of Life. *The Journal of Bone & Joint Surgery – American Volume* 95(24): 2170-2176, 2013.
17. Napierala *et al.*, Infection reduces return-to-duty rates for soldiers with Type III open tibia fractures. *Journal of Trauma Acute Care and Surgery* 77(3), Suppl. 2: S194-S197, 2014.
18. Olesen *et al.*, The cost of infection in severe open tibial fractures treated with a free flap. *International Orthopaedics (SICOT)* 41: 1049-1065, 2017.
19. Thakar *et al.*, The cost and consequences of proximal femoral fractures which require further surgery following initial fixation. *The Journal of Bone and Joint Infection [Br]* 92-B(12): 1669-1677, 2010.
20. Katsikogianni and Missirlis, Concise review of mechanisms of bacterial adhesion to biomaterials and of techniques used in estimating bacteria-material interactions. *European Cells and Materials* 8:37-57, 2004.
21. Lebeaux *et al.*, From in vitro to in vivo Models of Bacterial Biofilm-Related Infections. *Pathogens* 2: 288-356, 2013.
22. McLean *et al.*, Training the Biofilm Generation - A tribute to J. W. Costerton. *Journal of Bacteriology* 194(24): 6706-6711, 2012.
23. Williams and Costerton, Using biofilms as initial inocula in animal models of biofilm-related infections. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* 100B(4): 1163-1169, 2012.
24. Davies, Understanding Biofilm Resistance To Antibacterial Agents. *Nature Reviews Drug Discovery* 2: 114-122, 2003.
25. <https://www.cdc.gov/hai/patientsafety/ar-hospitals.html> (Accessed on 12th April 2021).
26. O'Neill, Review on Antimicrobial Resistance Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. London: Review on Antimicrobial Resistance. 2014. Available from: [https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations\\_1.pdf](https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf) (Accessed on 6th April 2021).
27. Organisation for Economic Co-operation and Development, Antimicrobial Resistance – Tackling the Burden in the European Union. Briefing note for EU/EEA countries. OECD Publishing, Paris; 2019.

28. <https://www.bactiguard.com/> (Accessed on 25th March 2021).
29. Data on file at Bactiguard (VMD-CE-019).
30. Data on file at Bactiguard (REP-15811).
31. Data on file at Bactiguard (Report 180502).
32. Data on file at Bactiguard (0172-5006-REV).
33. Data on file at Bactiguard (REP-15617).
34. Data on file at Bactiguard (REP-14495)
35. EC (European Commission) (2017). Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices.
36. Cao et al., Biological actions of silver nanoparticles embedded in titanium controlled by micro-galvanic effects. *Biomaterials* 32: 693-705, 2011.
37. Jin et al., Synergistic effects of dual Zn/Ag ion implantation in osteogenic activity and antibacterial ability of titanium. *Biomaterials* 35(27): 7699-7713, 2014.
38. Jin et al., Zn/Ag micro-galvanic couples formed on titanium and osseointegration effects in the presence of *S. aureus*. *Biomaterials* 65: 22-31, 2015.
39. Data on file at Bactiguard (1384-1004-ER).
40. Data on file at Bactiguard (2497-5006-ER).
41. Alberts et al., *Molecular Biology of the Cell*. 6th edition, New York: Garland Science; 2015.
42. Data on file at Bactiguard (REP-15696).
43. Gabriel et al., Effects of silver on adherence of Bacteria to Urinary Catheters: In vitro studies. *Current Microbiology* 30: 17-22, 1995.
44. Ahearn et al., Effects of Hydrogel/Silver Coatings on In Vitro Adhesion to Catheters of Bacteria Associated with Urinary Tract Infections. *Current Microbiology* 41: 120-125, 2000.
45. Data on file at Bactiguard (REP-15819; REP- 03042; REP-03041; REP-03040; REP-03039).
46. Karchmer et al., A Randomized Crossover Study of Silver-Coated Urinary Catheters in Hospitalized Patients. *Archives of Internal Medicine* 160: 3294-3298, 2000.
47. Lederer et al., Multicenter Cohort Study to Assess the Impact of a Silver-Alloy and Hydrogel-Coated Urinary Catheter on Symptomatic Catheter-Associated Urinary Tract Infections. *Journal of Wound Ostomy & Continence Nursing* 41(5): 1-8, 2014.
48. Banaszek et al., Effectiveness of silver alloy-coated silicone urinary catheters in patients with acute traumatic cervical spinal cord injury: Results of a quality improvement initiative. *Journal of Clinical Neuroscience* 78: 135-138, 2020.
49. Rupp et al., Effect of silver-coated urinary catheters: Efficacy, cost-effectiveness, and antimicrobial resistance. *American Journal of Infection Control* 32(8): 445-450, 2004.
50. Stenzelius et al., Noble Metal Alloy-Coated Latex Versus Silicone Foley Catheter in Short-Term Catheterization: A Randomized Controlled Study. *Scandinavian Journal of Urology and Nephrology* 45(4): 258-264, 2011.
51. Chung et al., A prospective interventional study to examine the effect of a silver alloy and hydrogel-coated catheter on the incidence of catheter-associated urinary tract infection. *Hong Kong Medical Journal* 23(3): 239-245, 2017.
52. Kai-Larsen et al., Foley catheter with noble metal alloy coating for preventing catheter-associated urinary tract infections: a large, multi-center clinical trial. *Antimicrobial Resistance & Infection Control* 10(40), 2021.
53. Goldschmidt et al., Prevention of Catheter-Related infections by Silver Coated Central Venous Catheters in Oncological Patients. *Zentralblatt für Bakteriologie* 283(2): 215-223, 1995.
54. Björling et al., Evaluation of central venous catheters coated with a noble metal alloy – A randomized clinical pilot study of coating durability, performance and tolerability. *Journal of Biomedical Material Research Part B: Applied Biomaterials*, 106B: 2337–2344, 2018.
55. Thorarinsdottir et al., Biofilm formation on three different endotracheal tubes: a prospective clinical trial. *Critical Care* 24: 382, 2020.
56. Tincu et al., Ventilator associated pneumonia: do silver-coated endotracheal tubes really work? [poster]. *Euroanesthesia*, Berlin 30th May – 2nd June 2015.
57. Karupiah et al., Efficacy And Safety Of Anti-Infective Noble Metal Alloy-Coated Orthopaedic Implants In Prevention Of Implant-Related Infection – A Cohort Study. *Virtual EFORT Congress*, abstract #1041, 30th June – 2nd July 2021.
58. Svensson et al., Osseointegration of titanium with an antimicrobial nanostructured noble metal coating. *Nanomedicine: Nanotechnology, Biology, and Medicine* 9: 1048-1056, 2013.
59. Data on file at Bactiguard (REP-03324)

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