

RVC OPEN ACCESS REPOSITORY – COPYRIGHT NOTICE

This is the peer-reviewed, manuscript version of an article published in *Veterinary Record*. The final version is available online: <https://doi.org/10.1136/vr.105223>.

The full details of the published version of the article are as follows:

TITLE: Reduced antimicrobial prescribing during autogenous staphylococcal bacterin therapy: a retrospective study in dogs with pyoderma

AUTHORS: Alison Wilson, Natalie Allers, David H Lloyd, Ross Bond and Anette Loeffler

JOURNAL TITLE: Veterinary Record

PUBLISHER: BMJ Publishing Group

PUBLICATION DATE: 2 May 2019 (online)

DOI: 10.1136/vr.105223

1 **Reduced antimicrobial prescribing during autogenous staphylococcal bacterin**
2 **therapy: A retrospective study in dogs with pyoderma**

3

4 Alison Wilson,¹ Natalie Allers,¹ David H. Lloyd,¹ Ross Bond,¹ Anette Loeffler¹

5 ¹Department of Clinical Science and Services, Royal Veterinary College, Hawkshead
6 Lane, North Mymms, Hertfordshire, AL9 7TA, UK

7

8 **Current address for:**

9 Alison Wilson: Rutland House Veterinary Hospital, Abbotsfield House, 4 Abbotsfield Rd,
10 Saint Helens, WA9 4HU, UK

11 Natalie Allers: Queens Road Veterinary Hospital, 2-4 Queens Road, Cheadle Hulme, SK8
12 5LU, UK

13

14

15

16

17 **Corresponding author:** Anette Loeffler, Royal Veterinary College, Hawkshead Lane,
18 North Mymms, Hertfordshire, AL9 7TA, UK. Email: aloeffler@rvc.ac.uk. Tel. +44 1707
19 666333.

20

21

22

23 **Conflicts of interest:** None

24 **Sources of funding:** Self-funded

25 **Word count:** 2519

26

27

28 **ABSTRACT**

29 Autogenous staphylococcal bacterins are commonly mentioned as treatment for canine
30 recurrent pyoderma but little evidence is known about their efficacy. This retrospective
31 study describes use and assesses efficacy of an autogenous *Staphylococcus*
32 (*pseudointermedius*) bacterin in dogs with pyoderma. Frequency and duration of systemic
33 antimicrobial therapy were compared 12 months before and after starting bacterin
34 (Wilcoxon-signed-rank test) with data extracted from general practice medical histories.

35 Bacterin orders had been received by the laboratory for 231 dogs over a 12.5-year period.
36 Complete medical records could be obtained for 22 dogs. All had received at least one
37 course (median 5, range 1-10) of systemic antimicrobials before starting bacterin. After
38 starting bacterin, five dogs (22.7%) did not receive any antimicrobials systemically; 17
39 (77.3%) received fewer courses and days compared to the preceding 12 months ($P=0.007$
40 for both courses and days). No bacterin-associated adverse effects had been recorded.

41 Although primary causes for pyoderma and the effect of topical therapy were not controlled
42 in this study, the data provide additional evidence of a beneficial effect of autogenous *S.*
43 *pseudointermedius* bacterin in the management of canine recurrent pyoderma. Autogenous
44 bacterin therapy should be studied further as an aid to treatment in the context of good
45 antimicrobial stewardship.

46 INTRODUCTION

47 With antimicrobial resistance as a major threat to human and animal health, veterinary
48 prescribing of antimicrobial drugs is under scrutiny, for both livestock and for companion
49 animals. Canine pyoderma remains one of the most common diseases diagnosed in small
50 animal practice,^{1,2} frequently leads to antimicrobial prescribing³ and is often recurrent due
51 to undiagnosed or uncontrolled underlying primary triggers.⁴⁻⁷

52 Repeated systemic antibacterial treatment is discouraged in order to reduce resistance
53 selection pressure on skin microflora and skin pathogens.⁸ However, other management
54 options for recurrent pyoderma are scarce, with topical antibacterial therapy as an
55 attractive, but not always practical, alternative.⁹⁻¹¹ Immunomodulation or immunisation
56 through staphylococcal vaccines have been explored for many decades, mainly for
57 application in bovine mastitis and in human furunculosis and rhinitis.¹²⁻¹⁵ In human
58 medicine, several vaccine candidates, targeting different antigens, have progressed
59 through to clinical trials but efficacy against invasive *S. aureus* infections in clinical phase
60 III stages have so far been disappointing.^{16,17}

61 Bacterins, defined as suspensions typically of lysed or attenuated bacteria used as
62 vaccines to increase immunity to particular pathogens or a disease, have been used
63 sporadically in dogs for staphylococcal blepharitis¹⁸ and for recurrent staphylococcal
64 pyoderma.¹⁹⁻²⁴ Clinical benefits have been reported but associated immunological changes
65 remain rarely studied²⁵ and poorly understood.

66 Two early bacterin studies published in the 1980s already indicated a beneficial effect as
67 adjunctive therapy in the management of superficial and deep canine pyoderma. One was
68 a *Propionibacterium acnes* (now referred to as *Cutibacterium acnes*)²⁶ suspension,¹⁹ the
69 other an autogenous '*S. aureus*' lysate (possibly *S. pseudintermedius* in current
70 taxonomy).²⁰ However, the intravenous injection route for the *P. acnes* product and the
71 high incidence of local and systemic adverse reactions with the *S. aureus* bacterin limited
72 practical clinical utility.

73 Later, two controlled studies assessed the efficacy of bacterins specifically in dogs with superficial
74 pyoderma. Staphage Lysate (SPL, Delmont Laboratories, Swarthmore, PA, U.S.A.), a phage
75 lysate of well-characterised *S. aureus* cultures, commercially available in the U.S.A. and selected
76 other countries, was tested in 21 dogs with superficial pyoderma against placebo in a double-
77 blinded design with twice weekly subcutaneous injections over 18 weeks and once or twice
78 weekly washing with a benzoyl peroxide shampoo for both groups.²¹ A beneficial effect was seen
79 in 77% of dogs in the treatment group with regard to milder or less frequent recurrence of
80 pyoderma or reduced need of antimicrobials compared to 37% improvement in the placebo group.
81 Efficacy was also reported for an autogenous *S. (pseud)intermedius* bacterin formulated through
82 phenol and formalin processing of the patient's own pathogenic staphylococcal isolate.²² After a
83 ten-week, single-blinded treatment period, lesion scores in the five control group dogs were
84 significantly higher than those in the five dogs receiving subcutaneous bacterin injections. In both
85 studies, systemic antibiotics were given initially in parallel to bacterin therapy for six and four
86 weeks respectively, reflecting the concept of bacterins as an aid to prevent recurrences rather
87 than a treatment for active infection. Lastly, two uncontrolled studies reported beneficial effects on
88 clinical signs in dogs with recurrent pyoderma. The SPL reduced pruritus scores in 13 atopic
89 dogs²³ and another *S. aureus* lysate, originally developed for use in bovine mastitis (Lysigin,
90 Boehringer Ingelheim Vetmedica, Inc. St. Joseph, MO, U.S.A.) reportedly improved pyoderma

91 lesions in all ten dogs with superficial pyoderma and in nine of eleven dogs with deep pyoderma
92 over a four-month period of subcutaneous injections.²⁴

93 Our retrospective study aimed to describe how the autogenous *S. (pseud)intermedius* bacterin
94 previously investigated by Curtis *et al.*²² is used in veterinary practice and to assess whether it
95 could reduce the need for systemic antimicrobial therapy in dogs with recurrent pyoderma.

96

97 **MATERIALS AND METHODS**

98 **Ethics**

99 The study had been approved by the Royal Veterinary College (RVC) Ethics and Welfare
100 Committee (URN 2014 1294).

101 **Bacterin orders and treatment recommendations**

102 Information on autogenous *Staphylococcus (pseud)intermedius* bacterins ordered for dogs
103 from the RVC microbiology laboratory between January 2002 and June 2014 was
104 reviewed. Bacterins had been formulated as previously described (production discontinued
105 since 2018) from clinical isolates of *S. pseudintermedius* (*S. intermedius* prior to 2009)
106 through processing with phenol and formalin.²² Bacteria had been isolated from clinical
107 samples submitted by veterinary surgeons (first opinion veterinarians and referral
108 veterinary dermatologists) for bacterial culture, antimicrobial susceptibility testing and
109 bacterin production, or isolates had been submitted for bacterin formulation via another
110 diagnostic laboratory on behalf of the submitting veterinary surgeon.

111 Bacterins were posted to submitting practices with instructions for subcutaneous
112 administration (Table 1). Antimicrobial treatment before and during the start of bacterin
113 therapy was at the veterinary surgeon's discretion but discontinuation approximately ten
114 days into bacterin treatment was recommended. Numbers of first orders, of subsequent
115 repeat orders and intervals between first orders and first and last repeat orders were
116 recorded. Based on volume (40ml per vial) and recommended injection protocol, one vial
117 was assumed to provide 81 days of induction course treatment and between 91 and 192
118 days of maintenance treatment at either weekly or fortnightly dosing. Orders submitted
119 after more than 192 days were included as new orders.

120 **Antimicrobial use and clinical characteristics**

121 Antimicrobial use before and during bacterin therapy, including treatment during the start
122 of bacterin injections, was investigated by retrospective analysis of the dogs' medical
123 records. Practices in the U.K. that had ordered bacterin for a dog with a methicillin-
124 susceptible *S. (pseud)intermedius* and for which addresses could still be obtained from the
125 RVC laboratory database were asked in writing to send patient medical histories covering
126 12 months before and 12 months after starting bacterin therapy. Practices were asked to
127 submit medical records coded with the study number provided on the covering letter and
128 with all owner identifiable data deleted. Medical histories were not requested if bacterins
129 had been ordered through another microbiology laboratory on behalf of the attending
130 veterinary surgeon. One follow-up phone call was made two to four weeks after the initial
131 request if histories had not been received.

132 Medical histories were analysed for signalment (recorded as close as possible to the start
133 of bacterin therapy), diagnosis of skin disease (as recorded by submitting practices or as

134 predicted from descriptions of lesion type), timing and duration of bacterin injections and
135 for systemic (days of drug prescribed for bacterial infections) and topical (prescribed or
136 not) antibacterial therapy. Pyoderma was classified based on clinical signs into superficial
137 (papules, pustules, epidermal collarettes) or deep (furuncles, sinuses, haemorrhagic
138 crusts). Records of adverse reactions in a timely association with bacterin injections were
139 noted.

140 **Statistical Analysis**

141 Data were described and analysed using SPSS Version 22.0 (IBM Corp. Released 2013.
142 IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY). Distribution of data was
143 tested for normality using the Shapiro-Wilk test. Differences between numbers of days and
144 numbers of courses of antimicrobial drugs prescribed for systemic use were compared
145 before and during bacterin therapy for each dog by Wilcoxon signed rank test. $P < 0.05$ was
146 considered statistically significant.

147

148 **RESULTS**

149 **Bacterin orders**

150 Totals of 231 new *S. (pseud)intermedius* bacterin requests (mean 18 per year, SD 6.7)
151 and of 480 repeat orders (mean 38 per year, SD 12.2) were received by the RVC
152 laboratory during the twelve-and-a-half-year study period. Of the 231 dogs for which
153 bacterin had been ordered, 137 (59.3%) continued with at least one repeat order. The
154 number of repeat orders per individual dog ranged from 1 to 16 (median 3) with repeats
155 ordered only once for 47 (20.3%) dogs, twice for 19 (8.2%) dogs and more than twice for
156 71 (30.7%) dogs. Orders for first repeat bacterin vials were received within 13 weeks of the
157 first order for 68 (50%) dogs, in compliance with the expected ordering interval according
158 to the dosing protocol. Of 305 ordering intervals available for consecutive repeat orders,
159 75.1% were within the appropriate predicted treatment duration.

160 **Clinical characteristics of bacterin-treated dogs**

161 Medical histories were requested for 144 of the 231 dogs from 47 different primary
162 practices. Medical records were not requested for the remainder as dogs either lived
163 outside the U.K. (n=12, all in Germany), bacterin had been ordered through another U.K.
164 diagnostic laboratory (n=39), addresses for submitting practices were no longer valid
165 (n=31) or medical records for the relevant period could not be accessed conveniently after
166 practices had changed from paper to computer records (n=5).

167 Records were returned for 45 of the 144 dogs (31.3% response rate) with information
168 covering the required 24-month period for 22 dogs (signalment in Table 2). In addition to
169 their pyoderma management, eleven dogs (50%) received ectoparasite prophylaxis
170 prescribed by their veterinary surgeons during their study periods. Allergic skin disease
171 was recorded as diagnosed or suspected based on clinical signs in 17 (77.3%) dogs.
172 Eleven of those (64.7%) received concurrent treatment with a systemic glucocorticoid (10
173 dogs) or ciclosporin (1 dog) for management of underlying allergic disease; there was no
174 difference between the number of dogs responding or not responding to bacterin
175 (antimicrobial courses reduced or not) between allergic patients receiving systemic anti-
176 inflammatory treatment and those that did not ($P = 0.65$ and $P = 0.98$, 2-tailed Fishers exact
177 for antimicrobial courses and days respectively). Other chronic diseases mentioned were

178 hypothyroidism in two dogs, a keratinisation disorder in one and heart disease in another
179 three dogs, all managed with systemic or topical medication in parallel to their pyoderma.

180 No adverse effects (at injection sites, or to general health) had been recorded in a timely
181 relation to bacterin therapy in any of the dogs.

182 **Antimicrobial use before and during bacterin therapy**

183 In the 12 months before starting bacterin therapy, all 22 dogs had received at least one
184 course or a minimum of 14 days of systemic antimicrobials (Table 2). In the 12 months
185 after starting bacterin therapy, five dogs (23%), four with superficial and one with deep
186 pyoderma, had not received any systemically used antimicrobials. Fewer courses and
187 fewer days of systemic antimicrobial therapy had been prescribed during the 12 months
188 following the start of bacterin therapy compared to the 12 months preceding bacterin
189 (P=0.007 for both courses and days comparing all 22 dogs). Ranges and medians are
190 shown in Table 2. When only comparing the 19 dogs for which at least one repeat bacterin
191 order had been received and which had therefore likely received at least 172 days of
192 bacterin therapy, antimicrobial prescribing before and after bacterin start was also reduced
193 for courses and days (both P=0.02).

194 Six different classes of systemic antimicrobial drugs had been prescribed for the 22 dogs.
195 All but one had received a β -lactam antibiotic on at least one occasion during their 24-
196 month study period (cephalexin prescribed for 20 dogs, amoxicillin-clavulanic acid for 13
197 dogs, cefovecin for 4 dogs on at least one occasion), clindamycin had been used in 5
198 dogs, a fluoroquinolone in 7, and 1 dog had been treated with trimethoprim-potentiated
199 sulphonamide. Topical antimicrobial therapy had been dispensed in addition to systemic
200 treatment in 15/22 (68%) dogs during the 24-month periods but prescriptions were too
201 infrequent to allow useful allocation into periods before and after starting bacterins.
202 Prescription-only, chlorhexidine-based shampoos (Malaseb, Dechra Veterinary Products,
203 Shrewsbury, U.K.; Microbex, Virbac Limited, Woolpit, U.K.) indicated for the management
204 of microbial skin infections had been used for 8/22 (36%) dogs, another six dogs had
205 received other antibacterial wash preparations (chlorhexidine, hypochloric acid or
206 chloroxylenol-based products) and one dog had received fusidic acid cream as the only
207 topical product. Of the five dogs that had been managed without systemic antimicrobials
208 after starting bacterin, three continued with antimicrobial shampoo therapy. Antimicrobial
209 eardrops had been prescribed for 10/22 dogs at least once during the 24 months periods.

210 **DISCUSSION**

211 Within the limitations of a retrospective study using general practice medical records, our
212 results suggest that autogenous *S. (pseud)intermedius* bacterin can help to reduce the
213 need for systemic antimicrobial therapy in the management of canine recurrent pyoderma.
214 For the first time in canine pyoderma, this study analysed the need for antimicrobial
215 medication during bacterin therapy over a long period, rather than clinical signs during
216 shorter trials as in previous studies. The reduced need for antimicrobial therapy is in line
217 with findings from a recent study in pigs where an autogenous *S. hyicus* vaccine used in
218 sows reduced the metaphylactic use of antimicrobials in their piglets during outbreaks of
219 exudative epidermitis but where management and other concurrent factors were well
220 controlled.²⁷ Reducing the need for systemic antimicrobials in dogs is of particular

221 relevance at a time when calls to reduce antimicrobial use in companion animals, and in
222 some countries restrictions on prescribing, are increasing.²⁸⁻³⁰

223 Acceptance of the bacterin therapy amongst owners and veterinary surgeons and safety in
224 the dogs appeared good based on repeat orders received for almost 60% of dogs after the
225 initial 80-day course and the lack of any mention of adverse reactions in the medical
226 records of the 22 dogs.

227 Important confounding factors in this study were the lack of standardisation or control of
228 diagnostic criteria and of primary causes for pyoderma. Diagnostic detail such as the level
229 of depth for pyoderma (superficial or deep) was recorded but diagnostic criteria had not
230 been determined prospectively. Although in one study, bacterin therapy was less effective
231 in dogs with deep pyoderma compared to those with superficial infections,²⁴ unfortunately,
232 this layer of analysis could not be included in this study. Furthermore, critical steps
233 towards successful management of recurrent canine pyoderma remain the investigation
234 and correction of primary diseases that lead to bacterial skin infection, most commonly
235 ectoparasite infestations and allergic skin disease.^{7 31} Unfortunately, diagnostic
236 investigations into such primary skin diseases seem rarely exhaustive in small animal
237 practice as highlighted by a recent observational study that found that definitive diagnoses
238 were only rarely reached before management decisions were made.³² Similarly, the results
239 from our study indicate that ectoparasite prophylaxis, topical antimicrobial therapy and
240 anti-inflammatory medication for dogs with allergic skin disease were probably underused
241 with only 50% of dogs receiving veterinary-prescribed ectoparasite control and only 50% of
242 allergic dogs receiving anti-inflammatory medication for their allergic skin disease.

243 In current clinical practice, a major challenge to the treatment of canine pyoderma is the
244 increasing prevalence of multidrug-resistant, methicillin-resistant *S. pseudintermedius*
245 (MRSP).¹⁰ Autogenous bacterins may be of value in reducing selection pressure on
246 opportunistic staphylococci by reducing the need for repeated systemic antimicrobial
247 therapy and thus the risk of selection for MRSP. However, bacterin therapy has not been
248 shown to speed up resolution of clinical signs, which should be the primary focus in the
249 management of any MRSP infection in order to reduce the risk of contagion and zoonotic
250 transmission. Furthermore, it remains unknown whether individual resistance genes are
251 destroyed during bacterin production. Until this has been resolved, bacterins should only
252 be prepared from methicillin-susceptible *S. pseudintermedius* to avoid the potential
253 dispersal of resistance genes.

254 In summary, the results from this study corroborate findings from the six earlier studies on
255 canine recurrent pyoderma¹⁹⁻²⁴ and expand the conclusions of a recent review that
256 staphylococcal bacterin therapy can be of value in the management of canine recurrent
257 pyoderma.³³ Further investigations to better understand underlying mechanisms and
258 optimise treatment are clearly needed. Such efforts would now be timely and relevant due
259 to the high level of morbidity associated with canine recurrent pyoderma and the public
260 health implications of repeated use of systemic antimicrobials that are classified as
261 critically important for human health by the World Health Organisation.³⁴

262 **ACKNOWLEDGEMENTS**

263 The authors thank Maggie Bushnell, Peter Dron and Sue Rodway from the RVC Pathology
264 and Diagnostic Laboratories for making records available and to the veterinary surgeons
265 for coding and providing animal medical records.

266

267 **REFERENCES**

- 268 1 Hill PB, Lo A, Eden CA, *et al.* Survey of the prevalence, diagnosis and treatment of
269 dermatological conditions in small animals in general practice. *Vet Rec* 2006; 158: 533-
270 39.
- 271 2 O' Neill DG, Church DB, McGreevy PD, *et al.* Prevalence of disorders recorded in dogs
272 attending primary-care veterinary practices in England. *PLoS One* 2014; 9: e90501.
- 273 3 Summers JF, Hendricks A, Brodbelt DC. Prescribing practices of primary-care
274 veterinary practitioners in dogs diagnosed with bacterial pyoderma. *BMC Vet Res*
275 2014; 10: 240.
- 276 4 Loeffler A, Lloyd DH. What has changed in canine pyoderma? A narrative review. *Vet J*
277 2018; 235: 73-82.
- 278 5 DeBoer DJ. Strategies for management of recurrent pyoderma in dogs. *Vet Clin North*
279 *Am Small Anim Pract* 1990; 1509-24.
- 280 6 Ihrke PJ. Recurrent canine pyoderma. The North American Conference 2005.
281 Proceedings. 274-5.
- 282 7 Curtis C. Canine idiopathic recurrent superficial pyoderma. *Vet Rec* 1998; 143: 344.
- 283 8 Nuttall T. Pulse antibiotic therapy: it's time to cut back. *Vet Rec* 2012; 171: 472-3.
- 284 9 Hillier A, Lloyd DH, Weese JS, *et al.* Guidelines for the diagnosis and antimicrobial
285 therapy of canine superficial bacterial folliculitis (Antimicrobial Guidelines Working
286 Group of the International Society for Companion Animal Infectious Diseases). *Vet*
287 *Dermatol* 2014; 25: 163-e43.
- 288 10 Morris DO, Loeffler A, Davis MF, *et al.* Recommendations for approaches to meticillin-
289 resistant staphylococcal infections of small animals: diagnosis, therapeutic
290 considerations and preventative measures.: Clinical Consensus Guidelines of the
291 World Association for Veterinary Dermatology. *Vet Dermatol* 2017; 28: 304-e69.
- 292 11 Loeffler A, Cobb M, Bond R. Comparison of a chlorhexidine and a benzoyl peroxide
293 shampoo as sole treatment in canine superficial pyoderma. *Vet Rec* 2011; 169: 249.
- 294 12 McCoy KL, Kennedy ER. Autogenous vaccine therapy in staphylococci infections.
295 *JAMA* 1960;174: 35-8.
- 296 13 Middleton JR, Luby CD, Adams DS. Efficacy of vaccination against staphylococcal
297 mastitis: a review and new data. *Vet Microbiol* 2009; 134: 192-8.
- 298 14 Broughan J, Anderson R, Anderson AS. Strategies for and advances in the
299 development of *Staphylococcus aureus* prophylactic vaccines. *Expert Rev Vaccines*
300 2011; 10: 695-708.
- 301 15 Williams JM, Mayerhofer HJ, Brown RW. Clinical evaluation of a *Staphylococcus*
302 *aureus* bacterin (polyvalent somatic antigen). *Vet Med Small Anim Clin* 1966; 61: 789-
303 93.
- 304 16 Giersing BK, Dastgheyb SS, Modjarrad K, *et al.* Status of vaccine research and
305 development of vaccines for *Staphylococcus aureus*. *Vaccine* 2016; 34: 2962-6.

- 306 17 Redi D, Raffaelli CS, Rossetti B, *et al.* *Staphylococcus aureus* vaccine preclinical and
307 clinical development: current state of the art. *New Microbiol* 2018; 41: Epub ahead of
308 print.
- 309 18 Chambers ED, Severin GA. Staphylococcal bacterin for treatment of chronic
310 staphylococcal blepharitis in the dog. *J Am Vet Med Assoc* 1984; 185: 422-5.
- 311 19 Becker AM, Janik TA, Smith EK, *et al.* *Propionibacterium acnes* immunotherapy in
312 chronic recurrent canine pyoderma. *J Vet Int Med* 1989; 3: 26-30.
- 313 20 Mayr A, Selmair J, Schels H. Erfahrungen mit einer Autovakzine-Therapie bei der
314 Staphylokokken-Pyodermie des Hundes. *Tierärztl. Umschau* 1987; 42, 112-8.
- 315 21 DeBoer DJ, Moriello KA, Thomas CB, *et al.* Evaluation of a commercial staphylococcal
316 bacterin for management of idiopathic recurrent superficial pyoderma in dogs. *Am J Vet*
317 *Res* 1990; 51:636-9.
- 318 22 Curtis CF, Lamport AI, Lloyd DH. Masked, controlled study to investigate the efficacy of
319 a *Staphylococcus intermedius* autogenous bacterin for the control of canine idiopathic
320 recurrent superficial pyoderma. *Vet Dermatol* 2006; 17:163-8.
- 321 23 Solomon SEB, Farias MR, Pimpao CT. Use of *Staphylococcus aureus* phage lysate
322 Staphage Lysate (SPL) for the control of recurrent pyoderma eczema in dogs with
323 atopic dermatitis. *Acta Scient Vet* 2016;44;1382.
- 324 24 Borku MK, Ozkanlar Y, Hanedan B, *et al.* Efficacy of staphylococcal bacterin for
325 treatment of canine recurrent pyoderma: an open clinical trial. *Revue Méd Vét* 2007;
326 158: 234-8.
- 327 25 DeBoer DJ, Schultz KT, Thomas CB, *et al.* Clinical and immunological responses of
328 dogs with recurrent pyoderma to injections of *Staphylococcus* phage lysate. In: von
329 Tscherner C & Halliwell REW, eds. *Advances in Veterinary Dermatology Vol 1.*
330 London: Bailliere-Tindall 1990;335-46.
- 331 26 Dréno B, Pécastaings S, Corvec S, *et al.* *Cutibacterium acnes* (*Propionibacterium*
332 *acnes*) and acne vulgaris: a brief look at the latest updates. *J Eur Acad Dermatol*
333 *Venereol* 2018;32; Suppl 2:5-14.
- 334 27 Arsenakis I, Boyen F, Haesebrouck F, *et al.* Autogenous vaccination reduces
335 antimicrobial usage and mortality rates in a herd facing severe exudative epidermitis
336 outbreaks in weaned pigs. *Vet Rec* 2018;182:744.
- 337 28 RUMA. Responsible Use of Medicines in Agriculture Alliance, 2009. Antibiotic use in
338 animal health - 'as little as possible, but as much as necessary'. *Vet Rec* 2009; 164,
339 444.
- 340 29 Bundesministerium für Ernährung und Landwirtschaft.
341 <https://www.bmel.de/SharedDocs/Downloads/Tier/Tiergesundheit/Tierarzneimittel/TÄH>
342 [AV_BgBl_280218.pdf? blob=publicationFile](https://www.bmel.de/SharedDocs/Downloads/Tier/Tiergesundheit/Tierarzneimittel/TÄH). Accessed 3 August 2018.
- 343 30 Lloyd DH, Page SW. Antimicrobial Stewardship in Veterinary Medicine. *Microbiol*
344 *Spectr* 2018; 6(3).
- 345 31 Seckerdieck F, Mueller RS. Recurrent pyoderma and its underlying primary diseases: a
346 retrospective evaluation of 157 dogs. *Vet Rec* 2018; 182: 434.

- 347 **32** Robinson NJ, Dean RS, Cobb M, *et al.* Factors influencing common diagnoses made
348 during first-opinion small-animal consultations in the United Kingdom. *Prev Vet Med*
349 2016; 131: 87-94.
- 350 **33** Glos K, Mueller RS. [Treatment of chronic recurrent idiopathic pyoderma in the dog
351 with vaccines containing bacterial antigens]. *Tierärztl Prax Ausg K Kleintiere Heimtiere*
352 2011; 39: 425-8.
- 353 **34** WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance
354 (AGISAR). Critically Important Antimicrobials for Human Medicine. 3rd Revision, 2011.
355 Available at: <http://www.who.int/foodsafety/publications/antimicrobials-third/en/>.
356 Accessed 3 August 2018.

357 **Table captions**

358 **Table 1:** Protocol and treatment recommendations provided to veterinary surgeons with
 359 each RVC *Staphylococcus* autogenous bacterin vial for injecting dogs.

360 **Table 2:** Characteristics and antimicrobial therapy in the 12 months before and after
 361 starting autogenous *Staphylococcus (pseud)intermedius* bacterin for bacterial skin
 362 infections in 22 dogs.

363

364 **Table 1:** Protocol and treatment recommendations provided to veterinary surgeons with
 365 each RVC *Staphylococcus* autogenous bacterin vial for injecting dogs

Recommendations	Treatment protocol	
Before starting induction bacterin therapy and during initial ten-day period	Antibiotics should be withdrawn approximately 10 days after the injections begin, assuming that pyoderma is controlled. Once opened, please keep the bacterin refrigerated and inject subcutaneously every 3-4 days as follows:	
	Day 1	1 ml
	Day 4	1 ml
	Day 8	2 ml
	Day 11	2 ml
	Day 15	3 ml
	Day 18	3 ml
Subsequent induction therapy and maintenance	Continue with 3 ml dose on a weekly basis.	
Continuation therapy	If after three months the animal is responding favourably, then the injection interval can be extended to ten days and gradually to two weeks.	

366

367
368

Table 2: Case characteristics and antimicrobial therapy before and after starting autogenous *Staphylococcus (pseud)intermedius* bacterin for bacterial skin infections in 22 dogs

Dog number	Breed	Sex	Body weight (kg)	Age (years)	Type of pyoderma as recorded in medical records	Number of repeat orders	Systemic antimicrobial therapy			
							Courses before	Courses after	Days before	Days after
1	Unknown	Not known	28	Not known	Deep interdigital	4	4	2	37	7
2	Dalmatian	F	30	6.5	Superficial and interdigital	3	11	7	81	77
3	Cairn terrier	M	13	7	Deep interdigital	3	3	4	27	77
4	Shar Pei	M	20	1.5	Superficial pyoderma	4	4	0	32	0
5	Italian Spinone	F	30	5.5	Superficial pyoderma	1	1	0	14	0
6	Doberman	M	39	2.2	Superficial and deep	11	6	2	96	27
7	Bullterrier	F	24	4.5	Deep pyoderma	12	6	5	237	65
8	German shepherd	F	29	5.4	Superficial pyoderma	4	3	8	76	77
9	Yorkshire terrier	F	4.5	11	Superficial pyoderma	2	9	6	190	196
10	Yorkshire terrier	F	4	10	Superficial pyoderma	3	6	2	116	27
11	Cavalier King Charles spaniel	M	12.5	8	Superficial pyoderma	1	3	6	59	46
12	Labrador retriever	M	35	6	Superficial pyoderma	1	6	3	43	65
13	Labrador retriever	M	32	6	Superficial pyoderma	1	6	5	65	133
14	Rhodesian Ridgeback	F	52	2	Superficial pyoderma	4	6	1	71	60
15	Unknown	M	43	Not known	Superficial pyoderma	2	4	3	90	28
16	Unknown	F	32	2.5	Superficial pyoderma	0	4	0	60	0
17	Labrador retriever	M	29	8	Superficial pyoderma	9	4	0	47	0
18	Crossbred	M	19	9	Superficial pyoderma	8	7	7	138	99

19	Dogue de Bordeaux	M	58	2	Superficial pyoderma	8	6	3	252	79
20	Boxer	F	24	4	Superficial pyoderma	0	1	1	15	5
21	Irish Setter	M	27	5	Deep pyoderma	3	3	0	98	0
22	Crossbred	F	37	4.5	Bacterial paronychia	0	7	3	228	203
Summary	14 different breeds	11 F, 11 M	Range 4-58 (median 29)	Range 1.5-11 (median 5.4)	68.2% superficial pyoderma, 9.1% superficial and deep, 18.2% deep pododermatitis, 1 bacterial paronychia	Range 1-12 (median 3)	Range 1-11 (median 5)	Range 0-8 (median 3)	Range 14-252 (median 74)	Range 0-203 (median 53)

369

M: male; F: female.