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1 **Title:** Investigation of field intradermal tuberculosis test practices performed by veterinarians
2 in France and factors that influence testing

3

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10

11 **Abstract:**

12 Bovine tuberculosis infection remains at a low but persistent level in French cattle herds and
13 requires for its surveillance the use of tests with limited sensitivity and specificity. It thus
14 appears essential to understand the reality of the field situation, to identify parameters which
15 could affect how veterinarians perform these tests and how it can affect the sensitivity of the
16 bovine tuberculosis surveillance system. We surveyed rural veterinarians (n=1,084), major
17 stakeholders of the bovine tuberculosis surveillance system, after judgement (non-random)
18 sampling to investigate their skin-test practices and their perception of the surveillance and
19 control programs for this disease.

20 The response rate was 19.4% (210/1,084). The responses highlighted that veterinarians were
21 aware of the importance of the fight against bovine tuberculosis and were resilient to the
22 challenges and issues faced during fieldwork. However, we identified several areas of
23 noncompliance with regulatory recommendations, particularly regarding the choice of
24 injection site, verifying the quality of the injection, the method of test reading, and the
25 reporting of non-negative test results. Multivariate analysis showed that veterinarians who had

26 worked for fewer years in large-animal practice had better skin-test procedures. A higher
27 proportion of performed comparative tests and a more positive perception of surveillance and
28 control programs by veterinarians were associated with better skin-test practices.

29 The areas of noncompliance identified in this study could be detrimental to the sensitivity of
30 bovine tuberculosis surveillance but our results suggest that improving the information
31 provided to veterinarians and increasing their awareness are feasible solutions to improve the
32 surveillance efficacy.

33

34 **Keywords:** bovine tuberculosis; *Mycobacterium bovis*; screening; intradermal tuberculin test;
35 survey.

36

37 **Highlights:**

- 38 - Discrepancies between regulatory recommendations and field skin-test practices
- 39 - Presumed impact of skin-test practices on the sensitivity of the surveillance system
- 40 - Strong awareness of veterinarians on the necessity of the bovine tuberculosis control
41 program
- 42 - Strong link between veterinarians' perceptions and skin-test practices

43

44 **Main text:**

45 1. Introduction

46 Bovine tuberculosis (bTB), caused mainly by *Mycobacterium bovis*, was a major and
47 prevalent pathogen in bovine herds in France during the 1950's, as more than 25% of farms
48 were infected. Because of the zoonotic threat of bTB, control and surveillance of this disease
49 has been progressively and successfully implemented. France was considered to be officially
50 tuberculosis-free, according to the European Union (EU) in 2001 (European Council, 2001),

51 as the country remained under the incidence threshold of 0.1% for six years, highlighting the
52 efficacy of the bTB control program conducted for decades (Bénet et al., 2006). Since 2004,
53 bTB has been considered to be reemerging in some parts of the country, with an increase of
54 the incidence (but remaining under the national threshold) and the possible involvement of
55 wildlife (Gortázar et al., 2012; Hardstaff et al., 2014). This raises the question of the current
56 efficacy and organization of bTB surveillance in the context of low-disease prevalence. The
57 French bTB surveillance system in cattle is based on: (i) *post mortem* inspection in slaughter
58 houses to identify lesions consistent with bTB; (ii) skin testing before introduction into herds;
59 and (iii) periodic mandatory skin-test screening of cattle herds. The periodicity of mandatory
60 skin test screening depends on the annual bTB prevalence in the area and whether the herd (or
61 area) is considered to be at increased risk for bTB because of specific practices (the
62 production of raw milk for example) or the epidemiological context.

63 The skin test refers to an intradermal tuberculin test which can be comparative or simple. This
64 test is the current first-line reference for bTB screening of herds, according to the EU
65 (European Council, 1964), and consists of the injection of tuberculin, a product that should
66 elicit delayed hypersensitivity by an increase in skin-fold thickness (measured three days after
67 injection), which occurs in case of bTB infection. Intradermal tuberculin tests are imperfect in
68 terms of sensitivity, as the values for the single intradermal test (SIT) ranges between 53%
69 and 100% depending on studies (conducted in variable conditions) with a reported median
70 value of 83.9% and between 52% and 100% with a median value of 80.0% for the single
71 intradermal comparative cervical tuberculin test (SICCT) (De La Rúa-Domenech et al., 2006;
72 Schiller et al., 2010; Bezos et al., 2014). A recent meta-analysis, attempting to summarize
73 data from literature reported a median sensitivity of 94%; 95% confidence interval (CI) [49;
74 100] for the SIT and of 63%; 95% CI [40; 94] for the SICCT (Nuñez-García et al., 2018;
75 Downs et al., 2018). Thus, the SIT consistently appears to be more sensitive. Many factors

76 can influence the sensitivity of these tests and may be related to the animal tested, the
77 tuberculin used for injections, the method of injection, or the method of reading (De La Rua-
78 Domenech et al., 2006). Imperfect sensitivity can lead to the under detection of bTB
79 infections in herds, as the national prevalence and the prevalence in infected herds are low.

80 In France, both tests (SIT and SICCT) can be used for mandatory screenings, depending on
81 the context (imposed by local veterinary authorities). For many years, the SIT was the
82 preferred method as a first-line test and the SICCT only used in situations where non-specific
83 exposure to atypical mycobacteria was suspected. For the past few years, in order to address
84 the difficulties of implementation of the SIT (especially linked to cattle handling issues), the
85 SICCT has been progressively introduced in some areas such as in the southwest of France.

86 The SICCT, which takes longer to perform, requires good cattle handling, enabling better
87 practices as a consequence. According to the EU directive, screenings can be annual or
88 performed every two, three, or four years depending on bTB prevalence in the area (European
89 Council, 1964). When a bTB suspicion is investigated, the SICCT is used. In infected herds, if
90 the removal of infected animals by testing and culling is chosen, the SIT is used in parallel
91 with gamma interferon assay.

92 It is important to investigate skin-test practices in the field, given the influence of such
93 practices on the efficacy of the bTB surveillance system and the potential for bTB infections
94 in herds. Indeed, French veterinarians are major stakeholders, since they implement two of the
95 three bTB surveillance system components (mandatory skin tests before introduction into
96 herds and mandatory periodic skin-test screening of herds). Quantitative and qualitative
97 studies have identified several discrepancies between field skin-test practices and EU
98 recommended methods (Humblet et al., 2011a, 2011b; Meskell et al., 2013). Such
99 noncompliance could lead to decreased sensitivity of bTb screening and harm the
100 performance of the surveillance system, possibly representing a risk factor for the persistence

101 and diffusion of bTB (Broughan et al., 2016; Humblet et al., 2009). A preliminary qualitative
102 study implemented in France in 2018 confirmed these discrepancies and highlighted several
103 field realities that impede perfect application of the recommended methods (Gully et al.,
104 2018). The main impediments were poor cattle handling, the time-consuming nature of
105 screening associated with a heavy administrative burden and low fees, imperfections of the
106 skin test, and the difficult position of the veterinarian, considering their dual role of private
107 and “sanitary veterinarian” (veterinarians responsible for official mandatory screening but
108 also the habitual veterinarian of the farm). The perception of the surveillance and control of
109 bTB by veterinarians also appeared to be a major factor that influences skin test practices
110 (Gully et al., 2018).

111 Our aim was to obtain quantitative data on the implementation of skin tests in France. The
112 first objective was to collect descriptive data concerning veterinarians’ skin-test practices and
113 their perception of bTB surveillance and control programs at a national level. The second
114 objective was to identify factors that influence veterinarians’ skin-test practices with an
115 analytical perspective. Such an approach, combining data on practices and perception, has
116 never been used before to better understand the field reality of bTB screening.

117

118 2. Materials and methods

119 2.1. Study population and sampling

120 In this cross-sectional national study, sampling focused on French geographical
121 administrative areas called *départements* (DPT) (France is divided into 96 DPT) in which all
122 large animal veterinarians (epidemiological unit of this study) were included. A non-
123 probability judgement sampling of DPT based on four criteria of interest was implemented to
124 represent diverse local bTB situations. The judgement criteria were: (i) number of cattle in the
125 DPT. Only DPTs with more than 40,000 cattle were sampled to retain DPTs with significant

126 cattle breeding activity. (ii) bTB incidence in the DPT during a five-year period (2012-2016),
127 highlighting the history of bTB in the DPT, which influences the veterinarians' bTB
128 experience. We considered five classes of incidence, because of the diverse bTB
129 epidemiological contexts, and selected several DPTs for each class, which included more than
130 10 outbreaks (high infection level); between five and nine outbreaks (mild infection level);
131 between one and four outbreaks, with at least one after January 1, 2015 (low infection level
132 with recent bTB outbreaks); between one and four outbreaks with no outbreak after January 1,
133 2015 (low infection level with no recent outbreaks); and no outbreaks (bTB-free DPT). (iii)
134 The frequency of bTB mandatory screening, which influences the veterinarians' bTB
135 experience. DPTs with different frequencies of screening were sampled: annual screening;
136 zoned annual screening (refers to annual screening in limited areas inside the DPT); screening
137 every two, three, or four years; and no screening. (iv) Type of cattle production, which can
138 influence field skin-test practices, mainly the efficacy of handling, which in turn influences
139 the conditions of implementation of the skin tests. DPTs with different dominant types of
140 cattle production were selected: dairy cattle, *Charolais* beef cattle, *Limousin* beef cattle,
141 *Blond d'Aquitaine* beef cattle, beef cattle of another predominant breed, and small or non-
142 classifiable cattle herd dominance.

143 By combining categories of the four criteria of interest, 34 DPTs were chosen to illustrate
144 the diversity of bTB contexts. As mentioned above, all large-animal veterinarians with a valid
145 electronic address in each chosen DPT were then selected from the 2017 directory of French
146 Veterinarians. The details of DPT selection, with the associated map, are available in
147 supplementary materials.

148

149 2.2. Design and administration of the questionnaire

150 Selected veterinarians were surveyed using an online questionnaire. The questionnaire was
151 divided into five sections: (i) personal data (including age, number of years in large-animal
152 practice, professional status, gender, training location, and geographic area of practice); (ii)
153 characteristics of the herds of the veterinarians' customers (number of herds, number of cattle,
154 and type of cattle production t); (iii) cattle handling devices used by the veterinarians'
155 customers (not analyzed in this study); (iv) skin-test practices, including injection site
156 identification and preparation, injection method, results-reading method, and results reporting;
157 and (v) veterinarians' perception of bTB-surveillance and control programs. All questions
158 (except additional comments) were closed and had to be answered. Opening of some sections
159 and sub-sections of the questionnaire was conditional. An English version of the detailed
160 questionnaire is available in supplementary materials.

161 The questionnaire was tested by a panel of nine veterinarians and minor changes were made.
162 The online questionnaire was available between July 5 and September 13, 2018. Selected
163 veterinarians received an electronic mail invitation with a presentation of the study and a link
164 to the survey. This first electronic mail was followed by two reminders, each one month apart.
165 All data were anonymously collected and all participants gave their informed consent after
166 reading the presentation of the study and before starting the questionnaire, which is in
167 compliance with French law on personal data.

168

169 2.3. Scoring scales

170 Before analysis of the collected data, two scoring scales were established: a skin-testing
171 practice scoring scale, which considers all steps of the skin-test and results-reporting, and a
172 scoring scale of the perception of bTB surveillance and control programs. The resulting scores
173 are referred to as the "intradermal test (IT) score" and "perception score", respectively.

174 The IT score is an adaptation of a score designed by Humblet *et al.* (Humblet et al., 2011b) to
175 monitor IT performed by field veterinarians. A score of 0, 1, or 2 was attributed to each
176 questionnaire answer concerning IT practice: 0 for an ideal answer, 1 for an acceptable
177 answer, and 2 for an unacceptable answer. Each step of the IT procedure was then weighted
178 by a factor adapted from the Humblet scoring scale. Such weighting highlights the possible
179 impact of the considered procedural step on the risk of not detecting reactors (false-negative
180 result generation). The final score was obtained by summing all items and then recoding to
181 fall between 0 and 1: 0 referring to the perfect practice of IT and 1 to the unacceptable
182 practice of IT (for detecting reactors). Details of the scoring scale are available in Table 1.

183 The perception score was obtained by attributing 0 or 1 for each answer concerning
184 perceptions of the bTB surveillance and control program: 0 was given if the answer expressed
185 a positive perception and 1 if it expressed a negative perception. The final score was obtained
186 by summing all items and also recoding to fall between 0 and 1: 0 referring to a completely
187 positive perception of bTB-surveillance and control programs by veterinarians and 1 to a
188 completely negative perception. Details of the scoring scale are available in Table 2.

189

190 2.4. Statistical analysis

191 Descriptive results of the study are presented as proportions with 95% CI (Clopper-Pearson
192 exact intervals).

193 Bivariate analyses were conducted to evaluate the association between the IT score and other
194 variables. These analyses were performed using simple linear regression, as the IT score is a
195 continuous variable. Associations were considered significant for $P \leq 0.05$.

196 Multivariate analysis was conducted considering the IT score as the dependent variable of a
197 linear mixed model. Normal distribution of the dependent variable was assessed graphically.

198 Exposition variables included in the model were those with a P value < 0.25 in bivariate
199 analysis: number of years in large-animal practice, professional status, gender, university or
200 school of formation, frequency of the use of self-locking feed-fences for handling herds of the
201 practice (perceived as the most convenient for cattle handling), proportion of SICCTs (among
202 all skin tests performed in the last year), and perception score. Three variables were forced
203 into the model based on the hypothesis of this study: mandatory performance of the screening
204 test (yes or no), type of cattle production, and the proportion of large-animal activities in the
205 veterinarians' practice. No strong correlation between these variables was observed.
206 Correlations were measured using the Variance Inflating Factor (VIF) and considered to be
207 "strong" above a threshold of 10 (Dohoo et al., 2009). DPTs and practices were implemented
208 in the model as random effects to account for potential clustering in the DPT (because of
209 uniform management by local veterinary authorities) and practice level (communication and
210 common procedures between veterinarians of the same practice). Inference for the fixed part
211 of the model was performed using Satterthwaite's method to provide accurate P values
212 (Kuznetsova et al., 2017). A stepwise method was used for model-building with the backward
213 elimination of effects (fixed and random) with P values obeying the principle of marginality
214 (Kuznetsova et al., 2017). Interactions between the perception score and number of years in
215 large-animal practice and between the perception score and proportion of SICCTs were tested
216 but were not significant. Hypotheses of the model (heteroscedasticity, Normal distribution of
217 residuals) were assessed graphically by examination of the residuals. All analysis were
218 performed using the R and R Studio software, "car" package for VIF calculation and
219 "lmerTest" package for linear mixed model building (Kuznetsova et al., 2017; R
220 Development Core Team, 2016).

221

222 3. Results

3.1. Study participation and characteristics of the respondents

A total of 240 veterinarians answered the questionnaire completely; 234 completed questionnaires were available to analyze data on the veterinarians' perception (six veterinarians didn't perform skin tests) and 210 to analyze data on skin-test practices (24 questionnaires were not usable because of inconsistency due to the selection of incompatible answers). This number of completed questionnaires corresponded to a participation rate of 19.4% (210/1084).

We compared the demographic characteristics of this sample to those of the general population of French large-animal practitioners for the year 2017 (Table 3). Some strata of the population, such as women, veterinarians over 61 years of age, and employees, were underrepresented, whereas men, 31-40 years of age, and clinic owners were overrepresented in sampled veterinarians. Given the small differences and the fact that all strata were well represented, this sample was considered to be representative and statistical inference was performed.

3.2. Skin-test practices of veterinarians during bovine tuberculosis screening

We investigated skin-test practices of veterinarians at each step of the procedure: choice of injection site, preparation of injection site, choice of material of injection, verification of injection quality, reading of skin-tests results, and reporting of the results. Extensive results for skin-test practices are provided in Table 4.

Concerning the choice of injection site, 64.3%; 95% CI [57.4; 70.8] of veterinarians claimed to always perform tuberculin injection on the neck. The other veterinarians (35.7%; 95% CI [29.2; 42.5]) did not always perform the injection at the recommended site (*e.g.* injection on the caudal fold or refusal to perform the injection). Preparation of the injection site was declared to be performed using scissors or clippers, which are the recommended tools in

248 France (even if scissors can be difficult to use under certain circumstances), by 87.1%; 95%
249 CI [81.8; 91.3] of veterinarians. The use of McLintock™ or Muto™ syringes, which are
250 recommended injection devices in France, was declared by 85.7%; 95% CI [80.2; 90.1] of
251 veterinarians. Systematic verification of injection quality, with reinjection of a full dose if
252 tuberculin release was observed, was performed by 39.5%; 95% CI [32.9; 46.5] of
253 veterinarians, whereas 56.2%; 95% CI [49.2; 63.0] declared not to check or to check but not
254 reinject if tuberculin release is observed. The evaluation of skin-fold thickness was performed
255 by systematic use of a caliper at Day 0 and Day 3 by 23.3%; 95 CI [17.8; 29.6]. This value
256 reached 73.3%; 95% CI [66.8; 79.2] if veterinarians who declared performing qualitative
257 reading at Day 3 and using calipers only if a palpable reaction is present were added. Reading
258 of the skin-test results was declared to be performed systematically by the same person who
259 performed the injection by 70.0%; 95% CI [63.3; 76.1]. Reading of the skin-test results was
260 postponed (and not performed earlier) if the veterinarian was not available at Day 3 in most
261 cases (96.2%; 95% CI [92.6; 98.3]).

262 Reporting of non-negative results obtained for a SIT to veterinary authorities was declared by
263 85.2%; 95 CI [79.7; 89.7] of veterinarians. Others retested reactors by themselves later or
264 interpreted the results as false positives. The isolation of reactors was performed by half of
265 veterinarians.

266 The SICCT appeared to be performed by veterinarians with less noncompliance, as 88.7%;
267 95% CI [81.6; 91.6] performed systematic evaluation of skin-fold thickness using a caliper at
268 Day 0 and Day 3 or only after palpable reaction at Day 3. Reporting of non-negative results
269 for the SICCT to veterinary authorities was declared by 90.8%; 95 CI [85.7; 94.6] of
270 veterinarians.

271

272 3.3. Veterinarians' perception of bovine tuberculosis surveillance and control programs

273 The perception results are presented in Table 5. The results brought to light a lack of
274 confidence in the skin tests, as only 23.1%; 95% CI [17.8; 29] of veterinarians considered
275 them to be the best tests for bTB screening, despite most veterinarians claiming to have the
276 necessary information from veterinary authorities (62.0%; 95% CI [55.4; 68.2]) and to be able
277 to correctly perform them (72.6%; 95% CI [66.5; 78.3]). Indeed, more than the half of
278 veterinarians considered the reading of skin-test results to be too subjective and 46.6%; 95%
279 CI [40.1; 53.2] feared false-positive results in case of a non-negative result. Some aspects of
280 bTB screening, such as administrative burden, lack of consistency between regulatory
281 recommendations and field reality and implemented measures in case of confirmation of an
282 outbreak, were considered to be important issues for a quarter of veterinarians.

283 Concerning hurdles to eradicating bTB, limitations of the SIT were mentioned by 69.2%;
284 95% CI [62.9; 75.1] of veterinarians, whereas only 34.6%; 95% CI [28.5; 41.1] mentioned
285 limitations of the SICCT. A large proportion of veterinarians (68.4%; 95% CI [62.0; 74.3])
286 considered that wildlife (which could act as bTB reservoir) could be an epidemiological
287 obstacle to eradicating bTB. Less than the half of veterinarians considered the low fees for
288 skin tests (41.9%; 95% CI [35.5; 48.5]), danger linked to bTB testing (38.9%; 95% CI [32.6;
289 45.5]), and double role of private and “sanitary veterinarians” (34.6%; 95% CI [28.5; 41.1])
290 as hurdles to eradicating bTB.

291 Concerning the bTB control program, 81.6%; 95% CI [76.1; 86.4] of veterinarians claimed
292 that it was essential because of the zoonotic threat of this pathogen and 84.2%; 95% [78.9;
293 88.6] because of the importance of retaining an official bTB-free status. The importance of
294 maintaining cattle herds free from pathogens (37.6%; 95% CI [31.4; 44.2]) and of ending a
295 control program, initiated decades ago (35.0%; 95% CI [28.9; 41.5]), were mentioned by a
296 minority of veterinarians.

297

298 3.4. Bivariate analysis between intradermal test scores and other variables
299 Results of the bivariate analysis between IT scores and several other variables collected
300 through the questionnaire are presented in Table 6. The mean global IT score (score between
301 0 and 1, 0 being the “ideal” situation and 1 the “worst”) was 0.29; 95% CI [0.27; 0.31].
302 Significant statistical associations with IT scores were observed for the school or university in
303 which veterinarians were trained, the frequency of the use of feed-fences in herds of the
304 practice, and the perception score. Other variables did not show any significant statistical
305 association. The strongest effect was observed for the perception score, as a variance of one
306 interquartile (0.182) led to a 0.079 difference in the IT score, meaning that a negative
307 perception of skin tests and control and surveillance programs was associated with poor skin-
308 test practices. Foreign universities were associated with better skin-test practices than the
309 Alfort, Nantes or Toulouse National Veterinary Schools. A high proportion of performed
310 SICCTs and the very frequent use of feed-fences in herds of the practice were also associated
311 with better skin-test practices.

312

313 3.5. Multivariate analysis integrating intradermal test scores as a dependent variable

314 A complete linear regression model was built and then adjusted. The variable selection
315 procedure (stepwise procedure) led to the exclusion of random effects (veterinary clinic and
316 DPT). Thus, the results are presented in Table 7 as in a classic multiple linear regression
317 model.

318 Intraclass correlation coefficients for veterinary clinics and DPTs were 7.24%; 95% CI [-40.4;
319 37.1] and 5.92%; 95% CI [-3.34; 19.7], respectively. Confidence intervals included 0, which
320 is consistent with the fact that these random effects were excluded during the variable-
321 selection procedure.

322 The final regression model, with the IT score as the dependent variable, included the number
323 of years in large-animal practice, proportion of performed SICCTs, and perception score,
324 meaning that each of the three variables is statistically associated with the IT score with
325 adjustment for the two others.

326 The variable with the greatest effect on IT score was still the perception score, as a variance
327 of one interquartile of this variable led to an increase of 0.083 of the IT score. The number of
328 years in large-animal practice and the proportion of performed SICCTs had lower effects
329 (increase of 0.047 of the IT score for a one interquartile variance of the variable “number of
330 years in large animal practice” and a decrease of 0.045 for a one interquartile variance of the
331 variable “proportion of performed SICCT”). These results show that a positive perception of
332 bTB control and surveillance programs, a low number of years in rural practice, and high
333 proportion of performed SICCTs are associated with better skin-test practices.

334

335 4. Discussion

336 A non-probability judgement sample was used in this study. This choice was made to take
337 into account the four criteria mentioned above, which are particularly relevant for bTB to
338 represent the diversity of local situations and local specifics of this disease. Such a sampling
339 method and study design exposed the study to selection bias, since all DPTs were not in the
340 sampling frame (coverage bias) and since it was based on voluntary participation (non-
341 response bias). The response rate (19.4%) was good relative to other web-based surveys
342 administered to veterinarians (Blanton et al., 2018; Fatjó et al., 2006). Nonetheless, this value
343 is still low and a non-response bias cannot be excluded. However, the demographic
344 characteristics of the sample population were relatively similar to those of the target
345 population (Conseil national de l’Ordre des vétérinaires, 2017). Veterinarians under 40 years
346 of age were perhaps underrepresented, as they are mainly employees and not well represented

347 in the directory of French veterinarians (no stable positions) and thus were outside of the
348 sampling frame, whereas clinic owners with stable positions were overrepresented in this data
349 base. This underrepresentation of young veterinarians may have led to underrepresentation of
350 women, given the age pyramid of French veterinarians (Conseil national de l'Ordre des
351 vétérinaires, 2017). The fact that older people are not as familiar with computers could
352 explain the underrepresentation of veterinarians older than 61 years of age (Bech and
353 Kristensen, 2009; Gelder et al., 2010). Despite judgement sampling based on bTB-related
354 criteria and the reasonable representativeness of this sample, based on demographic
355 characteristics, it is still difficult to ensure the representativeness of this sample for bTB
356 practices and the perception of bTB surveillance and control programs because of the non-
357 response bias mentioned above. We could not assess the impact of this bias as no data were
358 available for comparison.

359 This survey relied on an auto-administered online questionnaire and was thus exposed to
360 measurement bias (Gelder et al., 2010). Indeed, some questions dealt with regulatory aspects
361 and respondents could have claimed better practices than they actually apply because of the
362 sensitivity of the subject. This effect of “social desirability” would have been limited, as this
363 questionnaire was anonymous and many veterinarians declared non-conventional practices
364 (Gelder et al., 2010; Kreuter et al., 2009). Moreover, such a questionnaire (if well designed)
365 usually leads to good quality data (Gelder et al., 2010) and the descriptive results of the
366 veterinarians’ practices during bTB screening were consistent with previously published
367 studies on this subject (Humblet et al., 2011b, 2011a). However, all these previously
368 published studies were questionnaire based and thus exposed to the same bias.

369 The descriptive results of the veterinarians’ skin-test practices showed considerable
370 noncompliance relative to the regulatory framework. This noncompliance involved all steps
371 of the skin-test procedure. Hence, the systematic choice of the neck as injection site by only

372 two thirds of veterinarians and systematic verification of tuberculin injection quality by less
373 than 40% hampers the sensitivity of the skin test, because injection sites other than the neck
374 and an insufficient quantity of delivered tuberculin can lead to false-negative results (De La
375 Rua-Domenech et al., 2006). Qualitative reading of the skin test results (excluding the method
376 of using a caliper on Day 3 only if palpable reaction is present, which is only partially
377 qualitative) was only performed by one quarter of veterinarians and can also lead to decreased
378 sensitivity because of the subjectivity of this method. We decided to consider the use of a
379 caliper on Day 3 only if palpable reaction was present as a partially “acceptable” method
380 (with an attributed score of 1 in the IT score), even if it is not recognized by the EU. Indeed,
381 this method represents an intermediate situation between regulatory prescriptions (systematic
382 use of caliper) and other qualitative methods for the reading of the skin-test results (European
383 Council, 1964). This particular semi-qualitative reading method was also tolerated for a long
384 period in France and even if it has been banned since 2015, some veterinarians may still use
385 it. Reading of the results by a veterinarian other than the one who performed the injection can
386 also decrease sensitivity due to the subjectivity of the skin tests. This aspect is important as
387 the higher the subjectivity, the greater the tester bias, (conscious or unconscious), leading to a
388 higher risk of error (De La Rua-Domenech et al., 2006).

389 Veterinarians declared better practices when using the SICCT, maybe due to the rigorous
390 reading imposed by the test procedure itself (mandatory comparison between bovine and
391 avian tuberculin injection sites). This could lead to higher sensitivity of the screenings using
392 SICCT compared with SIT even if the theoretical sensitivity is lower for the SICCT (De La
393 Rua-Domenech et al., 2006). Nonetheless, efficient implementation of the SIT (enabling to
394 reach reported values of sensitivity) should strongly be recommended since this test, in
395 presence of bTB infection, would lower the probability of leaving infected animals and reduce
396 the delay for outbreak control.

397 Another crucial step that affects sensitivity of this surveillance system is the reporting of
398 results to animal-health authorities. We found that one quarter of veterinarians do not
399 systematically report non-negative results, which could lead to bTB outbreaks escaping the
400 surveillance linked to herd screening. Such practices could explain the fact that 39% of bTB
401 cases were detected in slaughterhouses between 2000 and 2006, whereas mathematical
402 models predicted between 15% and 20% (Bekara, 2014).

403 This study focuses on veterinarians' skin-test practices on the field and it is important to
404 mention that syringe revision and disinfection were not taken into account in the
405 questionnaire since they were not considered to be "skin-test practices", strictly speaking.
406 However, regular maintenance, as recommended by the manufacturer, is necessary to ensure
407 good test performances (Roy et al., 2018). Thus, the lack of data about this specific aspect
408 could act as a limitation of this study.

409 Better global IT scores were associated with a higher proportion of performed SICCTs, which
410 is linked with the already discussed descriptive results and thus may be linked to more
411 rigorous practices when performing the SICCT. It also appears that a higher number of years
412 in large-animal practice is associated with poorer skin-test practices. This phenomenon could
413 be explained by increasing field adaptation of the skin-test procedure linked to the greater
414 experience and expertise of the veterinarians. In such a case, lower IT scores may not reflect
415 lower sensitivity of the skin test, as such a score cannot fully take into account the expertise
416 and adaptation of veterinarians (increasing with years). This is true if we consider the concept
417 of "local universality" (flexible approach of a regulatory framework, which could initially
418 appear unchangeable, to ensure proper implementation in local contexts), which appears to be
419 important in the field of regulation of animal health (Enticott, 2011). Another non-conflicting
420 hypothesis is that older veterinarians have been confronted with a high prevalence of bTB,
421 and can accept lower sensitivity of the surveillance system and thus looser IT practices. Such

422 practices are nonetheless non-compatible with the actual herd prevalence of bTB in France (<
423 0.1%) (Cavalerie et al., 2015).

424 The descriptive results concerning the veterinarians' perception of bTB surveillance and
425 control programs showed a certain resilience when facing the constraints of bTB testing. The
426 administrative burden linked to bTB screening, insufficient test fees, danger, and difficulties
427 in implementing regulatory recommendations in the field were important according to our
428 results and previously published data, leading to only a moderate level of acceptance (Calba
429 et al., 2016; Meskell et al., 2013). However, they were secondary to concerns about the
430 zoonotic potential of *M. bovis* and the importance of preserving an official bTB-free status.
431 The zoonotic threat of bTB is real in low-income countries, with a major role of oral
432 contamination linked to raw milk consumption (Olea-Popelka et al., 2017). In France, the
433 threat of bTB is mainly economic and not public-health related, as the proportion of *M. bovis*
434 infections in all tuberculosis cases is very low (1-3%) (Antoine and Jarlier, 2010). This gap
435 between veterinarians' perception and the reality of a zoonotic threat could be linked to a
436 search for significance of their actions in cattle herds.

437 A major hurdle to eradicating bTB, as presented by veterinarians, was limitations of the
438 screening tests (SIT and SICCT), which is in agreement with their intrinsic characteristics
439 (sensitivity and specificity) (De La Rua-Domenech et al., 2006) and other reports on
440 veterinarians' perceptions (Calba et al., 2016; Ciaravino et al., 2017). From a veterinary point
441 of view, the SICCT had a higher level of acceptance in our study. This may be linked to the
442 higher specificity of this test (compared to the SIT), which reduces the occurrence of false-
443 positive results. False-positive results could indeed deteriorate the farmer – veterinarian
444 relationship, as such results lead to the blocking of farms for further investigation, sometimes
445 with the culling of test reactors (Ciaravino et al., 2017; Gully et al., 2018; Meskell et al.,
446 2013). Wildlife was also mentioned by veterinarians as a major hurdle to eradicating bTB.

447 Wild species can act as reservoirs of *M. bovis*, as shown in several countries (Fitzgerald and
448 Kaneene, 2013; Gortázar et al., 2012), and thus have an important role in the persistence of
449 bTB. In France, wild species do not currently appear to play such a role (Gortázar et al., 2012)
450 but act, instead, as spill-over hosts taking part in the transmission chains after infection from
451 cattle (Hauer et al., 2015). This other gap between the veterinarians' perception and the reality
452 of the epidemiological situation could be interpreted as the search for a rationale for the
453 persistence of bTB, which is not associated with herd screening (and thus with veterinarians'
454 skin-test practices).

455 Perception scores were strongly associated with skin-test performance (after adjustment for
456 other variables). Despite contradictory reports on whether task perception and significance is
457 a consequence or a cause of job performance, the data tend to show that such elements could
458 contribute to good job performance, especially in health-related fields (Grant, 2008; Tong,
459 2018). It should be noted that our data didn't show that working in a context of bTB infection
460 was associated with poorer (veterinarians experiencing difficulties to eradicate infection in
461 herds) or better (veterinarians experiencing efficacy of screening programs) perception scores
462 in comparison with a context of bTB-free situation.

463 The IT score used, despite robust establishment based on expert opinions (Humblet et al.,
464 2011b), does not directly quantify the decrease in sensitivity of the test due to noncompliance
465 with recommended practices. Indeed, the weighting of the score was applied only to take into
466 consideration the relative importance of each step of the test and thus allow a comparison
467 between veterinarians but not direct interpretation in terms of any decrease in sensitivity. This
468 may be a limitation of this study, but no data were available to precisely quantify a decrease
469 in sensitivity.

470 Some recommendations can be made to improve the performance of veterinarians when skin
471 testing cattle in France. In some countries (Ireland, for example), annual observation of
472 veterinarians' skin-test practices by an official veterinarian is performed (Duignan et al.,
473 2012). Such practices are not generalized but targeted in France. However, considering the
474 strong link between perception and performance, the utility of such actions could be
475 reconsidered, since the perception of veterinarians may not be improved but actually
476 worsened (in case of a conflicting relationship with veterinary authorities). Instead, increasing
477 the number of informational meetings could be a valuable means to reinforce veterinarians'
478 perception of the significance of bTB-surveillance and control programs, as shown in
479 previous studies conducted in France (Humblet et al., 2011a). As skin-test practices appear to
480 worsen with an increasing number of years in large-animal practice, awareness of the need of
481 good practices should also be reinforced through continuing education.

482 The fact that a high proportion of performed SICCTs is associated with better skin-test
483 performance is consistent with the current field observations (*e.g.* the transition from the SIT
484 to the SICCT in *Dordogne* DPT was associated with higher report rate of bTB suspicions).
485 Better SICCT practices could indeed balance the hypothetical loss of sensitivity due to poorer
486 practices when performing the SIT. Nonetheless, in bTB infected areas the good
487 implementation of the SIT would increase the probability of detection of the infected cattle
488 thanks to a higher reported sensitivity in comparison with the SICCT. A better
489 implementation of the SIT should be based on the use of caliper to measure skin folds which
490 requires good handling practices, even if the SIT needs less time than the SICCT to be
491 performed.

492 Our results could provide guidance for action plans to improve skin-test practices at the
493 national level by identifying certain factors associated with screening test performance in
494 cattle herds.

495

496 5. Conclusion

497 Given the goal of eradicating bTB in France, it was necessary to study the skin-test practices
498 of veterinarians at the national level because of their importance for the surveillance system.
499 Results of the online questionnaire administered to large-animal veterinarians show that,
500 despite discrepancies between the regulatory framework and the implementation of screening
501 tests in the field, veterinarians are aware of the necessity of effective bTB- surveillance and
502 control programs. Our results, obtained through an original approach integrating perception
503 data and using scoring systems, show that better skin-test practices are associated with a
504 larger proportion of performed SICCTs, fewer years in large-animal practice, and a more
505 positive perception of bTB-surveillance and control programs. Such results help to better
506 depict field practices and could be used to identify sound action plans to improve practices
507 during bTB screening.

508

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510

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516

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657

Table 1. Intradermal test and results reporting score (IT score)

0: answer is in agreement with mandatory recommendations; 1: acceptable answer (for test sensitivity);

2: non-acceptable answer (for test sensitivity).

Weighting of the score was performed as previously described by Humblet *et al.* (Humblet et al., 2011b), considering (a) the case of veterinarians who perform the single intradermal comparative cervical tuberculin test (SICCT) and single intradermal test (SIT) or (b) the case of veterinarians who perform only the SIT.

Scores were summed and the sum was recoded to fall between 0 and 1.

NA: not applicable

	Score	(a) Weighting if the SICCT and SIT are performed	(b) Weighting if only the SIT is performed
Site of injection			
Neck (systematically)	0		
Neck only for calm cattle, no skin test for others	1		
Neck only for calm cattle, other injection site (e.g. caudal fold) for others	1	8.2%	11.4%
No skin test if nervous cattle are present	2		
Other injection site (e.g. caudal fold) for all animals	2		
Injection preparation			
Scissors	0		
Clippers	0		
Razor	1	7.1%	9.8%
Marking without cutting hair (e.g. marker)	1		
Variable	2		
No preparation	2		
Injection material			
McLintock™	0		
Muto™	0		
Synthena™	1	3.4%	4.7%
Syringe and needle	1		
Dermojet™	2		
Injection quality check			
Systematic verification of tuberculin release and reinjection if necessary with a full tuberculin dose	0		
Systematic verification of tuberculin release and reinjection if necessary with a quantity adjusted for the estimated release	1	12.1%	16.8%

Systematic verification of tuberculin release but no reinjection if it occurs (because of fear of false-positive reaction)	2		
Systematic verification of tuberculin release but no reinjection if it occurs (because of drudgery)	2		
No verification of tuberculin release	2		
Person performing the reading of the skin test results			
Always the same veterinarian as the one who injected	0		
Occasionally a different veterinarian from the one who injected	2	9.3%	13.0%
Reading time			
Postponed to the day after if impossible on Day 3	0		
Performed earlier if impossible on Day 3	2		
Skin test reading method			
Calipers (systematically at Day 0 and Day 3)	0		
Use of calipers to measure the skin fold only if in doubt after qualitative reading and compared to a skin fold measured at Day 3 at a non-injected site	1		
Use of calipers to measure the skin fold only if in doubt after qualitative reading and compared to the skin fold measured at Day 0 before injection	1	22.8%	31.8%
Only qualitative reading (palpation)	2		
Test reading in case of cattle handling difficulties			
Following regulatory prescriptions	0		
Visual examination only	2		
Isolation of test reactors			
Isolation	0		
No isolation	2	3.7%	5.1%
Management of non-negative results			
Immediate reporting to veterinary authorities	0		
Postponed reporting to veterinary authorities	1		
No reporting and new intradermal test performed 6 weeks later	2	5.3%	7.4%
False-positive interpretation and no report	2		
Single intradermal comparative cervical tuberculin test (SICCT) practices			
Measurement of skin folds at the 2 injection sites before injection and in comparison with the 2 measurements performed at Day 3	0		
Measurement of the skin fold at only one site before injection and comparison with measurements performed at the 2 injection sites at Day 3	1	22.8%	NA
Measurement of skin folds at the 2 injection sites before injection and comparison with the 2 measurements performed at Day 3 only if there is palpable reaction	1		
No measurement before injection, 3 measurements at Day 3: 2 at the injection sites compared with a measurement of a non-injected site	2		
Management of non-negative results when performing single intradermal comparative cervical tuberculin (SICCT) tests			
Systematic reporting of all non-negative results	0		
No reporting if only one non-negative result is obtained	2		
No systematic reporting, even if more than one non-negative result is obtained	2	5.3%	NA
Reporting only if more than one non-negative result is obtained	2		

Table 2. Score of veterinarians' perception of bovine tuberculosis surveillance and control programs

0: answer linked to positive perception; 1: answer linked to negative perception.

Scores were summed and the sum was recoded to fall between 0 and 1.

	Score
Major consideration in case of non-negative result	
Thinks about a potential outbreak of a zoonotic disease	0
Thinks about a potential outbreak with a major economic impact for the farmer	0
Thinks about potential temporary blocking of the farm (false-positive result)	1
Has no specific consideration	1
Concerning intradermal skins tests	
Has the necessary information from the veterinary authorities	Yes = 0 / No = 1
Perceives him/herself as able to correctly perform skin tests	Yes = 0 / No = 1
Thinks a knowledge update on skin tests is necessary	Yes = 1 / No = 0
Thinks intradermal skin tests are the best available screening tests	Yes = 0 / No = 1
Thinks the interpretation of skin tests is too subjective	Yes = 1 / No = 0
Thinks it is necessary to reevaluate the administrative part associated with skin tests during screening (measurement reports, results transmission, ...)	Yes = 1 / No = 0
Thinks it is necessary to adapt prescriptions to field reality	Yes = 1 / No = 0
Thinks it is necessary to stop blocking herds for 6 weeks in case of a non-negative result	Yes = 1 / No = 0
Concerning hurdles to eradicating bovine tuberculosis	
Highlights limitations of the single intradermal skin test	Yes = 1 / No = 0
Highlights limitations of the single intradermal comparative cervical skin test	Yes = 1 / No = 0
Highlights the possible role of wildlife reservoirs	Yes = 1 / No = 0
Highlights the lack of consideration from sanitary authorities	Yes = 1 / No = 0
Highlights the low fees paid for skin tests	Yes = 1 / No = 0
Highlights the danger of performing skin tests	Yes = 1 / No = 0
Highlights the double role of private practitioner and "sanitary veterinarian"	Yes = 1 / No = 0
Concerning the of bovine tuberculosis control program	
Essential because it is a major zoonosis	Yes = 0 / No = 1
Essential to keep an official tuberculosis-free status	Yes = 0 / No = 1
Essential to prevent the circulation of infectious agents in cattle herds	Yes = 0 / No = 1
Essential to end this control program, initiated decades ago	Yes = 0 / No = 1
Useless because the bovine tuberculosis situation is favorable	Yes = 1 / No = 0
Useless because such a program will never have good results	Yes = 1 / No = 0

Table 3. Demographic characteristics of veterinarians sampled in the study and of the general population of large-animal veterinarians in France

	Sample of the study (n = 210) % and IC _{95%}	General population of French large-animal veterinarians % (Conseil national de l'Ordre des vétérinaires, 2017)
Gender		
Women	22.5 [17.4; 28.3]	34.4
Men	77.5 [71.7; 82.6]	65.6
Age (years)		
≤ 30	7.5 [4.5; 11.6]	11.1
31 - 40	39.2 [36.6; 50.9]	31.3
41 - 50	24.6 [19.3; 30.5]	22.4
51 - 60	24.2 [18.9; 30.1]	23.8
≥ 61	4.6 [2.3; 8.0]	11.4
Professional status		
Clinic owner	76.7 [70.8; 81.9]	64.6
Employee	19.6 [14.8; 25.2]	32.1
Private practitioner (without being a clinic owner)	3.8 [1.7; 7.0]	3.2

Table 4. Veterinarians' skin test practices in bovine tuberculosis screening

	%	IC _{95%}
Site of injection (n = 210)		
Neck (systematically)	64.3	[57.4; 70.8]
Neck only for calm cattle, no skin test for others	17.6	[12.7; 23.5]
Neck only for calm cattle, other injection site (e.g. caudal fold) for others	7.6	[4.4; 12.1]
No skin test if nervous cattle are present	6.2	[3.3; 10.4]
Other injection site (e.g. caudal fold) for all animals	4.3	[2.0; 8.0]
Site of injection preparation (n = 210)		
Scissors	41.4	[34.7; 48.4]
Clippers	45.7	[38.8; 52.7]
Razor	8.6	[5.2; 13.2]
Marking without cutting hair (e.g. marker)	0.5	[0.0; 2.6]
Variable	2.4	[0.8; 5.5]
No preparation	1.4	[0.3; 4.1]
Injection material (n=210)		
McLintock™	73.3	[66.8; 79.2]
Muto™	12.4	[8.2; 17.6]
Synthena™	12.4	[8.2; 17.6]
Syringe and needle	1.4	[0.3; 4.1]
Dermojet	0.5	[0.0; 2.6]
Injection quality check (n = 210)		
Systematic verification of tuberculin release and reinjection if necessary with a full tuberculin dose	39.5	[32.9; 46.5]
Systematic verification of tuberculin release and reinjection if necessary with a quantity adjusted for the estimated release	4.3	[2.0; 8.0]
Systematic verification of tuberculin release but no reinjection if it occurs (because of fear of false-positive reaction)	19.5	[14.4; 25.5]
Systematic verification of tuberculin release but no reinjection if it occurs (because of drudgery)	4.3	[2.0; 8.0]
No verification of tuberculin release	32.4	[26.1; 39.2]
Person performing reading of the skin test results (n = 210)		
Always the same veterinarian as the one who injected	70.0	[63.3; 76.1]
Occasionally a different veterinarian from the one who injected	30.0	[23.9; 36.7]
Reading time (n = 210)		
Postponed to the day after if impossible at Day 3	96.2	[92.6; 98.3]
Performed earlier if impossible at Day 3	3.8	[1.7; 7.4]
Skin test reading method (n=210)		
Calipers (systematically at Day 0 and Day 3)	23.3	[17.8; 29.6]
Use of calipers to measure the skin fold only if in doubt after qualitative reading and compared to a skin fold measured at Day 3 on a non-injected site	18.6	[13.6; 24.5]
Use of calipers to measure the skin fold only if in doubt after qualitative reading and compared to the skin fold measured at Day 0 before injection	50.0	[43; 57]
Only qualitative reading (palpation)	8.1	[4.8; 12.6]
Test reading in case of cattle handling difficulties (n = 210)		
Following regulatory prescriptions	84.3	[78.6; 88.9]
Visual examination only	15.7	[11.1; 21.4]
Isolation of test reactors (n = 210)		
Isolation	58.6	[51.6; 65.3]
No isolation	41.4	[34.7; 48.4]
Management of non-negative results (n = 210)		
Immediate reporting to veterinary authorities	21.4	[16.1; 27.6]
Postponed reporting to veterinary authorities	63.8	[56.9; 70.3]

No reporting and new intradermal test performed 6 weeks later	13.8	[9.4; 19.2]
False-positive interpretation and no reporting	1.0	[0.1; 3.4]
Single intradermal comparative cervical tuberculin test practices (n = 185)		
Measurement of skin folds at the 2 injection sites before injection and in comparison with the 2 measurements performed at Day 3	41.1	[33.9; 48.5]
Measurement of the skin fold at only one site before injection and comparison with measurements performed at the 2 injection sites at Day 3	8.1	[4.6; 13.0]
Measurement of skin folds at the 2 injection sites before injection and comparison with the 2 measurements performed at Day 3 only if there is a palpable reaction	47.6	[40.2; 55]
No measurement before injection, 3 measurements at Day 3: 2 at the injection sites compared with a measurement of a non-injected site	3.2	[1.2 ; 6.9]
Management of non-negative results when performing single intradermal comparative cervical tuberculin tests (n = 185)		
Systematic reporting of all non-negative results	90.8	[85.7; 94.6]
No reporting if only one non-negative result is obtained	1.6	[0.3; 4.7]
No systematic reporting, even if more than one non-negative result is obtained	7.0	[3.8; 11.7]
Reporting only if more than one non-negative result is obtained	0.5	[0.0; 3.0]

Table 5. Veterinarians' perception of bovine tuberculosis control and surveillance programs

	%	95% CI
Concerning intradermal skins tests (n = 234)		
Has the necessary information from the veterinary authorities	62.0	[55.4; 68.2]
Perceives him/herself as able to correctly perform skin tests	72.6	[66.5; 78.3]
Thinks a knowledge update on skin tests is necessary	17.9	[13.3; 23.5]
Thinks intradermal skin tests are the best available screening tests	23.1	[17.8; 29.0]
Thinks the interpretation of skin tests is too subjective	46.6	[40.1; 53.2]
Thinks it is necessary to reevaluate the administrative part associated with skin tests during screening (measurement reports, results transmission, ...)	26.9	[21.4; 33.1]
Thinks it is necessary to adapt prescriptions to field reality	33.3	[27.3; 39.8]
Thinks it is necessary to stop blocking herds for 6 weeks in case of a non-negative result	25.6	[20.2; 31.7]
Concerning hurdles to eradicating bovine tuberculosis (n = 234)		
Highlights limitations of the single intradermal skin test	69.2	[62.9; 75.1]
Highlights limitations of the single intradermal comparative cervical skin test	34.6	[28.5; 41.1]
Highlights the possible role of wildlife reservoirs	68.4	[62.0; 74.3]
Highlights the lack of consideration from sanitary authorities	29.1	[23.3; 35.3]
Highlights the low fees paid for skin tests	41.9	[35.5; 48.5]
Highlights the danger of performing skin tests	38.9	[32.6; 45.5]
Highlights the double role of private practitioner and "sanitary veterinarian"	34.6	[28.5; 41.1]
Concerning the bovine tuberculosis control program (n = 234)		
Essential because it is a major zoonosis	81.6	[76.1; 86.4]
Essential to keep an official tuberculosis-free status	84.2	[78.9; 88.6]
Essential to prevent the circulation of infectious agents in cattle herds	37.6	[31.4; 44.2]
Essential to end this control program, initiated decades ago	35.0	[28.9; 41.5]
Useless because the bovine tuberculosis situation is favorable	0.4	[0.0; 2.4]
Useless because such a program will never have good results	1.7	[0.5; 4.3]

Table 6. Results of bivariate analysis between the intradermal skin test score and other variables in a simple linear regression

CI: confidence interval

D: dichotomous variable

Ca: categorical variable

Ct: continuous variable

IQR: interquartile range

		Estimate	95% CI	P value
Gender (D)	Intercept (Female)	0.259	[0.219; 0.299]	0.100
	Male	0.038	[-0.007; 0.083]	
Professional status (D)	Intercept (Private)	0.296	[0.274; 0.318]	0.133
	Employee	-0.037	[-0.085; 0.011]	
Age (Ca)	Intercept (≤ 30)	0.284	[0.213; 0.354]	0.335
	31-40	-0.010	[-0.087; 0.067]	
	41-50	0.008	[-0.072; 0.088]	
	51-60	0.013	[-0.068; 0.095]	
	> 60	0.106	[-0.022; 0.234]	
University/School (Ca)	Intercept (Out of France)	0.226	[0.180; 0.271]	0.030
	Alfort	0.092	[0.030; 0.156]	
	Lyon	0.052	[-0.011; 0.116]	
	Nantes	0.072	[0.010; 0.134]	
	Toulouse	0.083	[0.023; 0.144]	
Large animal activity proportion (D)	Intercept ($\leq 60\%$)	0.302	[0.271; 0.332]	0.251
	> 60%	-0.023	[-0.062; 0.016]	
Mean herd size (Ct)	Intercept	0.291	[0.254; 0.328]	0.887
		-2.96e-05	[-4.40e-04; 3.81e-04]	
<i>1 IQR variation effect: -1.65e-03</i>				
Dominant herd type in the practice (Ca)	Intercept (Beef cattle different from <i>charolais</i>)	0.300	[0.266; 0.334]	0.732
	<i>Charolais</i> beef cattle	-0.017	[-0.063; 0.029]	
	Dairy cattle	-0.016	[-0.067; 0.034]	
Time in large-animal practice (Ct)	Intercept	0.259	[0.220; 0.297]	0.075
		1.68e-03	[-1.73e-04; 3.53e-03]	
<i>1 IQR variation effect: 0.032</i>				
Mandatory screening in herds (D)	Intercept (No)	0.279	[0.250; 0.309]	0.415
	Yes	0.016	[-0.023; 0.056]	
Proportion of single intradermal comparative cervical skin test (Ct)	Intercept	0.316	[0.286; 0.349]	0.021
		-5.89e-04	[-1.09e-03; -9.03e-05]	
<i>1 IQR variation effect: -0.047</i>				
Frequency of feed-fences in the practice (D)	Intercept (Less frequent)	0.307	[0.282; 0.332]	0.024
	Very frequent	-0.045	[-0.084; -0.006]	

Perception score (Ct)	Intercept	0.149	[0.094; 0.204]	< 0.001
		0.437	[0.275; 0.599]	
<i>1 IQR variation effect: 0.079</i>				

Table 7. Multivariate analysis results and effects of predictors on the intradermal skin test score

IQR: interquartile range

CI: confidence interval

Adjusted R²: 0.1601

F-statistic: 14.28

P value: 1.73e-08

Residual standard error: 0.1314 (206 degree of freedom)

	Estimate	95% CI	t	P value	IQR	Effect of one IQR variation
Intercept	0.125	[0.056; 0.195]	3.56	< 0.001		
Number of years in large-animal practice	2.48e-03	[7.62e-04; 4.21e-03]	-2.37	0.005	28-9	0.047
Proportion of single intradermal comparative cervical skin test	-5.58e-04	[-1.02e-03; -9.44e-05]	5.67	0.018	90-10	-0.045
Perception score	0.459	[0.299; 0.618]	2.84	< 0.001	0.409-0.227	0.083