

1 **SUPPLEMENTARY INFORMATION**

2  
3 **Modelling the effects of antimicrobial metaphylaxis and pen size on Bovine Respiratory Disease in**  
4 **high and low risk fattening cattle.**

5  
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16

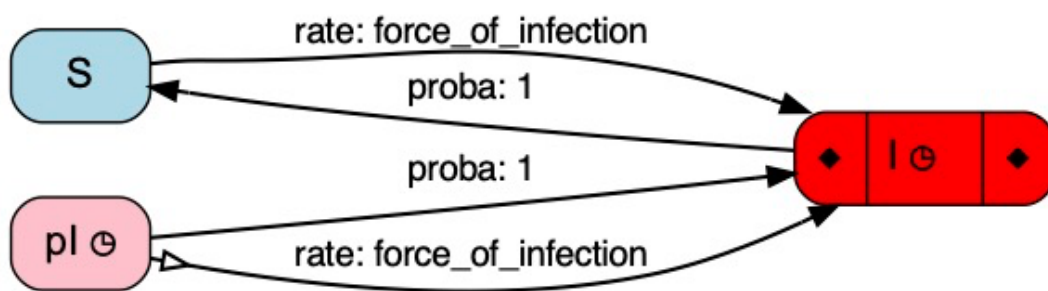
17

18 **1 Processes of the model**

19 In the model, five processes drive the states of individuals: infection (Fig. SI 1), clinical signs (Fig. SI 3),  
20 detection (Fig. SI 4) and treatment (Fig. SI 5). They are represented by a formalism broadly used in  
21 computer science, finite state machines, which is close to flow diagrams used by epidemiologists, with a  
22 higher expressiveness. Their textual description in the YAML format in the model file (SI section 4) is easy  
23 to read and can be automatically converted in a graphical representation by EMULSION.

24 To help understand the state machine diagrams, we present how the diagram summarising the infection  
25 process (Fig. SI 1) relates to the state machine specification (Fig. SI 2), extracted from the whole model  
26 (brd.yaml, see SI section 4). More details on how state machines differ from flow diagrams are available  
27 in the documentation: [https://sourcesup.renater.fr/www/emulsion-public/pages/Modelling\\_principles.html](https://sourcesup.renater.fr/www/emulsion-public/pages/Modelling_principles.html)

28



29

30 **Figure S1. State machine representing the infectious process at the individual scale.** Health states:

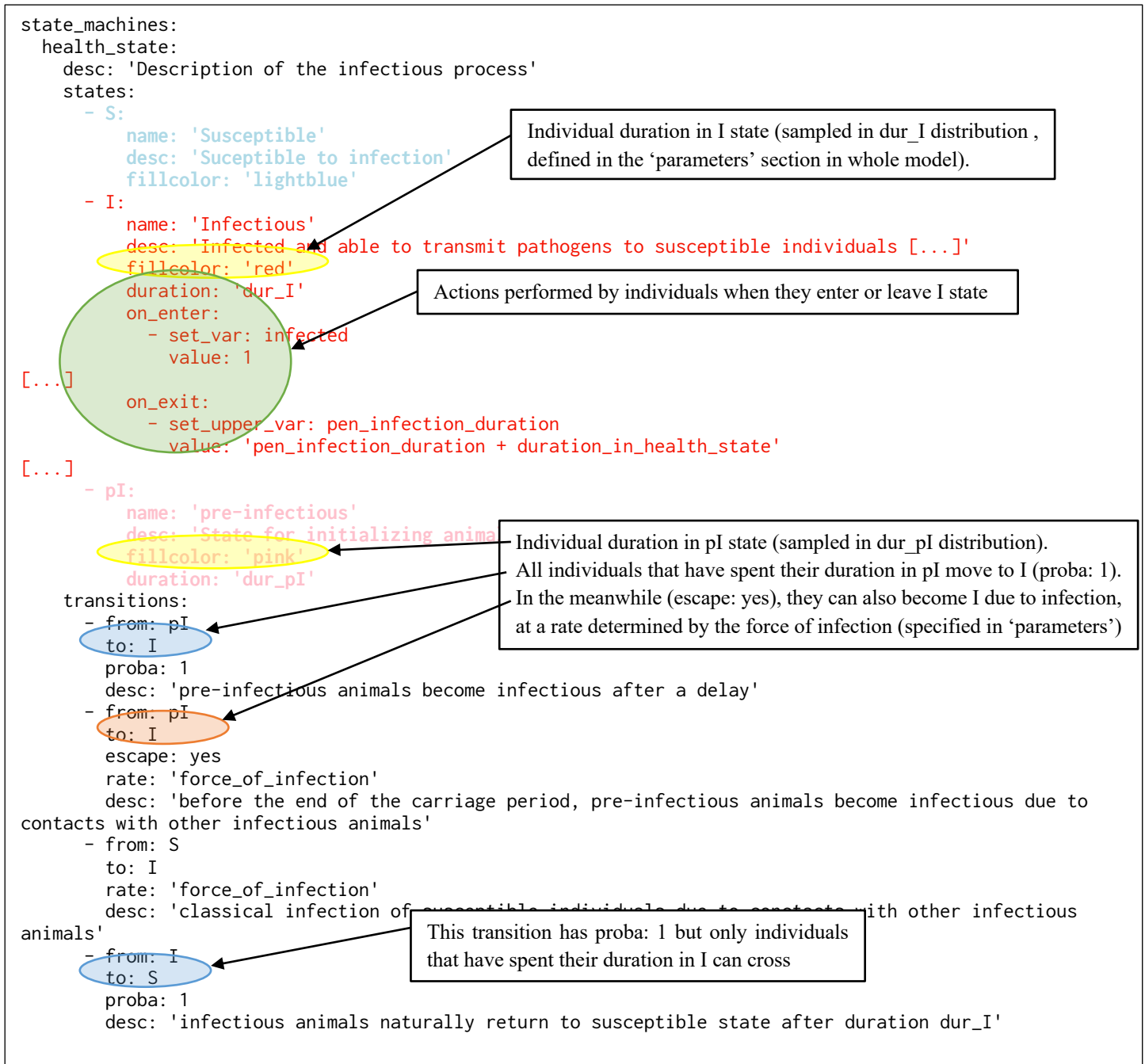
31 susceptible (S), infectious (I), asymptomatic carrier (pI). After a delay (denoted by the clock), pI  
32 individuals eventually become infectious (hence, they have a probability of 1 to move to I after the delay)

33 but can also become infectious at any moment (transition at the bottom with an open arrow at the  
34 beginning of the edge), due to contacts with infectious animals. Susceptible animals can become I only

35 through contacts with other I. Actions are performed when entering or leaving I state (denoted by the

36 lozenges), especially for controlling hyperthermia. After a delay, infectious individuals become

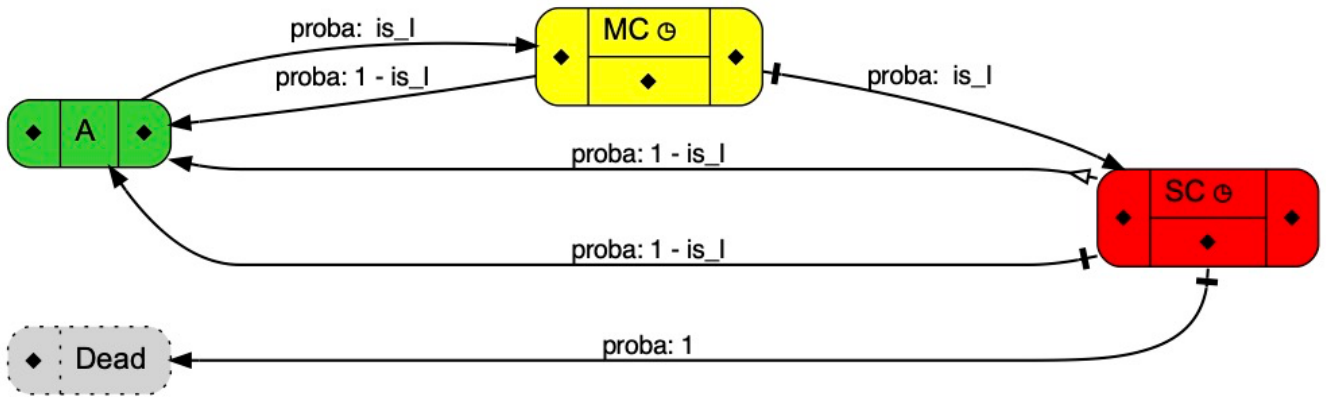
37 susceptible again.



**Figure S2. Annotated description of the 'health\_state' state machine.** This part of the BRD model produces the state machine diagram of Fig. SI 1

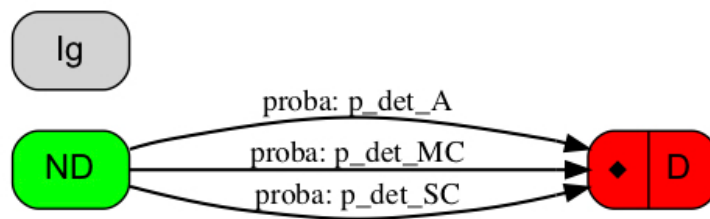
40

41



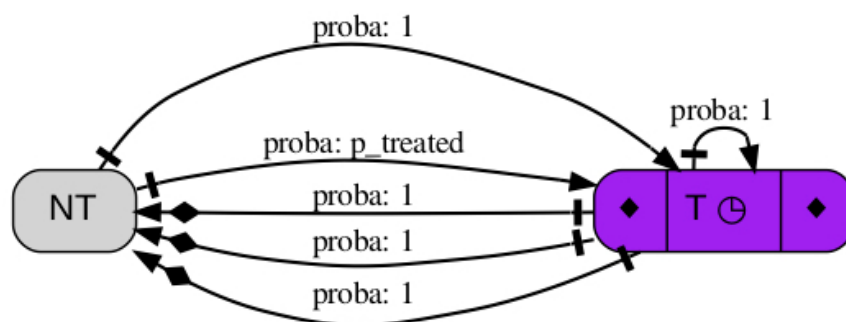
42

43 **Figure S3. State machine representing the onset of clinical signs.** States: asymptomatic (A), mildly  
 44 symptomatic (MildC) with low detection sensitivity, symptomatic with severe and more sensitive clinical  
 45 signs (SC), dead (Dead). Mild clinical signs appear with infection, then can either evolve towards severe  
 46 clinical signs, or disappear when infection is over. When entering SC state, individuals are subject to a  
 47 random trial to determine whether they will eventually die from BRD or return to A (denoted by the  
 48 vertical bar on the transitions from SC).



49

50 **Figure S4. State machine representing BRD detection.** States: undetected (ND), detected (D), Ignored  
 51 (Ig). Detection probabilities depend on the clinical status, based on the specificity for A (false positive),  
 52 and on the sensitivity for mild and severe clinical signs for MC and SC, respectively. State 'Ig' is set  
 53 when a treatment fails after the maximum allowed number of doses: in that case, the animal is no longer  
 54 considered for receiving further treatments.



56

57 **Figure S5. State machine representing the treatment protocol.** States: not under treatment (NT), under  
 58 treatment (T). Detected animals become T with a probability  $p_{\text{treated}}$  and receive a first antimicrobial  
 59 dose. A random trial determines the outcome of the treatment, which will be effective after a constant  
 60 delay (48h). Animals with a successful treatment or returned to asymptomatic in the meanwhile return to  
 61 NT. Otherwise, they are re-treated until receiving the maximum number of doses (here, 3), then the  
 62 treatment is abandoned, and the animal will not be re-treated anymore. For each of these disjoint  
 63 conditions, the decision is deterministic (hence ‘proba: 1’).

64

## 65 2 Complete EMULSION BRD model

66 The following file (brd.yaml) is meant to be run with the EMULSION framework (version 1.2b11 or later)  
 67 which can be installed according to the instructions provided on the software webpage:  
 68 <https://sourcesup.renater.fr/www/emulsion-public/>. The syntax of the EMULSION modelling language is  
 69 also fully described there.

70 Assuming EMULSION installed properly, running a scenario (defined by specific parameter values),  
 71 e.g. L-HR-C for 100 stochastic repetitions, requires the following command:

```
72 emulsion run brd.yaml -r 100 --output-dir L-HR-C -p pen_size=100 -p initial_prevalence=0.2 -p
73 use_antibioprevention=0 -p use_metaphylaxis=1 -p metaphylaxis_threshold=0.15
```

74 Simulation results are stored in directory ‘L-HR-C’ in a CSV file named ‘counts.csv’.

```

75  ---
76  #
77  # / -----|
78  # | | | | | | | | | | | | | | | | | | |
79  # | | | | | | | | | | | | | | | | | | |
80  # | | | | | | | | | | | | | | | | | | |
81  # \-----| \-----| | | | \-----| \-----|
82
83  #
84  # |---| | | | | | | | | | | | | | | | | | | |
85  # | | | | | | | | | | | | | | | | | | | | |
86  # | | | | | | | | | | | | | | | | | | | | |
87  # | | | | | | | | | | | | | | | | | | | | |
88  # |-----| | | | \---/| | | | | | | | | | | |
89
90
91  # NAME OF THE DISEASE
92  model_name: BRD_FR_US_VetRes
93
94  ## information
95  model_info:
96    authors:
97      - 'Sébastien Picault, INRAE, Oniris, BIOEPAR, 44300 Nantes, France'
98      - 'Pauline Ezanno, INRAE, Oniris, BIOEPAR, 44300 Nantes, France'
99      - 'Sébastien Assié, INRAE, Oniris, BIOEPAR, 44300 Nantes, France'
100   contributors:
101     - 'Brad White, Beef Cattle Institute, Kansas State University, USA'
102     - 'David Amrine, Beef Cattle Institute, Kansas State University, USA'
103   publications:
104     - 'Picault S, Ezanno P, Smith K, White B, Amrine D, Assié S. 2022 (under review). Modelling the
105       effects of antimicrobial metaphylaxis and pen size on Bovine Respiratory Disease in high and low risk
106       fattening cattle. Submitted to Veterinary Research (ModAH series)'
107
108  # -----
109  # |---| | | | | | | | | | | | | | | | | | | |
110  # | | | | | | | | | | | | | | | | | | | | |
111  # | | | | | | | | | | | | | | | | | | | | |
112  # | | | | | | | | | | | | | | | | | | | | |
113  # | | | | | | | | | | | | | | | | | | | | |
114
115  # TIME INFORMATION
116  time_info:
117    time_unit: hours
118    delta_t: 12
119    total_duration: '100*24'
120
121
122  #
123  # | | | | | | | | | | | | | | | | | | | |
124  # | | | | | | | | | | | | | | | | | | | |
125  # | | | | | | | | | | | | | | | | | | | |
126  # | | | | | | | | | | | | | | | | | | | |
127  # |-----| \---| \---| |-----| |-----|
128
129  # LEVELS OF AGENTS
130  levels:
131    beef_calves:
132      desc: 'level of individuals (young calves, if not males only, assuming no difference between
133        males and females in the infection processes)'
134      default_prototype: default_beef_calf
135    pen:
136      desc: 'level of the pen'
137      contains:
138        - beef_calves
139      aggregation_type: hybrid
140      default_prototype: default_pen
141      aggregate_vars:
142        - name: pen_nb_alive_treated_distinct
143          collect: 'treated'

```

```

44         operator: 'sum'
45     - name: pen_nb_alive_infected_distinct
46       collect: 'infected'
47         operator: 'sum'
48     - name: pen_nb_alive_detected_distinct
49       collect: 'detected'
50         operator: 'sum'
51     - name: pen_nb_doses_alive
52       collect: 'nb_doses_total'
53         operator: 'sum'
54     - name: pen_nb_treated_only_once
55       collect: 'treated_only_once'
56         operator: 'sum'
57
58 # -----
59 # |   \
60 # | |__| |-----|-----|-----|-----|
61 # | ___/ |___/ \ |___/ \ |___/ \ |___/ \ |___/ \
62 # | | | | | | ( ) | ( | | | | | | | | | | | | | |
63 # | | | | | | \ \ / \ \ \ \ \ | | | | | | | | | |
64
65 # LIST OF PROCESSES (IN ORDER)
66 processes:
67     beef_calves:
68         - health_state: infection
69         - clinical_state: clinical_signs
70         - detection_state: detection
71         - treat_state: treatment
72
73 # -----
74 # / ___|
75 # | | | | | | | | | | | | | | | | | | | | | |
76 # | | | | | | | | | | | | | | | | | | | | | |
77 # | | | | | | | | | | | | | | | | | | | | | |
78 # \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
79 #
80 #
81
82 # DESCRIPTION OF HOW TO GROUP INDIVIDUALS
83 grouping:
84     pen:
85         infection: [health_state]
86         treatment: [treat_state]
87         clinical_signs: [clinical_state, health_state]
88         detection: [detection_state, clinical_state]
89
90 # -----
91 # / ___| | | | | | | | | | | | | | | | | | | | |
92 # | ( ___| | | | | | | | | | | | | | | | | | | |
93 # \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
94 # ___) | | | | | | | | | | | | | | | | | | | |
95 # | ___/ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
96
97 # DESCRIPTION OF THE STATE MACHINES INVOLVED IN THE MODEL
98 state_machines:
99 #-----
00 # INFECTION
01 #-----
02 health_state:
03     desc: 'Description of the infectious process'
04     states:
05         - S:
06             name: 'Susceptible'
07             desc: 'Suceptible to infection'
08             fillcolor: 'lightblue'
09         - I:
10             name: 'Infectious'
11             desc: 'Infected and able to transmit pathogens to susceptible individuals. The duration of
12 infection (in the absence of control) is sampled in distribution dur_I.'

```

```

13     fillcolor: 'red'
14     duration: 'dur_I'
15     on_enter:
16         - set_var: infected
17           value: 1
18     on_exit:
19         - set_upper_var: pen_infection_duration
20           value: 'pen_infection_duration + duration_in_health_state'
21         - set_var: nb_consecutive_doses
22           value: 0
23 - pI:
24     name: 'pre-infectious'
25     desc: 'State for initializing animals that will eventually become infectious. This
26 represent an asymptomatic carriage of pathogens, which can lead to the onset of infectiousness just
27 after entering the pen or later. Pre-infectious individuals can however be infected (and become
28 infectious) due to contacts with infectious individuals'
29     fillcolor: 'pink'
30     duration: 'dur_pI'
31 transitions:
32 - from: pI
33   to: I
34   proba: 1
35   desc: 'pre-infectious animals become infectious after a delay'
36 - from: pI
37   to: I
38   escape: yes
39   rate: 'force_of_infection'
40   desc: 'before the end of the carriage period, pre-infectious animals become infectious due to
41 contacts with other infectious animals'
42 - from: S
43   to: I
44   rate: 'force_of_infection'
45   desc: 'classical infection of susceptible individuals due to contacts with other infectious
46 animals'
47 - from: I
48   to: S
49   proba: 1
50   desc: 'infectious animals naturally return to susceptible state after duration dur_I'
51
52
53 #-----
54 # CLINICAL SIGNS
55 #-----
56 clinical_state:
57   desc: 'Succession of clinical states experienced by infected animals.'
58   states:
59     - A:
60       name: 'Asymptomatic'
61       desc: 'Animal with no clinical signs'
62       fillcolor: 'limegreen'
63       on_enter:
64         - set_var: evolve_to_SC
65           value: 0
66           # the evolution from mild to severe clinical signs will
67           # be determined each time the animal enters MC
68       on_exit:
69         - set_upper_var: pen_nb_true_negative
70           value: 'pen_nb_true_negative + is_ND'
71           # if the detected animal leaves the asymptomatic state
72           # without detection, increase the number of true negative
73     - MC:
74       name: 'Mild clinical signs'
75       desc: 'Animal infected, which may have mild clinical signs which are difficult to detect.
76 Some of these animals will eventually develop severe clinical signs with probability
77 p_severe_clinical (assumed independent from infection duration), after a given duration'
78       fillcolor: 'yellow'
79       duration: 'dur_MC'
80       on_enter:
81         - set_var: evolve_to_SC

```



```

82     value: 'OR(random_bool(p_severe_clinical))'
83     # determine whether or not an animal with mild clinical
84     # signs will eventually develop severe clinical signs
85 on_stay:
86     - set_upper_var: pen_nb_MC_missed
87     value: 'pen_nb_MC_missed + is_ND * Eq(time,total_duration)'
88     # if no detection occurred before the end of the simulation, count as false negative
89 for MC
90     on_exit:
91     - set_upper_var: pen_nb_MC_missed
92     value: 'pen_nb_MC_missed + is_ND'
93     # if no detection occurred when leaving MC (either to SC or A), count as false negative
94 for MC
95     - set_upper_var: pen_mild_clinical_duration
96     value: 'pen_mild_clinical_duration + duration_in_clinical_state'
97     # record total duration of MC state
98 - SC:
99     name: 'Severe clinical signs'
100    desc: 'Animals with severe clinical signs (depression, anorexia) highly susceptible to
101 trigger detection. A small proportion of animals with severe clinical signs will eventually die from
102 BRD after dur_before_death'
103    fillcolor: 'red'
104    # assign default duration which is the time before dying from severe clinical signs
105    duration: dur_before_death
106    on_enter:
107    - set_var: evolve_to_death
108    value: 'OR(evolve_to_death, random_bool(p_death))'
109    # "OR" operator to ensure that animals tagged previously
110    # as going to die cannot escape their fate
111    - set_var: _time_to_exit_clinical_state
112    value: 'IfThenElse(evolve_to_death, _time_to_exit_clinical_state, 0)'
113    # if severe clinical signs are not expected to lead to
114    # death, reset duration to 0 to allow animals to go back
115    # to A as soon as they go back to S
116    on_stay:
117    - set_upper_var: pen_nb_SC_missed
118    value: 'pen_nb_SC_missed + is_ND * Eq(time,total_duration)'
119    # if no detection occurred before the end of the simulation, count as false negative
120 for SC
121    on_exit:
122    - set_upper_var: pen_nb_SC_missed
123    value: 'pen_nb_SC_missed + is_ND'
124    # if no detection occurred when leaving SC (either to A or Dead), count as false
125 negative for SC
126    - set_upper_var: pen_severe_clinical_duration
127    value: 'pen_severe_clinical_duration + duration_in_clinical_state'
128    # record total duration of SC state
129 - Dead:
130    name: 'Dead'
131    desc: 'Animals that die from BRD. When animals die, record durations if still I or H or T'
132    fillcolor: 'lightgray'
133    autoremove: yes
134    on_enter:
135    - record_change: pen_nb_deaths
136    - set_var: treated_only_once
137    value: 0
138    - set_upper_var: pen_infection_duration
139    value: 'pen_infection_duration + duration_in_health_state * is_I'
140    - set_upper_var: pen_nb_dead_treated_distinct
141    value: 'pen_nb_dead_treated_distinct + treated'
142    - set_upper_var: pen_nb_dead_infected_distinct
143    value: 'pen_nb_dead_infected_distinct + infected'
144    - set_upper_var: pen_nb_dead_detected_distinct
145    value: 'pen_nb_dead_detected_distinct + detected'
146    - set_upper_var: pen_nb_doses_dead
147    value: 'pen_nb_doses_dead + nb_doses_total'
148 transitions:
149 - from: A
150   to: MC

```

```

51     proba: ' is_I'
52     desc: 'Infected animals develop mild (undetectable) clinical signs, some of them will
53 eventually develop severe clinical signs later'
54     - from: MC
55     to: SC
56     cond: evolve_to_SC
57     proba: ' is_I'
58     desc: 'Animals develop detectable (severe) clinical signs after dur_MC if they were marked to
59 develop severe clinical signs (when entering C) and still infected'
60     - from: MC
61     to: A
62     proba: '1 - is_I'
63     desc: 'Animals return to Asymptomatic after dur_MC if they are not infected anymore'
64     - from: SC
65     to: Dead
66     cond: ' evolve_to_death'
67     proba: 1
68     desc: 'the few animals that have very severe clinical signs will eventually die from BRD (if
69 not successfully treated in the meanwhile)'
70     - from: SC
71     to: A
72     escape: 'NOT(evolve_to_death)'
73     proba: '1 - is_I'
74     desc: 'animals that are not marked as going to die return to Asymptomatic as soon as
75 infection is over even before duration in SC'
76     - from: SC
77     to: A
78     cond: 'NOT(evolve_to_death)'
79     proba: '1 - is_I'
80     desc: 'animals that are not marked as going to die return to Asymptomatic as soon as
81 infection is over'
82
83 #-----
84 # DETECTION
85 #-----
86 detection_state:
87     desc: 'Description of the state of individuals regarding detection'
88     states:
89     - ND:
90         name: 'Undetected'
91         desc: 'Animal considered healthy by the farmer (whatever its real health state).'

```

```

20     value: 'IfThenElse(pen_time_first_detection < 0, time, pen_time_first_detection)'
21     - set_upper_var: pen_do_collective_treatment
22     value: 'MAX(pen_do_collective_treatment, compute_collective_treatment_decision)'
23     - set_upper_var: pen_previous_half_day_incidence
24     value: 'IfThenElse(pen_do_collective_treatment * use_daily_incidence, 0,
25 pen_previous_half_day_incidence)'
26     - set_upper_var: pen_half_day_incidence
27     value: 'IfThenElse(pen_do_collective_treatment * use_daily_incidence, 0,
28 pen_half_day_incidence)'
29     - set_upper_var: pen_cumulate_incidence
30     value: 'IfThenElse(pen_do_collective_treatment * (1 - use_daily_incidence), 0,
31 pen_cumulate_incidence)'
32     # if collective treatment decided, ensure that next incidence will be 0
33     # (to avoid restarting collective treatment over and over) otherwise do not change
34 anything
35     - Ig:
36         name: 'Ignored'
37         desc: 'Animal previously detected but which successive treatments failed, hence no more
38 considered for further treatments'
39     transitions:
40     - from: ND
41       to: D
42       proba: p_det_A
43       desc: 'False positive detection due to the lack of specificity'
44     - from: ND
45       to: D
46       proba: p_det_MC
47       desc: 'Detection of an animal with mild clinical signs'
48     - from: ND
49       to: D
50       proba: p_det_SC
51       desc: 'Detection of an animal with severe clinical signs'
52
53
54 #-----
55 # TREATMENTS
56 #-----
57 treat_state:
58     desc: 'Description of treatment protocol'
59     states:
60     - NT:
61         name: 'Non Treated'
62         desc: 'Non treated animal'
63         fillcolor: 'lightgray'
64     - T:
65         name: Treated
66         desc: 'Treated animal'
67         fillcolor: 'purple'
68         duration: dur_T
69         on_enter:
70         - set_var: treated
71           value: 1
72         - set_var: nb_consecutive_doses
73           value: '1 + nb_consecutive_doses'
74         - set_var: nb_doses_total
75           value: '1 + nb_doses_total'
76         - set_var: treated_only_once
77           value: 'Eq(nb_doses_total, use_antibioprevention + 1)'
78         - set_var: treatment_successful
79           value: 'random_bool(p_recovery)'
80         on_exit:
81         - set_upper_var: pen_do_collective_treatment
82           value: 0
83     transitions:
84     - from: NT
85       to: T
86       cond: 'AND(NOT(is_Ig), pen_do_collective_treatment)'
87       proba: 1
88       desc: 'When a collective treatment is implemented, treat all animals not currently treated

```

```

89 unless they already received the maximum number of doses'
90   - from: NT
91     to: T
92     cond: 'AND(NOT(pen_do_collective_treatment), is_D, StrictLessThan(nb_consecutive_doses,
93 nb_doses_max))'
94     proba: p_treated
95     desc: 'Treat individual animals as the result of individual detection. Avoid to re-treat
96 animals which are still detectable but already got the max number of treatments (such animals stay in
97 NT and will be re-detectable after they return to S at the natural end of disease) or animals that
98 have been already treated even some time ago but will obviously die from BRD'
99   - from: T
100     to: NT
101     cond: 'is_A'
102     proba: 1
103     on_cross:
104       - become: healthy      # to ensure that pI -> S
105       - set_var: nb_consecutive_doses
106         value: 0
107       - become: undetected # temporarily no more considered for treatments
108     desc: 'stop treatment after duration dur_T if the animal has no more clinical signs (recovery
109 occurred before end of treatment)'
110   - from: T
111     to: NT
112     cond: 'AND(OR(is_SC, is_MC), treatment_successful)'
113     proba: 1
114     on_cross:
115       - become: healthy      # I -> S (which induces H -> N)
116       - set_var: nb_consecutive_doses
117         value: 0
118       - become: undetected
119     desc: 'recovery occurs after treatment of duration dur_T assuming the treatment was
120 successful'
121   - from: T
122     to: T
123     cond: 'AND(OR(is_SC, is_MC), NOT(treatment_successful), StrictLessThan(nb_consecutive_doses,
124 nb_doses_max))'
125     proba: 1
126     desc: 'restart treatment after duration dur_T assuming no recovery occurred despite
127 treatment, and number of doses below the authorized threshold'
128   - from: T
129     to: NT
130     cond: 'AND(OR(is_SC, is_MC), NOT(treatment_successful), Eq(nb_consecutive_doses,
131 nb_doses_max))'
132     proba: 1
133     on_cross:
134       - become: ignored
135     desc: 'if no recovery occurred after the maximum number of treatments: abandon (do not reset
136 the number of doses received to avoid restarting treatment immediately - this will be done when
137 leaving I state)'
138
139 # -----
140 # |  _  \               | |
141 # | |__ ) | _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | | _ _ _ _ _ _
142 # |  _ _ / ' _ / ' _ / ' _ / ' _ / ' _ / ' _ / ' _ / ' _ / ' _ / ' _ / ' _ /
143 # | | | ( _ | | | ( _ | | | | | | | _ / | | _ / | \ _ \
144 # | _ | \ _ , - | _ | \ _ , - | _ | | _ | \ _ \ _ \ _ \ _ | | _ _ _ /
145
146 parameters:
147 # -----
148 # CLINICAL SIGNS PARAMETERS
149 # -----
150 dur_MC:
151   desc: 'Distribution of the durations of mild clinical signs caused by infection, before the
152 apparition of severe clinical signs likely to trigger treatment (hours)'
153   value: 'dur_MC_fact * random_beta(1.08, 1.69)*111 + 12'
154   source: 'Timsit et al 2011, fig. 4. Min-Max = 12-123; Approx. quartiles: 42, 51, 75. Estimated
155 beta distribution from Q2 and Q3: alpha=1.08, beta=1.69'
156   mean_dur_MC:
157     desc: 'average value of the dur_MC distribution (hours) - beware: to update according to dur_MC'

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58     value: 55
59 dur_MC_expected:
60     desc: 'expected value of dur_MC, which is mean_dur_MC for individuals that develop severe
61 clinical signs, and mean_dur_I for the others'
62     value: 'p_severe_clinical * dur_MC_fact * mean_dur_MC + (1 - p_severe_clinical) * mean_dur_I'
63 mean_dur_SC:
64     desc: 'average value of the duration of severe clinical signs for animals that will not die from
65 BRD (hours)'
66     value: 'mean_dur_I - mean_dur_MC'
67 dur_SC_expected:
68     desc: 'expected value of dur_MC, which is mean_dur_SC for individuals that will not die from BRD,
69 and dur_before_death for the others'
70     value: '(1 - p_death) * mean_dur_SC + p_death * dur_before_death'
71 dur_A_expected:
72     desc: 'expected value of the duration of asymptomatic state, which is longer than the simulation
73 time (range of values: about 150 days on average in [White and Rentner 2009], but 10 months in [Assié
74 et al 2009])'
75     value: '200 * 24'
76 p_severe_clinical:
77     desc: 'probability that an animal with mild clinical signs eventually develops severe clinical
78 signs'
79     value: 0.5
80     source: 'expert opinion'
81 p_death:
82     desc: 'probability that an animal with severe clinical signs eventually dies from BRD'
83     value: 0.05
84     source: 'expert opinion'
85 dur_before_death:
86     desc: 'distribution of the durations of severe clinical signs before death (only for animals that
87 will die from BRD)'
88     value: '10*24'
89     source: 'expert opinion'
90
91 # -----
92 # EPIDEMIOLOGICAL PARAMETERS
93 # -----
94 dur_I:
95     desc: 'distribution of durations in the infectious state'
96     # value: 'poisson(mean_dur_I)'
97     value: 'random_gamma(dur_I_shape, mean_dur_I/dur_I_shape)'
98     source: 'trying gamma distribution which is equivalent to N(=10) consecutive geometric
99 distribution which slowly converges towards a constant distribution - quartiles 92.7, 116, 143 (h)'
00 dur_I_shape:
01     desc: 'shape of the gamma distribution for I durations - high values: close to constant, low
02 values: long tail'
03     value: 10
04 mean_dur_I:
05     desc: 'average duration in infectious states (in hours)'
06     value: '5*24'
07     source: 'expert opinion for an average pathogen'
08 dur_pI:
09     desc: 'Distribution of the durations of asymptomatic carriage of BRD pathogens, shifted by the
10 use of long-acting antimicrobials when antibioprevention is performed'
11     value: 'default_dur_pI + use_antibioprevention * shifted_dur_pI'
12 mean_dur_pI:
13     desc: 'average duration in carriage state (in hours)'
14     value: '3*24'
15     source: 'previously calibrated for scenarios: FR/FRref: 2*24 ; USLR/USHR/USHRM: 6*24 - set to
16 arbitrary value 3*24 in generic study'
17 dur_pI_shape:
18     desc: 'shape of the gamma distribution for pI durations - high values: close to constant, low
19 values: long tail'
20     value: 5
21 default_dur_pI:
22     desc: 'Default distribution of the durations of asymptomatic carriage of BRD pathogens'
23     value: 'random_gamma(dur_pI_shape, mean_dur_pI/dur_pI_shape)'
24     source: 'testing alternative distributions : gamma law to have a few high values'
25 shifted_dur_pI:
26     desc: 'Shift in the distribution of the durations of asymptomatic carriage of BRD pathogens due

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27 to the use of long-acting antimicrobials'
28   value: 'random_gamma(shift_dur_pI_shape, mean_shift_dur_pI/shift_dur_pI_shape)'
29 mean_shift_dur_pI:
30   desc: 'average duration of the delay induced by long-acting antimicrobials'
31   value: '24 * 15'
32   source: 'calibration'
33 shift_dur_pI_shape:
34   desc: 'shape of the gamma distribution for pI shift'
35   value: 20
36 pathogen_transmission_rate:
37   desc: 'average value of individual transmission rate (per hour)'
38   value: '0.008'
39   source: 'calibrated for FR/US system'
40 force_of_infection:
41   desc: 'The force of infection experienced by each susceptible animal depends on the sum of
42 individual infectiousness and exposure to general microbism of the farm'
43   value: 'pathogen_transmission_rate * total_I / total_pen + external_risk'
44   source: 'assuming frequency-dependent force of infection'
45 external_risk:
46   desc: 'contribution of the microbism of the herd (outside of the pen) to the force of infection.
47 Set to 0 to represent isolated pens'
48   value: 0
49 pen_nb_infected_distinct:
50   desc: 'total number of distinct animals infected at least once in the pen over time'
51   value: 'pen_nb_alive_infected_distinct + pen_nb_dead_infected_distinct'
52 pen_nb_detected_distinct:
53   desc: 'total number of distinct animals detected at least once in the pen over time'
54   value: 'pen_nb_alive_detected_distinct + pen_nb_dead_detected_distinct'
55
56 #-----
57 # DETECTION
58 #-----
59 Se_MC:
60   desc: 'sensitivity of BRD detection based on mild clinical signs'
61   value: 0.3
62   source: 'Timsit et al 2016 - TODO discuss'
63 Se_SC:
64   desc: 'sensitivity of BRD detection based on severe clinical signs'
65   value: 0.6
66   source: 'White & Rentner 2009 - TODO discuss'
67 Sp:
68   desc: 'specificity of BRD detection assuming no difference between MC/SC'
69   value: 0.9
70   source: 'Timsit et al 2016 - TODO discuss'
71
72 p_det_MC:
73   desc: 'probability to detect a BRD case with mild clinical signs, each step (calculated from the
74 sensitivity, the average duration in MC state, and the duration of one time step)'
75   value: 'is_MC * (1 - (1 - Se_MC)**(1 / dur_MC_expected))'
76 p_det_SC:
77   desc: 'probability to detect a BRD case with severe clinical signs, each step (calculated from
78 the sensitivity, the average duration in SC state for animals not going to die from BRD, i.e.
79 actually the average duration of infection minus the average duration with mild clinical signs)'
80   value: 'is_SC * (1 - (1 - Se_SC)**(1 / dur_SC_expected))'
81 p_det_A:
82   desc: 'probability to detect a false positive BRD case though asymptomatic, each step (calculated
83 from the specificity and the duration over which this specificity was calculated'
84   value: 'is_A * (1 - Sp ** (1 / dur_A_expected))'
85 pen_daily_incidence:
86   desc: 'daily incidence at pen scale calculated from detections'
87   value: 'pen_half_day_incidence + pen_previous_half_day_incidence'
88
89 #-----
90 # TREATMENT
91 #-----
92 dur_T:
93   desc: 'Constant duration before assessing the efficacy of the treatment (hours)'
94   value: 48
95   source: 'average treatment protocol (discussed with professors in veterinary medicine)'

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96 p_treated:
97   desc: 'probability that a detected animal is treated'
98   value: 1
99   source: 'expert opinion'
00 p_recovery:
01   desc: 'probability that a treated animal recovers (for 1 dose)'
02   value: '0.8'
03   source: 'treatment protocol discussed with professors in veterinary medicine'
04 nb_doses_max:
05   desc: 'maximal number of consecutive doses for the same animal'
06   value: 3
07   source: 'treatment protocol discussed with professors in veterinary medicine'
08 use_antibioprevention:
09   desc: 'Boolean to indicate whether antibioprevention is used or not. With antibioprevention, all
10 animals in the pen start with one dose (but initial_prevalence must be adjusted subsequently to
11 account for treatment, e.g. * (1 - p_recovery))'
12   value: 0
13 pen_nb_treated_distinct:
14   desc: 'total number of distinct animals treated at least once in the pen over time'
15   value: 'pen_nb_alive_treated_distinct + pen_nb_dead_treated_distinct'
16 pen_nb_doses:
17   desc: 'total number of doses given at pen scale over time'
18   value: 'pen_nb_doses_alive + pen_nb_doses_dead'
19 use_metaphylaxis:
20   desc: 'Boolean to indicate whether metaphylaxis i.e. collective treatment during fattening is
21 used. With metaphylaxis, when the incidence (daily or cumulate depending on pen size) reaches a given
22 threshold, all animals get treated immediately'
23   value: 0
24 metaphylaxis_threshold:
25   desc: 'threshold to trigger collective treatment'
26   value: 0.15
27 use_daily_incidence:
28   desc: 'Boolean to indicate the method for deciding to implement a collective treatment. 1:
29 implement when daily incidence > metaphylaxis_threshold ; 0: implement when cumulate incidence >
30 metaphylaxis_threshold'
31   value: 0
32 compute_collective_treatment_decision:
33   desc: 'decide whether a collective treatment must be done or not - which can be triggered either
34 by a daily incidence threshold, or by a cumulate incidence threshold'
35   value: 'use_metaphylaxis *
36           (IfThenElse(use_daily_incidence,
37                       pen_daily_incidence,
38                       pen_cumulate_incidence) >= metaphylaxis_threshold * total_pen)'
39 #-----
40 # INITIAL CONDITIONS
41 #-----
42 pen_size:
43   desc: 'initial size of the pen'
44   value: 100
45   source: 'French system: Assie, 10 animals - US system: White & Amrine, 100 animals'
46 initial_prevalence:
47   desc: 'initial proportion of (pre-)infected animals'
48   value: 0.1
49   source: 'calibrated values for scenarios: FR/FRref 0.1 ; USLR: 0.01; USHR: 0.14; USHRM: 0.06'
50
51 # -----
52 # SENSITIVITY ANALYSIS
53 # -----
54 dur_MC_fact:
55   desc: 'multiplicative factor used to modulate dur_MC (esp. in sensitivity analysis)'
56   value: 1
57
58 #
59 # / ----- | | |
60 # | (----- | |----- | |-----
61 # \___ \ | ___/ \ | ___/ \ \ / / / \ | '___/ ___|
62 # ___) | || ( | | | ___ \ \ / / ( | | | \___ \
63 # |-----/ \___ \, -| \___ \___| \_/ \___, -| | | ___/
64

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65 # VARIABLES OF THE AGENTS
66 statevars:
67 #-----
68 # AGGREGATE VARIABLES AT PEN SCALE
69 #-----
70 pen_time_first_detection:
71   desc: 'date of first detection in the pen'
72 pen_infection_duration:
73   desc: 'cumulate infection duration at pen scale'
74 pen_mild_clinical_duration:
75   desc: 'cumulate duration of the presence of animals with mild clinical signs in the pen'
76 pen_severe_clinical_duration:
77   desc: 'cumulate duration of the presence of animals with severe clinical signs in the pen'
78 pen_nb_alive_treated_distinct:
79   desc: 'total number of distinct animals treated in the pen over time'
80 pen_nb_dead_treated_distinct:
81   desc: 'total number of distinct animals that were treated in the pen at least once but died'
82 pen_nb_alive_infected_distinct:
83   desc: 'total number of distinct animals infected at least once in the pen over time'
84 pen_nb_dead_infected_distinct:
85   desc: 'total number of distinct animals infected at least once in the pen over time but died'
86 pen_nb_alive_detected_distinct:
87   desc: 'total number of distinct animals detected at least once in the pen over time'
88 pen_nb_dead_detected_distinct:
89   desc: 'total number of distinct animals detected at least once in the pen over time but died'
90 pen_nb_doses_alive:
91   desc: 'total number of doses given at pen scale over time'
92 pen_nb_doses_dead:
93   desc: 'total number of doses given to animals that died'
94 pen_nb_deaths:
95   desc: 'total number of dead animals over time'
96 pen_nb_MC_detections:
97   desc: 'total number of detections based on mild clinical signs, over time'
98 pen_nb_MC_missed:
99   desc: 'total number of undetected animals though having mild clinical signs, over time'
00 pen_nb_SC_detections:
01   desc: 'total number of detections based on severe clinical signs, over time'
02 pen_nb_SC_missed:
03   desc: 'total number of undetected animals though having severe clinical signs, over time'
04 pen_nb_false_positive:
05   desc: 'total number of false positive detections (asymptomatic animals considered diseased), over
06 time'
07 pen_nb_true_negative:
08   desc: 'total number of true negative animals (asymptomatic animals never detected while
09 asymptomatic), over time'
10 pen_cumulate_incidence:
11   desc: 'total number of detected animals (true or false positive), over time'
12 pen_prev_cumulate_incidence:
13   desc: 'total number of detected animals (true or false positive) until previous time step, over
14 time'
15 pen_half_day_incidence:
16   desc: 'total number of detected animals (true or false positive) during the current time step'
17 pen_previous_half_day_incidence:
18   desc: 'total number of detected animals (true or false positive) during the previous time step'
19 pen_do_collective_treatment:
20   desc: 'boolean to indicate whether a collective treatment is currently ongoing or not'
21 #-----
22 # INFECTION (Animal Level)
23 #-----
24 _time_to_exit_health_state:
25   desc: 'time step after which agents are allowed to leave current health state (EMULSION built-
26 in)'
27 # infection_duration:
28 #   desc: 'total duration of infection of an animal over time'
29 infected:
30   desc: 'boolean, 1 if animal infected at least once, 0 otherwise'
31 #-----
32 # CLINICAL SIGNS
33 #-----

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34   evolve_to_death:
35     desc: 'indicate whether or not an animal with severe clinical signs will eventually die from BRD'
36   evolve_to_SC:
37     desc: 'indicate whether or not an animal with mild clinical signs will eventually develop severe
38 clinical signs if still infected after dur_MC'
39   _time_to_exit_clinical_state:
40     desc: 'time step after which agents are allowed to leave current clinical state (EMULSION built-
41 in)'
42 #-----
43 # DETECTION
44 #-----
45 detected:
46     desc: 'boolean, 1 if animal detected at least once, 0 otherwise'
47 #-----
48 # TREATMENT
49 #-----
50 treated:
51     desc: 'boolean value, 1 if animal treated at least once, 0 otherwise'
52 nb_consecutive_doses:
53     desc: 'number of consecutive doses given to the animal during the same episode'
54 nb_doses_total:
55     desc: 'total number of doses given to the considered animal'
56 treated_only_once:
57     desc: 'boolean, 1 if the animals was treated exactly once (not accounting for possible
58 antibioprevention) and still alive, 0 if not treated or treated multiple times or dead'
59 treatment_successful:
60     desc: 'boolean value, 1 if the treatment will succeed, 0 otherwise'
61
62 #
63 # |-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
64 # | |-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
65 # | |-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
66 # | |-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
67 # | |-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
68 # | |-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
69 # | |-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
70 #
71 # SPECIFICATION OF INITIAL VARIABLE VALUES FOR SPECIFIC CASES
72 prototypes:
73   pen:
74     - default_pen:
75       desc: 'prototype to initialize pen variables'
76       pen_infection_duration: 0
77       pen_severe_clinical_duration: 0
78       pen_mild_clinical_duration: 0
79       pen_nb_dead_treated_distinct: 0
80       pen_nb_dead_infected_distinct: 0
81       pen_nb_dead_detected_distinct: 0
82       pen_nb_doses_dead: 0
83       pen_cumulate_incidence: 0
84       pen_prev_cumulate_incidence: 0
85       pen_previous_half_day_incidence: 0
86       pen_half_day_incidence: 0
87       pen_nb_MC_detections: 0
88       pen_nb_SC_detections: 0
89       pen_nb_MC_missed: 0
90       pen_nb_SC_missed: 0
91       pen_nb_false_positive: 0
92       pen_nb_true_negative: 0
93       pen_nb_deaths: 0
94       pen_time_first_detection: -1
95       pen_do_collective_treatment: 0
96   beef_calves:
97     #-----
98     # INITIALIZATION PROTOTYPES
99     #-----
100    - default_beef_calf:
101      desc: 'default prototype applied to all animals before any further modification'
102      treat_state: NT

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03     clinical_state: A
04     detection_state: ND
05     nb_consecutive_doses: 0
06     treated: 0
07     treated_only_once: 0
08     infected: 0
09     detected: 0
10     evolve_to_death: 0
11     evolve_to_SC: 0
12     nb_doses_total: 'use_antibioprevention'
13     health_state: S
14 - initial_healthy_beef:
15     desc: 'prototype for healthy and susceptible animals'
16     health_state: S
17 - initial_carrier_beef:
18     desc: 'prototype for asymptomatic carriers'
19     health_state: pI
20 #-----
21 # MODIFICATION PROTOTYPES
22 #-----
23 - healthy:
24     desc: 'prototype for making individual return to S'
25     health_state: S
26     clinical_state: A
27     nb_consecutive_doses: 0
28 - undetected:
29     desc: 'restore the Undetected status'
30     detection_state: ND
31 - ignored:
32     desc: 'animal no more considered for further treatments'
33     detection_state: Ig
34 - detected:
35     desc: 'mark an animal as detected'
36     detection_state: D
37
38
39 #
40 # |-----|      ( ) | ( )      | |
41 # | | | | | | | | | | | | | | | | | |
42 # | | | | | | | | | | | | | | | | | |
43 # | | | | | | | | | | | | | | | | | |
44 # |-----| | | | | | | | | | | | | | |
45
46 #
47 # |-----|      ( ) | ( )
48 # |-----|-----|-----|-----|-----|-----|
49 # / _ / _ \ | ' _ \ / _ ' | | _ | | / _ \ | ' _ \ |
50 # | ( | ( ) | | | | ( | | | | | ( ) | | | \ \ \
51 # \ \ \ \ / | | | \ \ \ , | | | \ \ \ / | | | | /
52
53 initial_conditions:
54   pen:
55     - prototype: initial_healthy_beef
56       amount: 'round(pen_size * (1 - initial_prevalence))'
57     - prototype: initial_carrier_beef
58       amount: 'round(pen_size * initial_prevalence)'
59
60 #
61 # / _ \      | |      | |
62 # | | | | | | | | | | | | | | | | | |
63 # | | | | | | | | | | | | | | | | | |
64 # | | | | | | | | | | | | | | | | | |
65 # \ \ \ \ / \ \ \ , \ \ \ / \ \ \ / | | | /
66 #
67 # | |
68 # | |
69 # TYPE AND PERIODICITY OF OUTPUTS
70 outputs:
71   type: csv

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72 pen:
73   period: 1
74   extra_vars:
75     - total_pen
76     - pen_time_first_detection
77     - pen_nb_deaths
78     - pen_cumulate_incidence
79     - pen_prev_cumulate_incidence
80     - pen_half_day_incidence
81     - pen_previous_half_day_incidence
82     - pen_daily_incidence
83     - pen_nb_dead_treated_distinct
84     - pen_nb_treated_distinct
85     - pen_nb_treated_only_once
86     - pen_nb_infected_distinct
87     - pen_nb_detected_distinct
88     - pen_infection_duration
89     - pen_severe_clinical_duration
90     - pen_mild_clinical_duration
91     - pen_nb_doses
92     - pen_nb_MC_detections
93     - pen_nb_SC_detections
94     - pen_nb_MC_missed
95     - pen_nb_SC_missed
96     - pen_nb_false_positive
97     - pen_nb_true_negative
98     - pen_do_collective_treatment
99   ...
```