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RIVM

To
Ministry of Agriculture, Mrs A. Burger,
Ministry of Public Health, Mr P.H. Huyts

Subject
Advice for culling policy and killing methods of goats infected with Q-fever.

Date
15 December 2009

Dear Mrs Burger, dear Mr Huyts,

On Friday afternoon I received your request for advice regarding the various options of killing methods for pregnant goats and sheep at infected farms. During the meeting on 14 December four other questions were laid down before the experts.
Two of those questions were elaborately answered in the letter from the CVI (Mr Bianchi) to the CVO (Ms Bruschke). The other experts whom we consulted support the advice of the CVI. We have attached the CVI report.
The other questions I have put before veterinary experts and an 'arbo' (= employment) expert.
The experts emphasise that the advices regarding the killing methods are focused on limiting the dispersion of C. burnetii from infected animals by minimising the number of handling the animals and limiting the locations where animals are taken to. It is important to keep the risk for employees as low as possible.
I will give you the substantiations and answers point by point.

Question 1.
Concerning non-vaccinated farms with positive bulk milk test.
What effect can we expect from vaccinating pregnant animals?

Considerations
There are no reliable data available. Part of these animals will already be infected, even when the test is not (yet) positive. In such cases vaccination does not reduce the spreading of Coxiella burnetii. A number of these animals will not yet be infected. There is doubt about the effect of vaccination of pregnant animals, but also a lack of useful data regarding goats.

Advice
The experts believe that vaccination of pregnant animals does not result in the desired effect on excretion of C. burnetii. See further comment and substantiation given by the CVI.

Question 2.
Concerning vaccinated farms with positive bulk milk test.
Would it be possible to make a distinction between high and low contamination farms?

Considerations
As indicated in the advice of 10 December a distinction between high and low contamination is arbitrary, and as indicated in the CVI advice as such legally liable. On further consideration by the veterinary experts it turned out that based on the laboratory results of bulk milk testing it was impossible to make a reliable distinction between high and low contamination levels. The test, available at present, as a one-off test for indicating infection with individual goats has insufficient predicting value whether the animal will excrete the bacteria or not. There is no indicating level that provides sufficient security.

Advice
The veterinary experts consider it to be impossible to make an effective distinction between high and low contamination farms. One-off individual testing for infection offers insufficient indications to exclude bacteria excretion in the near future. See further comment and substantiation given by the CVI.

Question 3.
Concerning vaccinated farms with positive bulk milk test.
Does it have a useful effect to test not-pregnant animals and distinguish between infected and not-infected animals (and then cull only the infected animals)?

Considerations
Not-pregnant infected animals excrete the Q-fever bacteria in low quantities. The experts estimate the risk from these animals for public health to be low. Furthermore they note that the bacteria will already be spread all around the farm, which will probably lead to new human cases even with maximum intervention in 2010.

Advice
Culling not-pregnant infected animals will have no added value re public health. A selective culling policy of positive animals could help the farms in question to reach the negative status sooner.

Question 4.
Concerning non-vaccinated farms with negative bulk milk test.
Is the current policy sufficient to limit the public health problems in the coming season?

Considerations
In the coming season several farms will become positive which have as yet negative results in the bulk milk tests. Based on knowledge from past experience the number of positive farms could grow to several tens extra in the coming kidding season. Especially these farms could cause public health problems in the direct surroundings, because the (new) infection at not-vaccinated farms could lead to an ‘abortion-storm’.

Advice
As already indicated in the 4 December advice, it is of upmost importance to find these farms swiftly. The experts therefore advise to speed up the testing frequency. Logistically it should be possible to submit all (negative) farms to bulk milk testing every two weeks. Bulk milk testing has its limitations, even with a more than every two months frequency. Abortions could already be going on at a farm before bulk milk tests positive. Therefore the criteria for notification (5% abortions or 3 animals at small farms) should be maintained in order to take measures in time. With early notification to the Public Health Service (GGD) people in the neighbourhood (of these farms) can be informed and guided.

The following questions (already put on 11 December 2009 by Ms. Burger) concern methods of killing.

Question 5.
Killing at the slaughterhouse, in order to use the products for human and animal consumption.

Considerations
For this option pregnant animals will have to be transported to the slaughterhouse. Transporting as well as processing the animals gives extra risk of spreading C. burnetii. Transport will cause stress for the pregnant animals thus increasing the risk of abortion (during transport) en therefore of spreading the Q-fever bacteria. Furthermore, transport is not allowed in the last two weeks of pregnancy anyway (animal welfare).
Slaughtering infected pregnant animals, in order to use the products for human consumption would not be permitted within EU rules, according to a consulted farm vet (1).
If you would decide to use these products for animal consumption anyway, the uterus and foetus should be carefully cut out and removed separately for destruction. Making any mistakes in this procedure will cause an unacceptably high risk of releasing high quantities of C. burnetii for the slaughterhouse workers and possibly neighbouring people as well. In various literature one finds sufficient clues that slaughterhouse workers can contract Q-fever. (2, 3 and 4)
Making any mistakes in the slaughtering procedure, the meat intended for consumption could become contaminated with C. burnetii. It is therefore inadvisable to use the meat of such animals for consumption, because during the processing before heating a risk of exposure cannot be eliminated.
Lastly various literature describes that people in the neighbourhood of slaughterhouses can contract Q-fever due to airborne dust of contaminated slaughter disposal of infected animals. (5)

Advice
The experts vigourously dissuade this option to reduce the risks for transporters, slaughterhouse workers and possible neighbouring people. While transporting live pregnant animals the risk of an abortion is higher and therefore the risk of spreading the disease likely.
Processing the carcasses causes unacceptable health risks to workers, neighbouring people and consumers of the products.

Question 6.
Killing at the slaughterhouse or at the destruction unit, with shooting mask and pentobarbital, while disposing of the carcasses to Rendac for destruction (incineration).

Considerations
This option as well, has an extra transport moment with more people involved and more risk of exposure for these people. See further arguments and comments in question 5.
The risk of spreading the bacteria with this option is lower than with option 5 because the animals are not slaughtered and therefore the risk of slaughter mistakes is limited. However measures must still be taken to protect the workers and to disinfect the lorry and the slaughterhouse. The killing methods will be discussed in question 7.

Advice

The experts dissuade this option to reduce the unnecessary risks for transporters, slaughterhouse workers and possible neighbours. Transporting live pregnant animals causes unacceptable risk, because one cannot rule out abortions* during transport.

Question 7.
Killing animals at farm with shooting mask and euthesate, while disposing of the carcasses to Rendac for destruction (incineration).

Considerations
The veterinary experts have indicated that an injection with an overdose pentobarbital (euthesate, euthasol, euthanimal) is regarded to be the most humane killing method for pregnant animals (as well as for the unborn foetus). (6)
The animals will quietly fall asleep and die without pain. The unborn foetus will also get the stuff in through the placenta and will also die painless. Using a shooting mask the animal temporarily looses consciousness and will then have to be killed by 'bleeding' or by still administering an overdose of pentobarbital. Using the shooting mask has no surplus value.
Killing the animals at farm gives the animals no extra stress and therefore a lower risk of spontaneous abortion. Although killing the animals at farm is an emotionally heavy burden for the farmer and the vet, which should not be disregarded or underestimated, this does not compare to the risk of spreading of C. burnetti during transport of live pregnant animals.

Advice
The veterinary experts advise to kill the pregnant animals at farm with an overdose pentobarbital, conform article 4 of the *Ministerial regulation for killing animals*. The cadavers must then be covered and directly disposed of to Rendac for destruction (incineration).

* **The experts of the Animal Health Service (GD) however believe, contrary to the other experts, that the risk of spontaneous abortion is only relevant for highly pregnant animals. (see advice 6)**

Additional advice:
- Employees who come into contact with infected animals or their products should be informed and should take proper protection measures (this will be worked out by arbo-experts). Employees who are in the Q-fever risk-groups (patients with heart valve problems and persons with lower resistance due to f.i. transplantation, cancer, chronic kidney disease or pregnancy) should be excluded from working with infected animals or their products.
- Those who ever had a Q-fever infection have a strongly reduced chance of medical problems after new exposure. It is therefore recommended to preferably use those employees, of whom the company physician after screening has established a previous Q-fever infection, for working with infected animals and their products.
- Lastly the experts advise you to offer psychological care to employees involved in culling and to the farmers' families.

Sincerely,

Prof. Dr. R.A. Coutinho
Director of the Centre for Infectious Diseases Control

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RIVM

To
Ministry of Agriculture, Mrs A. Burger,
Ministry of Public Health, Mr P.H. Huyts

Subject
Additional advice Q-fever control measures of the experts' meeting of 10 December 2009

Date
10 December 2009

Dear Mrs. Burger, dear Mr. Huyts,

This advice is an addition to the advice letter of 4 December. The current advice was achieved during a telephone meeting on 10 December with a limited number of experts. In the letter of 4 December the effects of the various veterinary strategies for the human Q-fever epidemic were assessed by experts.
In this additional advice we deal with the specific questions that the ministries of Agriculture and Public Health have put before us.
The experts emphasise that the advices aim to reduce the number of abortions with infected animals so that excretion of *C. burnetii* will be significantly reduced in 2010. At this moment we will not go into the desired policy for 2010.
The additional questions focus on the possible effect of individual testing of animals. This concerns:

1) Executing strategies 5 en 6.
The attached schedule of decision making (see below), created by the ministries, shows what the decision points are for executing strategies 5 and 6 and to what situations the additional questions relate.

2) Hereunder we give the asked questions and the experts' answers categorised by the blocks in the schedule. The red blocks indicate that consensus is clear.

Ad A: Not-infected pregnant animals at timely vaccinated positive farms
How high is the risk for public health of pregnant but presently not infected goats to become infected soon after all because they stay in an infected barn or to shed the bacteria after all?

Answer:
A small number of animals will be tested negative *wrongly*. Besides there is a risk of *new* infections for a small percentage of the animals. Because of the previous vaccination all these animals will probably not abort. Abortion does cause excretion of billions of bacteria. Full term births by infected animals however also disperse millions of Q-fever bacteria. Because of this the experts believe it is justified to individually test the animals at these farms and only remove the positive ones. In case of a highly contaminated farm the risk of new infections with so far negative tested animals is higher.
Therefore we give you in consideration to also remove the not-infected pregnant animals at highly infected farms. The distinction line between high and low at contaminated farms is arbitrary. This line could be specified soon by veterinary experts. A suggestion at this moment could be at more or less than 50% infections of pregnant animals.

Ad B: Infected not-pregnant animals at timely vaccinated positive farms
This concerns strategy 5b in the advice. On what grounds should an infected not-pregnant animal be spared?

Answer:
This concerns not-pregnant animals (meaning they are or were not pregnant in the 2009/10 breeding season) which are considered to have limited C. *burnetii excretion.* As the advices aim to reduce large amounts of *C. burnetii* excretion due abortion and kidding of infected animals, removing these animals will have no surplus value for 2010.

Ad C: Not-infected not-pregnant animals at timely vaccinated positive farms
This concerns strategy 6. How high is the risk of vaccinated animals becoming infected in due time?

Answer:
There is a limited risk of new infections for these animals. However, with a breeding ban for contaminated farms these animals will not become pregnant and excretion of *C. burnetii* will be limited. There will be no significant surplus value in 2010 to remove these animals.

Ad D and ad E: Infected and not-infected not-pregnant animals at non-vaccinated positive farms
Strategy 6 as well, whereby it is indicated in the 4 December letter of advice that there will be little surplus value with regard to strategy 5a.

Your questions:
1) How is this little surplus value substantiated?

Answer:
See answers at B and C

2) What are the arguments to proceed with this on account of public health?

Answer:
There are no arguments for 2010.

3) What is the surplus value of this strategy for the specific infected farm (f.i. rapid sanitation)?

Answer:
There is no surplus value for 2010.

4) Is there surplus value for 2010 or just for the longer term, knowing that compulsory vaccination will be started at these farms?

Answer:
The surplus value can be considered a strategy to lead these farms to a negative status rapidly.

5) Could the surplus value be quantified and could the possible surplus value be compared to the risk for public health coming from other animal species (like meat sheep)?

Answer:
The surplus value cannot be quantified.

Additional advice:
- The experts advise you to increase the bulk milk testing frequency during the kidding season (until July 2010) to once per two weeks, in order to detect sooner the negative farms becoming positive after all.
- When scanning the animals for pregnancy this test should be repeated for better safety when the first result was negative and scanning was performed early in the possible pregnancy period.
- The execution of the measures taken should start as soon as possible with those flocks of which kidding is expected to start in December and beginning of January.

Sincerely,

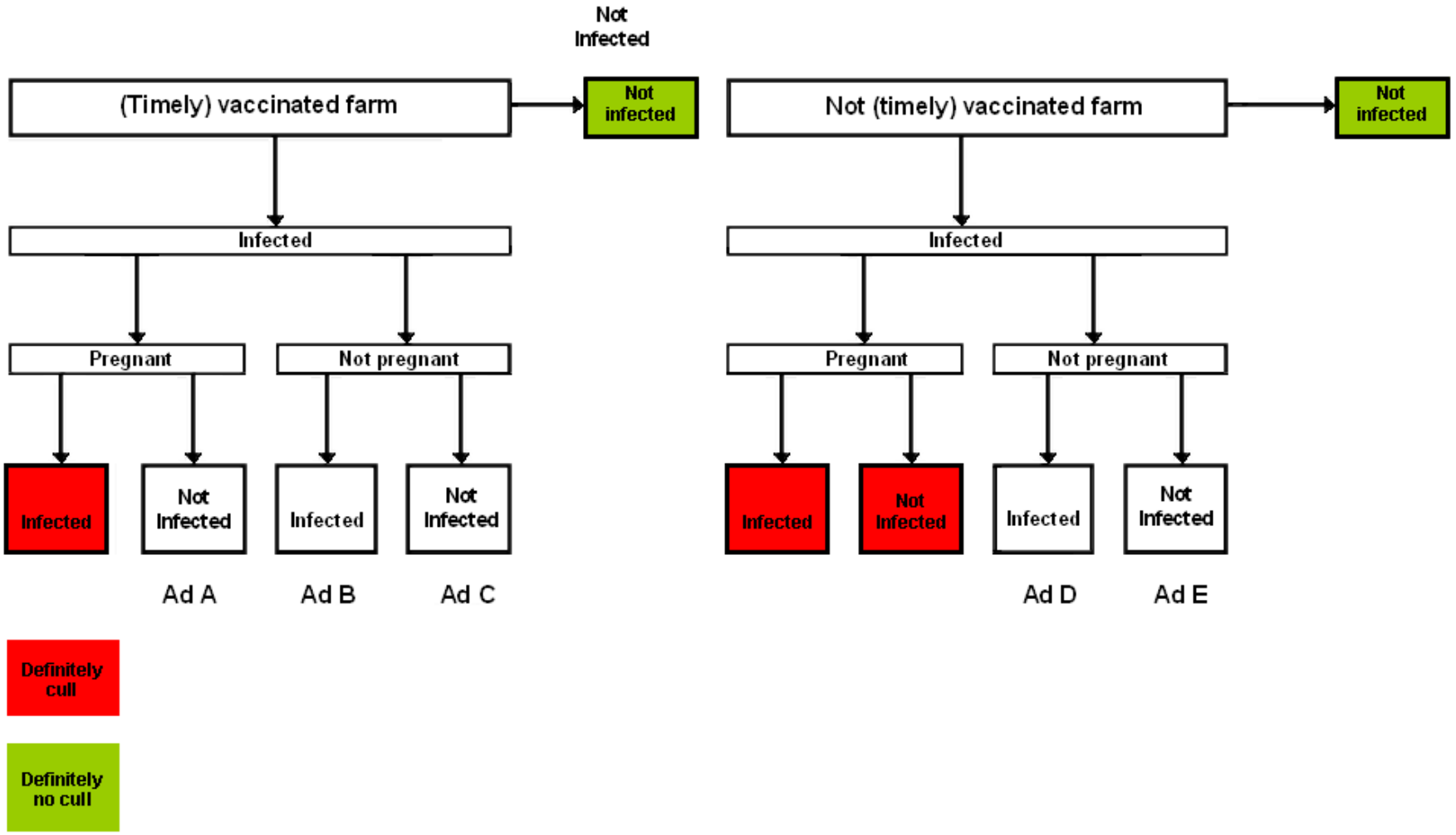
Prof. Dr. R.A. Coutinho
Director of the Centre for Infectious Diseases Control

Attachments:
Decision schedule
Map of Q-fever contaminated farms (plus 5 kilometer zones)
CVI advice

Only the original Dutch text is authentic

English translation: European Livestock Association

Decision schedule for culling yes/no



Q-koorts 11-12-2009

Bedrijfslokaties waar
Q-koorts is geconstateerd

Legenda

- Besmette bedrijfslocaties
- 5Km buffer
- Provinciegrens
- Bebouwd gebied
- Rivieren
- Snelwegen
- Grotere wateren
- Bos

Ministerie van Landbouw, Natuur en Voedselkwaliteit

Q-koorts
Besmettingen

N

0 3 6 12 18 24 30 km

1:1.400.000

Bron:

Gis Competence Center, Assen

CENTRAL VETERINARY INSTITUTE
WAGENINGEN UR

13 December 2009

Mrs. Dr. C.J.M. Bruschke
Ministry of Agriculture, Nature and Food Quality

Dear Mrs Bruschke,

Referring to your questions in your letter of 11 December 2009, you may find our advice herewith:

Question 1: The minister aims to kill as little animals as possible. She would prefer to spare not-infected pregnant animals at not-vaccinated farms. These animals should however have to be vaccinated immediately in order to eliminate the risk. She would like to be advised in this by veterinary experts about the expected safety and effectivity of vaccinating pregnant dairy goats and sheep at infected farms.

Substantiation of the advice:

At positive, not-vaccinated farms one can distinguish pregnant animals into not-infected and infected animals. Testing pregnant animals at one moment by PCR on vaginal swabs or milk samples distinguishes only between test-positive and test-negative animals. Test-positive are infected animals. Test-negative animals can be subdivided in infected ("false negative test) and not-infected animals that could as yet become infected in the coming period. The problem of infected animals that are test-negative due to intermittent excretion and differences between various excretion routes is even more important for your second question. We will therefore elaborate on this aspect in the answer to the second question.

At this moment there are no data regarding your problem about the effect of vaccination in relation with excretion using this vaccine on pregnant goats and sheep in the Netherlands. We must therefore rely on available literature data.

Literature data about the effects of vaccinating animals in infected flocks or herds in relation with excreting the germ are scarce; especially longitudinal studies that track the effect through time in relation with excretion of Coxiella bacteria are lacking.
Although the best documented study concerns cattle, we believe it is useful to substantiate our advice. It concerns a longitudinal study on six infected dairy cattle farms in France (Guatteo et al., 2008. Prevention of C. burnetii shedding in infected dairy herds using a phase 1 C. burnetii inactivated vaccine, Vaccine 26; 4320-4328). In this study 336 cows and heifers, pregnant and not pregnant, were vaccinated with the vaccine now used in the Netherlands or a placebo vaccine.
The conclusions of this result were that a pregnant cow vaccinated with the vaccine had the same chance to become excreter (in milk, faeces, vaginal excretion) as a pregnant cow administered with the placebo. Also the

amount of excreted bacteria did not differ significantly; only the animals that were not yet pregnant at the moment of vaccination had five times lower probability of becoming excreters as the placebo group. Animals (pregnant and not-pregnant) that were already infected at the moment of vaccination were not protected: the number of excreters and the amount of excretion did not differ from the animals in the placebo group. This confirms previous studies on goats where it was proven that vaccinating (not-pregnant) animals already infected at the time of vaccination, does not prevent or reduce excretion. As possible explanation for this vaccine failure with pregnant animals one mentions the negative (disadvantageous) effect of pregnancy on the immune response after vaccination (possible immuno-depression particularly frustrating the T-helper 1 type immune response). Vaccination is therefore most effective in not-infected flocks, especially for not-pregnant animals.

We are not familiar with studies (both field studies as experimental infections) on administering and the effect of the vaccine with pregnant (not-infected of infected) goats.
If however one could expect any effect from the above, it will take at least 5-6 weeks after vaccination (administering twice with an interval of 3 weeks) to show.

The vaccine could probably be administered to pregnant animals without a lot of side effects. In the current information leaflet the vaccine producer recommends not to use the vaccine with pregnant animals. At the moment the producer has applied for a more extensive registration for using the vaccine with pregnant animals as well.

Advice CVI:
Based on the above arguments we believe that administering the vaccine to pregnant animals will not lead to the desired effect of reducing the number of excreters and the amount of excretion per animal. Disregarding whether the test-negative animals are infected or not-infected at the moment of vaccination.

Question 2: The experts' advice of 10 December 2009 indicates that at vaccinated farms not-infected pregnant animals could be spared. The experts suggest that killing the pregnant animals at heavily infected vaccinated farms could be justified because a number of animals will be falsely declared not-pregnant or not-infected. Infected pregnant animals are a risk. The distinction between heavily and not heavily infected farms is arbitrary and could be put at 50%. The minister would like the CVI to further elaborate the line between heavily and lightly infected and to receive a substantiated advice on what line (percentage infected animals) to choose.

Substantiation of the advice:

The situation at vaccinated farms is considerably more complicated than at non-vaccinated farms. Serological monitoring (of possibly disputable value) into prevalence is impossible. Besides it is impossible to retrieve whether these farms were already infected at the moment of vaccination, and therefore with regard to excretion there is no surplus value to the effect of vaccination of already infected animals.

Based on the current experience in the Netherlands and on literature data the vaccine will prevent abortions in the larger part of the population, thus preventing the excretion of billions of bacteria, but infected animals can still excrete a considerable amount of bacteria, especially during a normal partus. This was the basis for the advice of the expert group to remove all pregnant animals. In second term the option to only remove the infected pregnant animals at vaccinated farms was put before the experts' group.

The status of infected or not-infected of individual, pregnant animals at an infected farm can at the moment only be established by a one-off analysis of a milk sample or vaginal swab (when animal is not lactating) with a PCR-test. As already indicated at question 1 the negative result of this test with healthy animals is no guarantee that the animal is not infected.
From literature data (Rousset et al., 2009. Coxiella burnetii shedding routes and antibody response after outbreaks of Q-fever-induced abortion in dairy goat herds. Microbiol.75; 428-433) one can deduct that even after abortion or

normal partus infected animals excrete intermittently and that it is (therefore) necessary to repeatedly sample the animals and take samples from all known excretion routes (faeces as well as milk and vaginal swabs) in order to reduce false negative results. This procedure should even more be applied during the period before partus.

The experts' consultation has indicated that culling all pregnant animals at all infected vaccinated farms will lead to removing not-infected animals and that if possible a difference could be made between farms with high prevalence and low prevalence. Because, a farm that was indicated positive through bulk milk testing, could have been found positive by just one single or just a few high excreters(s). At farms with a very low prevalence the number of test-negative, but yet infected animals should therefore be lower. The CVI believes that distinction between high and low infection farms cannot be related to bulk milk testing. The distinction shall therefore, if one were to decide to test at vaccinated farms, have to be based on yet to perform PCR-tests. Pre-drawing a line for the number of test-positive animals to make this distinction is impossible according to the CVI; every line is arbitrary and legally questionable.

CVI advice:
The CVI believes that if the precautionary principle is used and one aims at maximum excretion reduction at vaccinated farms, culling all pregnant animals is the only (justified) option. We realise that this way not-infected animals will be sacrificed unintentionally.

Making an absolute distinction between infected and not-infected animals at these farms is impossible, because there is a great chance of false negative test results when based on a one-off moment before an abortion or normal partus. This chance cannot be quantified with the current knowledge and at short notice.

In conclusion:
Your request for a substantiated percentage of test-positive animals in order to make a distinction between high and low infection farms, on account of such possibility given in the additional experts' advice, is at this moment impossible to answer due to all the uncertainties that we have described above.

Yours sincerely,

Dr. A.T.J. Bianchi

Only the original Dutch text is authentic

English translation: European Livestock Association