Development of a milk quality assurance program for Johne's disease by modelling

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Abstract

A new surveillance program was developed that guarantees a certain maximum number of *Mycobacterium avium* subsp. *paratuberculosis* (*Map)* bacteria per litre of bulk milk. In the new program dairy herds are distinguished in two categories, 'green' and 'red', where 'green' stands for the pool of certified herds which guarantee a preset bulk milk quality. The program is based on 3 parts: (1) an intake-procedure (certification), (2) a surveillance-procedure to monitor 'green' herds, and (3) a control-procedure on 'red' herds. Models were developed to study the development in time of the group of 'green' herds and of the group of 'red' herds (group size, prevalence, *MAP* in bulk milk). Several test regimes (based on blood or faeces tests) were combined with absence or presence of management measures and of purchase of animals. Results of epidemiological models were used in an economical decision analysis.

Results were as follows. It is very important for 'green' herds to exclude animal trade. Management measures are less important during the first 8 years, but are very important on 'red' herds. The intake- and surveillance test scheme itself is less important than presence or absence of animal trade and of management measures. However, on 'red' herds the control test scheme does matter.

Only if a milk price differentiation for milk produced by 'green' herds is introduced, the 'green' herds will join the program. The majority of all dairy herds in the Netherlands will be certified as 'green' after intake. When a farmer receives a 'red' status, the preferred decision is to stop immediately joining the program even if the milk price differentiation is € 0.01 per litre milk.

Introduction

In the Netherlands a certification- and surveillance program for *Mycobacterium avium* subsp. *paratuberculosis (Map)* has been developed, aiming at eradication of *Map* at the herd level. In the program, herds can obtain a *Map* 'free' status following five annual herd examinations, provided all faecal culture results are negative. The first herd examination is done by ELISA and faecal culture of ELISA-positive animals, and the 2nd through 5th by pooled faecal culture (Benedictus et al., 1999). Because the program aims at eradication of *Map* at the herd level, it is inherently expensive while incentives for farmers to participate are lacking. Therefore, only low numbers of farmers participate. However, the most important goal from a food safety point of view is to reduce the number of *Map* bacteria per litre of bulk milk. Thus, an important research question is: can we design a new program that guarantees a certain maximum number of *Map* bacteria per litre of bulk milk, that is simple and cheap and that gives farmers enough incentives to join and to keep joining the program for many years?

In the present study a new certification and surveillance program was developed for farms with 'low-risk' or 'low-*Map*' bulk milk. These farms will guarantee a certain quality of their bulk milk, which is based on a preset maximum of the number of *Map* bacteria per litre bulk milk. In the certification and surveillance program dairy herds are distinguished in two categories, 'green' and 'red', where green stands for the certified herds which guarantee the preset quality. An intake test scheme determines which farms will receive a green or red status. With the help of a surveillance test scheme the green herds are monitored regularly. Management improvements and trade restriction may help to improve the milk quality in the green pool, and may restrict the number of green herds becoming test-positive in the next future (and thus move to the pool of red herds). In red herds, a control procedure will be applied in order to receive a green status (again) after a certain time. The control consists of test and cull of positive animals, whether or not combined with management improvements (step 1, 2 and 3 of PPN, the Paratuberculosis Program in the Netherlands, see Groenendaal et al., 2002 and 2003) and/or trade restrictions (here: purchase of life animals from green farms only).

Materials and Methods

Various alternative programs for certification-and-surveillance-and-control of *Map* on low-prevalence Dutch dairy herds were evaluated in this study, assuming an initial herd-level prevalence in the country of 30%, i.e. at the start (before the intake procedure) we assume that 30% of the dairy herds is infected with *Map*, and 70% is free from *Map*. This prevalence was recently found in the Netherlands (van Weering et al., 2004).

Evaluated test schemes are based on sampling individual animals for blood or faeces (individual faeces test, pooled faeces test, serum Elisa). Testing of bulk milk samples for *Map* at a large scale is not (yet) possible, so this test method was not evaluated in this study. With models we make the step from number of test-positive animals in a herd to number of *Map* bacteria in milk. To evaluate the effectiveness of the various programs three models were used in this study:

(1) The simulation model JohneSSim for within-herd transmission of *Map* in a closed herd. This is a stochastic and dynamic simulation model that simulates (a) the herd dynamics, (b) the disease dynamics within the herd, (c) the control of Johne's disease and (d) the economic consequences at the herd level. Details and input parameter values can be found in Groenendaal et al. (2002) and in Weber et al. (2005). With this model the effectiveness of the intake- and surveillance procedure in closed herds were determined, as well as the control procedure in red herds. The economical and epidemiological output of this simulation model served as input for the other two models (see below).

Preventive management in the simulated herds was set to reflect the observed distribution of management practices in the Dutch dairy industry (background management, see Groenendaal et al., 2002). Alternatively, we simulated that *all* herds took the following preventive management measures: improved hygiene around birth (step 1 of PPN), colostrum from own dam only, and feeding of artificial milk replacer only (step 2), and effective separation of young stock from adult cows from birth to the end of the first year (step 3). Because these measures also affect other animal diseases, only 50 % of all costs of these management measures were attributed to the control of paratuberculosis in this study. Some of these input parameters were updated in Febuary 2004 and are presented in van Roermund et al. (2004) and Weber et al. (2005).

The expected number of *Map* bacteria per quantity of bulk milk is the sum of *Map* shed directly into milk, and the numbers added through contamination of milk by faeces from faecal shedders. Faecal contamination of milk was estimated to amount on average 40 mg per litre (Stadhouders and Jørgensen, 1990). For an extensive overview of *Map* bacteria and/or CFU's in milk and in faeces, see van Roermund et al., 2004. Based on these data, assumptions were made on the on-farm *Map* contamination of bulk milk (Table 1). Faecal contamination was considered the prime source of *Map* in milk. The expected concentration C_{Map} of *Map* bacteria in bulk milk was approximated by the average concentration of *Map* in milk in all animals in the herd.

Table 1. Assumed concentration of Map bacteria in milk for each stage of the infection-and-disease process in adult cattle.

Stage	Proportion of animals	Direct shedding of *Map* in milk (bacteria per litre)	Faecal contamination of milk (g per litre)	*Map* concentration in faeces (bacteria per gram)	*Map* in milk through faecal contamination (bacteria per litre)	Total *Map* in milk (bacteria per litre)
Latent infected		0	0.04	0	0	0
Lowly infectious	0.8	0	0.04	0	0	0
	0.2	0	0.04	10^2	4	4
Highly infectious	0.6	10^2	0.04	10^2	4	104
Highly infectious	0.24	10^2	0.04	10^4	400	500
Highly infectious	0.16	10^2	0.04	10^7	400	$4.001 \cdot 10^5$
Clinical disease		10^4	0.04	10^9	$4 \cdot 10^6$	$4.001 \cdot 10^7$

It is not known which concentration of *Map* bacteria in on-farm bulk milk can be considered acceptable. In the present study a maximum concentration of 10^3 *Map* bacteria per litre bulk milk was decided as acceptable by experts from Dutch dairy organisations (NZO/NIZO), based on their knowledge on the effect of pasteurisation.

Intake-, surveillance- and control- schemes were first studied separately and then integrated in simulations with JohneSSim. The selected ones can be found in Table 2. In the integrated simulations, herds were permitted to migrate between the statuses green and red. At the intake, test-negative herds were designated as green while test-positive herds were designated as red. Thereafter, green herds were re-classified as red if a test-positive animal was found in the herd during surveillance. Red herds were re-classified as green following the required number of negative herd-examinations, as determined in a separate analyses of the intake and control schemes (see Results).

Table 2: Intake and surveillance of green herds and control in red herds simulated with the JohneSSim model. A positive result of the ELISA or pooled faecal culture (PFC) during intake and surveillance was confirmed by individual faecal culture (IFC). During control in red herds IFC-positive animals and their lastborn calf were culled. However, results of ELISA during control in red herds were not confirmed by another test; ELISA-positive individuals and their lastborn calf in red herds were culled.

Scheme		Intake			Surveillance				Control		
		test (once)	animals		test	interval	animals		test	interval	animals
i1-s1-c1	i1	ELISA	All, ≥3yr	s1	ELISA	1 yr	All, ≥3 yr	c1	ELISA	1 yr	All, ≥3 yr
i1-s1-c7	i1	ELISA	All, ≥3yr	s1	ELISA	1 yr	All, ≥3 yr	c7	IFC	2 yr	All, ≥2 yr
i1-s2-c1	i1	ELISA	All, ≥3yr	s2	ELISA	2 yr	All, ≥3 yr	c1	ELISA	1 yr	All, ≥3 yr
i1-s2-c7	i1	ELISA	All, ≥3yr	s2	ELISA	2 yr	All, ≥3 yr	c7	IFC	2 yr	All, ≥2 yr
i5-s1-c1	i5	PFC	All, ≥2yr	s1	ELISA	1 yr	All, ≥3 yr	c1	ELISA	1 yr	All, ≥3 yr
i5-s1-c7	i5	PFC	All, ≥2yr	s1	ELISA	1 yr	All, ≥3 yr	c7	IFC	2 yr	All, ≥2 yr
i5-s2-c1	i5	PFC	All, ≥2yr	s2	ELISA	2 yr	All, ≥3 yr	c1	ELISA	1 yr	All, ≥3 yr
i5-s2-c7	i5	PFC	All, ≥2yr	s2	ELISA	2 yr	All, ≥3 yr	c7	IFC	2 yr	All, ≥2 yr
i5-s5-c7	i5	PFC	All, ≥2yr	s5	PFC	2 yr	All, ≥2 yr	c7	IFC	2 yr	All, ≥2 yr

(2) The analytical model. For the total population of dairy herds, which can interact with each other by trade of living animals, a new model was developed. This mathematical model describes a large group of herds (divided in green herds and red herds) and therefore needs to be less detailed. The model is deterministic, and variation between herds is modelled by distributions. Input parameters of this model were tuned with those used in JohneSSim, such as the distribution of initial prevalences within herds, life expectancy of animals (infected or not), relative infectiousness in various stages of infection, test sensitivity in various stages of infection, and the within-herd transmission rate of paratbc. For the within-herd dynamics of paratuberculosis in each herd, the transmission is described by one parameter (beta), which default value was based on simulation results with JohneSSim. This mathematical model was used to study the development in time of the group of green herds and of the group of red herds (group size, prevalences in the two groups, *Map* in bulk milk etc).

Animal trade, i.e. here purchase of life animals from green herds, is based on actual data of the Netherlands of the year 2000. In that year 37% of all dairy herds purchased animals, and 63% did not. The average number of purchased life animals by *open* cattle herds was 7 per herd per year (Velthuis, 2004). In the model for the 'open herds' scenario (animal trade allowed), 63 % of the herds was treated as closed, and 37 % of the herds purchased animals (7 per herd per year). Of course for the 'closed herds' scenario (no animal trade), no animals were purchased by all herds.

(3) The economical decision analysis determines the preferred decision for a farmer: should I join the new program or not? The decision of an individual farmer whether to join the program or not will be based on many different aspects (e.g. former experiences with other programs, the amount of labour, the time it will take, the yearly costs, the investments, the benefits and the chances of receiving these benefits, beliefs, etc.). A way to determine the economically preferred decision of a farmer, given the set of alternatives he has, is by analysing a decision tree. A decision tree includes three aspects of the decision making process, namely the costs, the benefits and the risks. In a decision tree all alternative actions available for the decision maker and the choices determined by chance are structured in a chronological order. The choice of the preferred action is based on the decision criterion, which is in this case the highest Expected Monetary Value (EMV). A detailed description of the economical decision analysis of this study is given by Velthuis et al. (2006, this volume) and by van Roermund et al. (2004). The input for the decision analysis is the output of JohneSSim and of the analytical model.

In the modelled decision tree the costs, losses and the probabilities to go from a green status to a red status and vice versa are included. The decision tree weighs the economic elements with the risks and shows the preferred decision based on this. When the preferred decision is not to join the program the decision tree estimates the milk price differentiation for green farms that is needed to change the preferred decision to joining the program. This milk price differentiation serves as an incentive for farmers to join the program. The 36 alternative programs for paratuberculoses which have been evaluated in this study are the 9 test schemes of Table 2, each with and without management measures and with and without animal trade (9x4).

Results

Epidemiology. We assumed an initial prevalence of paratuberculosis of 30%, i.e. 30% of the herds is considered infected and 70% is considered to be free. As a result, 90% and 83% of the herds receive a green status after intake I1 (Elisa) and I5 (faecal culture) respectively. After that, the pool of green herds is decreasing in size during the first 10 years. This is due to the green but still infected herds which are detected later in time, and then move to the pool of red herds. Only with management measures an increase in number of green herds can be seen, due to the red herds becoming green again after a certain lag period, depending on the control scheme on those red herds (C1=Elisa or C7=faecal culture). As an example the percentage green herds after 8 years is given in Table 3 (to compare with 90% at the start in year 0 after intake I1). For codes I, S and C, see Table 2.

Tabel 3. Percentage green herds after 8 years.

Test scheme	*Management: yes Herd: closed*	*Management: no Herd: closed*	*Management: yes Herd: open*	*Management: no Herd: open*
I1-S1-C1	77	73	57	31
I1-S2-C1	81	77	70	35
I1-S2-C7	85	74	69	34

So the pool of green herds is decreasing in number during the first years. Due to the detection of green but infected herds, the prevalence of infected animals and the *Map* bacteria per litre bulk milk in the pool of green herds is decreasing immediately in time, showing an improvement of the 'quality' in the pool of green herds in time (not shown here; see van Roermund et al, 2004).

Immediately after the intake procedure, the PVN (predictive value negative) is very high: about 97.8% and 99.7% of the green herds produces milk with *Map*<10^3 bacteria/litre after intake I1 (Elisa) and I5 (faecal culture) respectively. However, the small fraction of green herds producing milk with *Map*>10^3 bacteria/litre have a huge effect on the *average Map* content of milk of all green herds together, being still above this level for the first 5 years (for I1). This is due to the very skewed distribution of *Map* bacteria in milk per herd. After intake procedure I5 (faecal culture) the average *Map* content of milk in the pool of green herds drops immediately to the level of 10^3 bacteria/litre (see van Roermund et al, 2004).

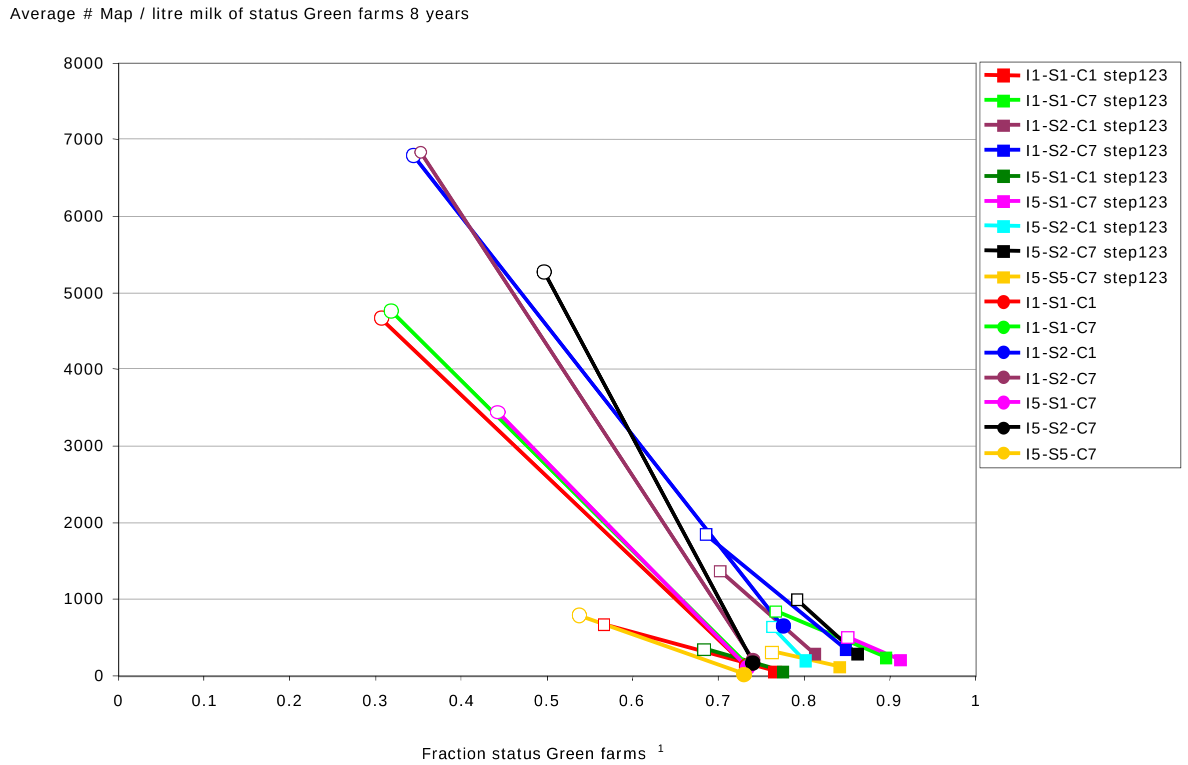

Figure 1. *Map* bacteria per litre bulk milk in the pool of green herds versus fraction of farms in the green pool, 8 years after the start of the program. Open dots or squares represent open farms, closed dots or squares represent closed farms. Squares represent farms with management measures (=step123), dots represent farms without management measures.

Figure 1 shows *Map* bacteria in bulk milk versus the fraction of herds in the pool of green herds in year 8. Most idealistic programs are in the lower-right corner of this figure: these programs result in a high fraction of herds in the green pool, and in a low average *Map* content of bulk milk in this pool of herds (after 8 years). From this figure it becomes clear that animal trade (purchase from green herds; open farms: open dots) has a strong negative effect on both outputs. Programs in the lower-right corner are I5-S1-C7, I1-S1-C7, I5-S2-C7, I1-S2-C7, and I5-S5-C7, all with management measures + no animal trade. Only the test scheme I5-S5-C7 (always faecal culture) is always successful when looking at the average *Map* content of milk in the pool of green herds, even without management measures and with animal trade.

It seems that the intake procedure (I) and the surveillance procedure (S) themselves are less important than the control procedure on red herds (best is: faecal culture C7), and the presence of management measures + the absence of animal trade. With control scheme C7 red herds go back to the pool of green herds sooner (after two negative test rounds) than C1 (Elisa), and this explains the larger size of that pool. In absence of animal trade, the effect of management measures seems relatively low (compare closed squares with closed circles), but this is due to the short period of 8 years.

When found test-positive, a green herd shifts to the pool of red herds. The criterium for red herds to move back to the pool of green herds is taken equal to that of unknown herds to become green after the intake procedure: the PVN value (see above). For the pool of red herds it was found that 6 ELISA or 2 faecal culture test-negative herd examinations are needed to reach a PVN value of 97.8-99.7% (depending on intake I1 or I5).

For the pool of red herds management measures are very important (see van Roermund et al., 2004). They have a large effect on the % infected animals and *Map* content of milk of red herds. Animal trade does not have an important effect, as purchase of an infected animal has a small effect on the prevalence of an already infected herd. The average *Map* content of milk in the group of red herds is always above the level of 10^3 bacteria/litre, except for a short time immediately after cull of faecal culture-positive animals (control C7) when management measures are applied on the farm. But within one year the *Map* content is back to levels of at least $7x10^3$ bacteria/litre (see van Roermund et al., 2004).

Decision analysis. If there is no milk price differentiation for milk produced by green farms the preferred decision for a farmer is not to join any program. When a farmer receives a red status (at the intake procedure or after a test round during the surveillance procedure) the preferred decision is to stop immediately joining the program even if the milk price differentiation is € 0.01 per litre milk. Higher milk price differentiations are not studied here. One exception is program I1-S1-C7 (without management measures). For this program the optimal decision for a red farm after the intake procedure (thus where the herd was tested positive) is to join the control-procedure for another test round (at a milk price differentiation of at least € 0.003). When tested positive again, the optimal decision is to stop joining the program.

The minimal milk price differentiation needed to change the decision from 'no' to 'yes' to join the intake-procedure is between € 0.0005 and € 0.0051. If a program is designed in such a way that a farmer cannot stop joining the program before the 6th test round of the surveillance procedure, the milk price differentiation is higher and should be between € 0.0009 and € 0.0080, depending the program. The higher milk price differentiation is due to the higher costs, for instance program costs during 6 test periods. The programs I1-S2-C1, I1-S1-C1 and I1-S2-C7 (without management measures) have the lowest costs for participants. The average yearly costs for green and for red farms are € 388 and € 1065 for program I1-S2-C1, € 609 and € 1085 for program I1-S1-C1 and € 386 and € 1647 for program I1-S2-C7. With management measures these costs are much higher: € 2110 and € 2538 for program I1-S2-C1, € 2332 and € 2529 for program I1-S1-C1 and € 2007 and € 3183 for program I1-S2-C7. For a more extensive overview and for benefits, see Velthuis et al. (2006, this volume) and van Roermund et al. (2004).

A cost - effectiveness analysis is presented in Figure 2. In this figure the milk price differentiation between green and red farms (needed to give a farmer enough incentive to join voluntary a quality assurance program) is set out against the average number of *Map* bacteria per litre of 'green' milk. Two clusters can be distinguished in this figure: the programs with management measures (step123, right lower corner) and the programs without management measures (left). This shows that management measures results in a higher milk price differentiation and in a lower number of *Map* bacteria in milk. The difference in the upper and lower end of each line indicates the effect of allowing animal trade or not. The number of *Map* bacteria in milk is much lower when no trade is allowed. However, the effect of 'not allowing trade' is much higher for programs where no management measures are included (left). The 'cheapest' programs that are most effective (where *Map* is below 10^3/litre) do not include management measures but include trade restriction.

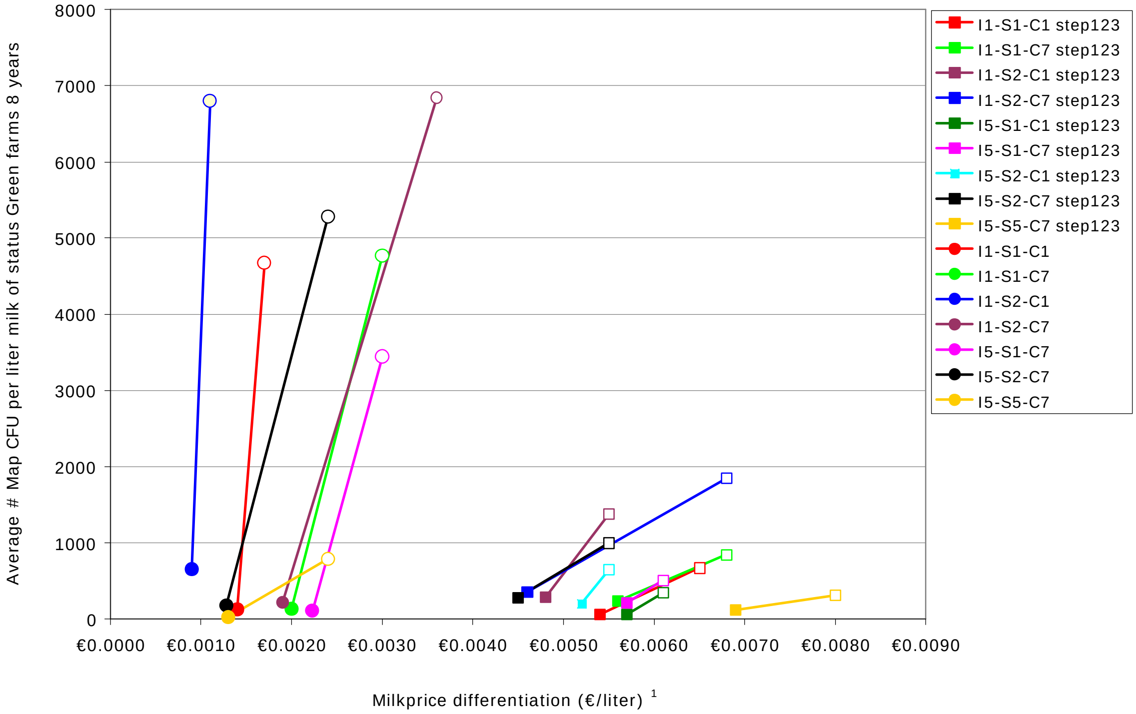

Figure 2. Milk price differentiation needed to give a farmer enough incentive to join voluntary a quality assurance program for *Map* in relation to the average number of *Map* per litre of milk of green farms per year. The milk price differentiation is based on the assumption that a farmer joins the program for the intake procedure and at least 6 test rounds during the control procedure. The lower end of each line (closed dots or squares) represents closed farms in a program where no trade is allowed, whereas the upper end (open dots or squares) represents open farms where trading is allowed.

When aiming at a milk quality of, on average, less than 10^3 *Map* bacteria per litre for green farms it can be concluded that the programs with animal trade and without management measures are not appropriate (Figure 2). There is one exception, namely the program I5-S5-C7 (always faecal culture) that is effective with animal trade and without management measures and does not need a high milk price differentiation (for the scenario that a farmer cannot stop joining the program before the sixth test round of the surveillance and control procedures). When management measures are applied almost all programs (with or without animal trade) are suitable to bring the milk quality of the green farms to the aimed level (Figure 2).

In short, management improvements on farms brings about high costs for participants and thus cause a higher milk price differentiation for green farmers. For the pool of green farms, management measures are less important than reducing animal trade. However, the effect of management measures is getting more important when animal trade is allowed. Furthermore, management measures are important on red farms, and if they are not taken, the pool of green farms will never increase in size. The alternative program where management measures are taken only on red farms and where animal trade is excluded only on green farms was not studied here.

Discussion and conclusions

According to the models, it is very important for green herds to exclude animal trade. Management measures are less important when animal trade is restricted (during the first 8 years), but are always very important on red herds. The intake- and surveillance scheme itself is less important than the effect of animal trade and of management measures. The control C7 (individual faecal culture) on red herds is important for the size of the pool of green herds due to the shorter lag time of becoming green again (2 negative test rounds), and C7 is important for lower *Map* numbers in milk of red herds. If there is no milk price differentiation for milk produced by green farms the preferred decision for a farmer is not to join any program. If a milk price differentiation is introduced, the green farms will join. The majority of all dairy farms in the Netherlands will be certified as green. When a farmer receives a red status (at the intake procedure or after a test round during the surveillance procedure) the preferred decision is to stop immediately joining the program even if the milk price differentiation is € 0.01 per litre milk. This will happen with 10-14% of the farms, which will become red immediately after the intake procedure, and with farms tested positive during the following surveillance procedure.

As for each modelling study, results depend on the model assumptions. Most insecure assumptions in our models due to lack of data are the amount of *Map* bacteria in milk and the effect of management measures on the within-herd transmission of the infection. Both were studied in a sensitivity analysis (see van Roermund et al., 2004 and Weber et al., 2005). In the models *Map* in milk is mainly caused by a small fraction of the highly infectious animals plus by the clinical animals (see Table 1). This skewed distribution should be verified in the field. It is important to realise that effects of management measures in the models are still based on expert opinions (see Groenendaal et al., 2002) which are not proven yet.

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