Economic aspects of antiviral agents to control Classical Swine Fever epidemics

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Preface

Outbreaks of contagious animal diseases such as Classical Swine Fever have detrimental effects on the livestock sector in an affected country as well as on society at large. The development of antiviral agents to control these epidemics can reduce the consequences of such outbreaks. The economic impact of applying these antiviral agents is until now unknown. In this report these consequences are investigated. This report is the result of a close cooperation between two institutes of Wageningen UR: LEI and CVI. It shows that an effective multi-disciplinary approach leads to better insights into complex problems.

We trust that the results of this research will assist policy makers and producers of antiviral agents in choosing the optimal strategy in the case of an outbreak of Classical Swine Fever.

L.C. van Staalduinen MSc
Managing Director LEI Wageningen UR

Summary

S.1 Key findings

The maximum price of antiviral agents to control Classical Swine Fever (CSF) epidemics has been determined. The price tolerance per dose (including application costs) amounts to approximately €10 if only treatment with antiviral agents in a 2-km radius around infected premises is considered (culling in a 1-km radius is applied as the reference eradication strategy). The price tolerance is about €7 per dose if a combination of vaccination (of finishers and piglets) and treatment with antiviral agents (of sows) in a 2-km radius around infected premises is considered (a 2-km emergency vaccination of finishers and piglets is taken as the reference eradication strategy). A price per dose below these prices makes a control strategy with treatment of antiviral agents the economically preferred eradication strategy in the case of a CSF outbreak in a densely populated livestock area in the Netherlands. See Chapter 5

Table S.1	**Maximum price per dose (euro)**			
Eradication strategy a)	**vac1_av1**	**vac2_av2**	**av1**	**av2**
EU	921	581	67	49
cul1	158	116	10	**10**
vac1_EU	15	29	-1	3
vac2_EU	-22	**7**	-4	1

a) EU measures (EU) always apply; additionally, animals are either pre-emptively culled (cul), emergency vaccinated (vac), treated with antiviral agents (av) or vaccinated and treated (vac_av) depending on herd type. The number denotes the control radius in km around detected farms.

S.2 Complementary findings

- The maximum price per dose depends on the eradication strategy applied and the chosen reference strategy.
- The maximum price per dose depends only to a limited extent on the size of an outbreak.
- The maximum price per dose will be higher when export losses, ripple effects, spill-over effects and/or enforcement costs are also accounted for. See paragraph 3.2

S.3 Method

- Based on the results of an epidemiological simulation study, a number of strategies were evaluated on their economic merits. Strategies focused on the effects of using antiviral agents. For this a partial budgeting approach was used. See paragraph 2.3
- Application of antiviral agents during outbreaks of epidemic livestock diseases like CSF is a potential tool as a complementing eradication strategy in the case of an outbreak of CSF. Antiviral agents provide instantaneous protection without culling the susceptible animal, and do not induce an anti-CSF-virus antibody response, facilitating serological testing to regain the CSF-free status. See paragraph 1.1

Samenvatting

S.1 Belangrijkste uitkomsten

Er is een maximumprijs vastgesteld voor antivirale middelen die worden gebruikt voor het bestrijden van epidemieën van klassieke varkenspest. De prijstolerantie per dosis (inclusief toedieningskosten) bedraagt circa € 10 als een behandeling met antivirale middelen wordt overwogen in een straal van 2 km rond het besmette pand (het ruimen van varkens in een straal van 1 km wordt toegepast als de referentiestrategie). De prijstolerantie is circa € 7 per dosis als een combinatie van vaccinatie (van slachtvarkens en biggen) en behandeling met antivirale middelen (van zeugen) wordt overwogen in een straal van 2 km rond het besmette pand (noodvaccinatie van slachtvarkens en biggen in een straal van 2 km wordt toegepast als de referentiestrategie). Een prijs per dosis die lager is dan deze bedragen maakt een strategie op basis van behandeling met antivirale middelen de economisch meest aantrekkelijke uitroeiingsstrategie in het geval van een uitbraak van de klassieke varkenspest in een dichtbevolkt veehouderijgebied in Nederland.

Tabel S.1	**Maximumprijs per dosis (euro)**			
Uitroeiingsstrategie a)	**vac1_av1**	**vac2_av2**	**av1**	**av2**
EU	921	581	67	49
Ger1	158	116	10	**10**
vac1_EU	15	29	-1	3
vac2_EU	-22	**7**	-4	1

a) EU-maatregelen (EU) zijn altijd van toepassing; daarnaast worden dieren preventief geruimd (cul), krijgen ze een noodvaccinatie (vac), worden ze behandeld met antivirale middelen (av) of worden ze gevaccineerd en behandeld (vac_av), afhankelijk van de besmettingshaard. Het getal is de straal in km rond de gedetecteerde bedrijven waarbinnen de ziekte wordt bestreden.

S.2 Overige uitkomsten

- De maximumprijs per dosis is afhankelijk van de toegepaste uitroeiings-strategie en de gekozen referentiestrategie.
- De maximumprijs per dosis is slechts in beperkte mate afhankelijk van de omvang van een uitbraak.

- De maximumprijs per dosis zal hoger zijn wanneer er tevens rekening wordt gehouden met exportverliezen, verspreidingseffecten, spill-overeffecten en/of handhavingskosten.

S.3 Methode

- Op basis van de resultaten van een epidemiologische simulatiestudie is een aantal strategieën beoordeeld op de economische verdiensten. De strategieën waren gericht op de effecten van het gebruik van antivirale middelen. Hiervoor werd een 'partial budgeting'-aanpak gebruikt.
- De toepassing van antivirale middelen bij een uitbraak van epidemische veeziekten als de klassieke varkenspest kan dienen als een aanvullende uitroeiingsstrategie in geval van een uitbraak van klassieke varkenspest. Antivirale middelen bieden direct bescherming en zorgen ervoor dat het dier niet hoeft te worden geruimd. Bovendien maakt het dier bij gebruik van deze middelen geen antilichamen aan tegen de klassieke varkenspest, zodat door middel van serologische tests de status varkenspestvrij kan worden verkregen.

1 Setting the scene

1.1 Introduction

Epidemic livestock diseases like Classical Swine Fever (CSF) present a threat to the productivity of the livestock sector and can have substantial effects on national economies. Therefore a rapid detection and eradication is of utmost importance. In the case of an outbreak of CSF, the Competent Authorities apply control measures to eliminate the infection from its territory and to avoid spread to other member states (MSs).

Given the importance of this epidemic livestock disease for MSs and EU economy the EU agreed upon a minimal set of measures to be applied in the case of an outbreak of CSF (Council Directive 2001/89/EC). Especially in MSs with a large, concentrated and intensive livestock sector the EU minimum measures do not lead to a swift and efficient containment of the epidemic and additional measures need to be applied. These measures can consist of preventive culling in a circle around infected farms, the application of movement restrictions and/or vaccination in an area around infected farms. These specific additional control measures can only be applied after approval by the EU Commission.

Control measures are associated with costs. Detection and culling of infected farms, preventive culling of high risk farms, movement restrictions to prevent further spread of infection, vaccination as well as other additional preventive measures are accompanied with substantial cost for the government as well as the livestock production chain. Besides these direct costs, costs related to export bans and (temporary) loss of export markets within and outside the EU occur. For exporting MSs like the Netherlands, Belgium and Denmark these export losses may even be larger than the direct costs of an outbreak. In Appendix 1 the present control measures as described in the Dutch Contingency Plan CSF are summarised (in Dutch).

Application of antiviral agents during outbreaks of epidemic livestock diseases like CSF is a further potential tool in the pallet of additional measures. Antiviral agents provide instantaneous protection without culling the animal, and do not induce an anti-CSF-virus antibody response, facilitating serological testing to regain the CSF-free status. They can be used to protect sows that are not vaccinated in the current Dutch contingency plan strategy, or used as an alternative control measure where all animals are treated with antiviral agents (i.e., sows, piglets and finishing pigs).

In a previous study the use of antiviral agents as an alternative or additional strategy to control CSF epidemics was reported in terms of epidemiological effects (Backer, 2011). A number of the evaluated strategies in the epidemiological study were used to evaluate the economic effects of using antiviral agents to contain CSF outbreaks. The results of this economic study are presented below.

Economic effects of an outbreak of CSF

When evaluating the costs of an epidemic of a contagious disease like CSF, different components can be distinguished:

- Direct costs related to the control of the epidemic.
  These include the costs for the infrastructure for the control of the epidemic, the costs associated with culling and destroying of infected and contact animals, the costs associated with destruction of feed on detected farms, the compensation and vaccination costs.
- Enforcement costs.
  Costs related to the enforcement of movement restrictions (police and other inspection services).
- Costs related to trade restrictions.
  Due to an epidemic the national and international market access for animals of susceptible species and their products is restricted. An epidemic of CSF will result in trade restrictions that are mostly related to the epidemic per se and do not depend on the specific characteristics of the control strategy chosen. After the last outbreak it takes time until all the restrictions in trade are lifted and the situation from before the epidemic is restored. For example after an outbreak of CSF in a country, trade with third countries of pigs and pork products is restricted for 6 months. For trade within the EU, the Commission can decide that this period can be shorter depending on the measures taken by the MS.
- Ripple effects.
  The effects from outbreaks of CSF that are felt upstream and downstream along the livestock value chain: breeding, feed production, input supply, slaughter, processing, final sale and consumption.
- Spill-over effects.
  Spill-over effects are effects of an outbreak outside the affected livestock production chain. These are for example the effects from outbreaks of CSF on tourism and other services. Since other than typical agricultural production is becoming more important for the rural economy, these spill-over effects are likely to become a large part of the total epidemic costs.

The duration of the trade restrictions has a large effect on the economic consequences for an infected country. For a country like the Netherlands, which depends to a large extent on export of pigs and pig meat, the duration of a trade restriction from infected areas within and outside the EU determines these economic effects for a large part.

1.2 Objective of the research

The following research questions were answered to obtain an insight into the economic aspects of the application of antiviral agents in the control of an outbreak of CSF in a densely populated livestock area (DPLA) in the Netherlands:

1. What are the economic differences between the eradication strategies?
2. What is the 'price tolerance' of the application of antiviral agents?

2 Material and Methods

2.1 Epidemiological data

The epidemiological data as presented in Backer (report 2011, publication in preparation) were used as input for the economic calculations. In total 8 strategies were analysed.

Control strategies

Table 2.1 Overview of control strategies evaluated in the economic evaluation a)

Control strategy	**Animal type**		
	Finishers	**Piglets**	**Sows**
EU	EU	EU	EU
cul1	cul1	cul1	cul1
vac1_EU	vac1	vac1	EU
vac1 _av1	vac1	vac1	av1
vac2 _EU	vac2	vac2	EU
vac2 _av2	vac2	vac2	av2
av1	av1	av1	av1
av2	av2	av2	av2

a) EU measures (EU) always apply; additionally, animals are either pre-emptively culled (cul), emergency vaccinated (vac), treated with antiviral agents (av) or vaccinated and treated (vac_av) depending on herd type. The number denotes the control radius in km around detected farms.

The benchmark strategies
EU: The EU demands a minimal control strategy, as required by Council Directive 2001/89/EC. All animals on infected detected farms are culled, transport is regulated in protection and surveillance zones, and dangerous contacts are actively screened and traced.

The measures of the EU strategy always apply; additional measures are taken in the following control strategies:

cul1: Additional pre-emptive depopulation in a 1-km radius around infected premises is the preferred strategy of the EU in a DPLA.

vac1_EU: Emergency vaccination of finishing pigs and piglets in a 1-km radius around infected premises instead of preventive culling. Sows are excluded from vaccination to minimise the risk of persistently infected piglets.

vac2_EU: Emergency vaccination of finishing pigs and piglets in 2 km around infected premises instead of preventive culling. This is the preferred strategy in The Netherlands. Sows are excluded from vaccination to minimise the risk of persistently infected piglets.

Strategies that include treatment with antiviral agents

In the case of treatment with antiviral agents the following assumptions are made:

- If sows are treated, the suckling piglets are assumed to be protected via the milk.
- Antiviral treatment will take place for the duration of 15 days but this period can become longer when another infected herd is newly detected within the control radius. However, the maximally allowable treatment duration is set at 30 days.

The following strategies were evaluated:

av1: EU control measures always apply. On top of this, all susceptible animals in a control radius of 1 km are treated with antiviral agents.

av2: As av1, but now all animals are treated in a radius of 2 km.

vac1_av1: EU control measures always apply. Emergency vaccination of finishers and piglets in a 1-km radius around infected premises. Sows are excluded from vaccination to minimise the risk of persistently infected piglets. Non-vaccinated sows are treated with antiviral agents in a 1-km radius around infected premises.

vac2_av2: As vac1_av1, but with emergency vaccination of finishers and piglets in a 2-km radius around infected premises and non-vaccinated sows are treated with antiviral agents in a radius of 2 km around infected premises.

A summary of the epidemiological data is provided in Table 2.2 (originating from the calculations of Backer in 2011).

Table 2.2 Mean epidemiological results a)

Control strategy	Duration (days)		Number of infected farms		Number of pre-emptively culled farms		Number of vaccinated farms		Number of treated farms with antiviral agents		Number of culled animals (x 1,000)		Number of vaccinated animals (x 1,000)		Number of antiviral doses (x 1,000)	
EU	724	(249-1,227)	546	(79-1,003)	0	(0-0)	0	(0-0)	0	(0-0)	793	(133-1,248)	0	(0-0)	0	(0-0)
cul1	162	(69-342)	48	(21-101)	212	(84-436)	0	(0-0)	0	(0-0)	399	(162-786)	0	(0-0)	0	(0-0)
vac1_EU	192	(85-383)	56	(24-113)	11	(2-27)	230	(84-470)	0	(0-0)	96	(48-176)	340	(125-671)	0	(0-0)
vac1_av1	167	(77-342)	50	(21-104)	11	(2-27)	204	(75-421)	97	(36-199)	88	(43-156)	304	(109-606)	615	(216-1,315)
vac2_EU	118	(56-234)	34	(18-63)	11	(2-27)	345	(154-631)	0	(0-0)	62	(34-106)	508	(224-918)	0	(0-0)
vac2_av2	102	(51-200)	30	(17-55)	11	(2-27)	310	(138-577)	147	(69-278)	55	(31-96)	455	(214-840)	1,030	(445-2,002)
av1	207	(86-577)	57	(22-187)	11	(2-27)	0	(0-0)	242	(82-651)	104	(46-278)	0	(0-0)	7,654	(2,402-21,135)
av2	120	(65-281)	32	(17-70)	11	(2-27)	0	(0-0)	334	(157-694)	65	(35-131)	0	(0-0)	11,825	(5,192-24,587)

a) 5%-95% confidence interval between brackets.
Source: Backer et al. (2011).

2.2 Economic data used

To evaluate the economic consequences of the different control strategies an existing economic model was used (Backer et al., 2009). Since the main objective of this research is to compare the effects of different control strategies, only those costs and benefits that were expected to differ substantially between the evaluated alternatives are included. The costs that are included in the calculations are in Table 2.3. In the next section the costs that are included or excluded in the model are addressed. Also, the assumed values are given.

Price data of 2012 were used. In case they are unknown (e.g. because some costs can only be determined after an outbreak) they are based on historical data indexed for a price level of 2012. Price indexes of CBS (www.cbs.nl) were used.

Table 2.3 Economic input parameters used in the economic evaluation (2012 price level)

Screening and sampling			**Vaccination costs**		
Taking samples as suspect	298,684	€/infected farm	Sows	0.00	€/animal
Execution of screening	244,444	€/infected farm	Piglets	2.26	€/animal
Total screening and sampling	543,128	€/infected farm	Fattening pigs	2.26	€/animal
Taxation and materials per culled farm	7,180	€/culled farm	Value of compensated animals including feed		
Destruction (transport included)			Sows	467	€/animal
Sows	109	€/animal	Piglets	45	€/animal
Piglets	0.00	€/animal	Fattening pigs	106	€/animal
Fattening pigs	15	€/animal	Empty farm buildings during outbreak		
Clearing and disinfection			Sows	0.99	€/animal/day
Sows	502	€/animal	Piglets	0.00	€/animal/day
Piglets	0.00	€/animal	Fattening pigs	0.20	€/animal/day

Table 2.3	**Economic input parameters used in the economic evaluation (2012 price level) (continued)**				
Screening and sampling			**Vaccination costs**		
Fattening pigs	188	€/animal	Costs of transportation prohibition of non-infected farms with fattening pigs, first 6 weeks	11.01	€/animal
Repopulation costs					
Sows	181	€/animal			
Piglets	0.00	€/animal			
Fattening pigs	12	€/animal			

- *Screening and sampling*
  These are costs related to screening and sampling, as well as costs of crisis centres, tracking and tracing, clinical examination and clinical inspection, based on the total cost of the 2001 epidemic in the Netherlands (Huirne et al., 2002).

- *Costs of clearing and disinfection*
  The labour costs of culling of animals and disinfection of farms, based on Huirne et al. (2002).

- *Compensation for culled pig herds*
  The costs of culled animals are the number of culled animals times the value of each animal. The costs of destructed feed are the number of culled animals times the average value per animal of the stock of feed present on the farm. The value of culled animals was based on value tables that are regularly updated.[1] Values were calculated as averages over all ages, since the stage in the production cycle is unknown for individual farms.

[1] To improve the process of valuation of animals culled during an epidemic the Dutch Competent Authorities and the livestock sector agreed upon a method for valuation ('Waardetabellen'). Based on this procedure an annually updated value table prepared by LEI for different types of animals has been created.

- *Costs of empty housing*
  These are costs of empty housing between the moment of culling and the moment of repopulation after the epidemic and a 30-day period after the last detection.

- *Costs of repopulation*
  The culled farms incur costs after repopulation because of suboptimal utilisation of their capacity.

- *Costs of transportation prohibition of non-infected farms and welfare slaughter*
  The costs were calculated of non-infected farms in an area with transport prohibition for a 6-week period because of missed returns. Only these costs were calculated for finisher pigs. It is assumed that sows will not have welfare problems and will not lose value during a transport prohibition.

- *Costs of empty houses and repopulation of non-infected farms in infected compartments*
  Pigs are sufficiently available in the Netherlands in the area with movement restrictions to prevent empty housing.

- *Costs of vaccinating*
  The labour costs of vaccination of animals and the vaccine costs.

- *Value loss of vaccinated animals*
  The value loss of vaccinated animals is the number of vaccinated animals times the average value loss of each animal if sold on the Dutch market. The estimates for the value loss of products from vaccinated pigs were based on previous research by Van Asseldonk and Bergevoet (2011, unpublished data).

- *Costs of logistic processing of vaccinated animals*
  During the epidemic and the 30-day period after last detection, vaccinated pigs are processed similarly to non-vaccinated animals. Vaccinated animals that are still alive after this period have to be logistically slaughtered and corresponding costs were calculated. Vaccinated hobby animals were not slaughtered and incurred no additional costs.

- *Costs of antiviral drugs*

Since determination of the price tolerance of the antiviral drugs (and their application) is the objective of the present study, no price for the antiviral agents (and their application) is included in the initial calculations. Also, it assumed that there are no restrictive measures associated with respect to the withdrawal period[1] and market access that could hamper the sale of products originating from animals treated with these agents.

Excluded from the calculation

- *Enforcement costs:* costs of police involvement and other control agencies in the enforcement of movement restrictions. A sensitivity analysis is conducted based on assumptions presented in Appendix B. Enforcement costs are substantial. There are two issues with respect to these enforcement costs: 1) They are not eligible for reimbursement under the EU Veterinary Fund and 2) They are difficult to estimate, since they depend on the location of the outbreaks, the enforcement deemed necessary by the competent authorities and the expected cooperation of farmers in the affected areas.
- *Ripple effects:* costs that occur in the pig value chain.
- *Spill-over effects:* costs that can occur during an epidemic of CSF in branches not primarily affected such as horses, poultry, sheep, pigs and cattle farming and arable land and the costs of non-agricultural industry as tourism are also not analysed (i.e.).
- Export market losses were excluded in the economic analysis since they strongly depend on the duration of the outbreak.
- In this evaluation only the economic effects of the occurrence of the first outbreak in a Densely Populated Livestock Area (DPLA) are evaluated; the effects of a first outbreak in a Sparsely Populated Livestock Area (SPPA) are not evaluated.

[1] The withdrawal period is the period between the last application of the antiviral drugs and the moment the animal can be slaughtered and the products are safe for human consumption. After the last outbreak it will take at least 42 days before movement restrictions are lifted and animals can be slaughtered. However, in the case of a long duration of an outbreak, animal welfare problems on farms affected by movement restrictions might occur. In such cases, farmers can be allowed to slaughter animals in dedicated slaughter houses under strict restrictions. To enable this welfare slaughter on treated farms, the withdrawal time determines the minimal time after treatment this welfare slaughter can occur.

2.3 Methods used for the economic analysis

The method of economic evaluation comprised three steps.

1. Calculating economic differences between the different eradication strategies.
2. The total costs of the evaluated strategies were pairwise compared and presented in a matrix structure.
3. Determining the price tolerance.

The 'price tolerance' of antiviral agents is the price level per dose and their application at which two strategies are indifferent (i.e. with anti-viral agents compared with a reference strategy). Two reference strategies were investigated, namely with and without vaccination as part of the eradication strategy.

In the evaluated strategies the number of 'demanded' doses depends on the strategy chosen but also to a large extent on the evolvement of the epidemic under a given control strategy. Besides the price tolerance based on mean values, we also explore if the size of an outbreak and the number of doses of antiviral agents used have an impact on the maximum price. For the situation without and with vaccination the outbreaks were ranked. The maximum price per dose was determined per iteration by the using the following formula:

$$\text{Price}_{\text{int } t} = (\text{Cost strategy- av}_{\text{int, } t} - \text{Cost strategy+ av}_{\text{int, } t}) / (\text{\# doses}_{\text{int, } t})$$

In which 'Cost strategy- av$_{\text{int, } t}$' are the total costs for the tth iteration in which no antiviral agents were applied and 'Cost strategy+ av$_{\text{int, } t}$' are the total costs for the tth iteration with application of antiviral agents, while '# doses $_{\text{int, } t}$' are the number of doses needed for the tth iteration.

3 Results

In the following paragraphs a number of tables and graphs with summarised results are presented. The numbers in *italics* in the tables are discussed in the text. In the strategies were antiviral agents are applied the results are *exclusive the costs (of application) of the antiviral agents.*

3.1 Total costs and differences between control strategies

In Table 3.1 the control costs are presented. The distribution of the total costs of the different control strategies is given in Figure 3.1 to Figure 3.3. Unless mentioned otherwise, the main text presents results of the variant excluding enforcement costs, which are presented in Appendix 3).

Table 3.1 Costs of different control strategies in the case of an outbreak of CSF in a DPLA in the Netherlands, in million euros (excluding enforcement costs)

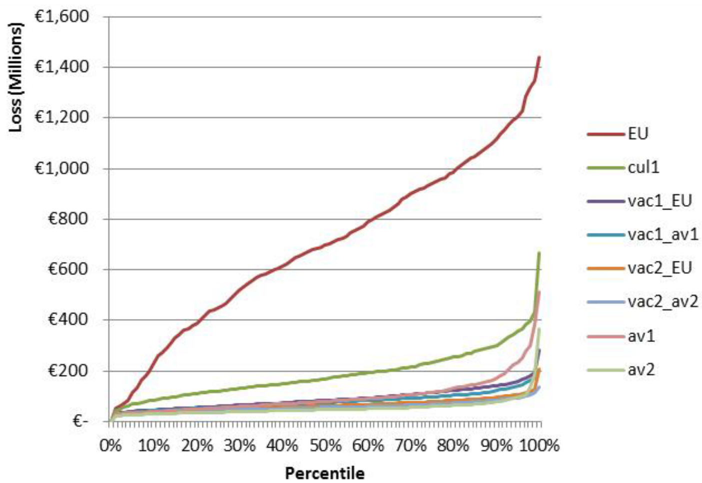
	Total costs		
	Mean	**(5%**	**95%)**
EU	*692*	114	1204
cul1	185	70	356
vac1_EU	90	40	158
vac1_av1 a)	80	37	142
vac2_EU	65	34	107
vac2_av2 a)	*58*	31	94
av1 a)	98	35	234
av2 a)	53	26	95

a) The cost of the antiviral agents and their application are not included in the calculations.

The total costs (excluding enforcement costs) differ substantially between the evaluated strategies (Table 3.1 and Figure 3.1). The EU strategy is the most expensive strategy (average of €692m per outbreak). The other strategies have substantially lower average costs. Strategy vac2_av2 has the lowest average costs (€58m). Large differences occur in possible outcomes between iterations (Figure 3.1). Costs gradually increase with increasing percentiles. Only at higher percentile values (>95% percentile) costs rise steeply. The EU strategy has the highest costs at each percentile value followed by cul1.

Note that the control costs are the largest part of the total costs of the outbreak. In the situation *enforcement costs excluded*, the proportion of the costs borne by farmers amounts to 21% for cul1 and 47% for vac2_av2. In the situation where the *enforcement costs are included*, the fraction of the costs borne by the farmers varies between 13% for av1 and 26% for vac2_EU.

Figure 3.1	**Distribution of outcomes of the simulations a)**



a) The x axis gives the percentile and the y axis gives total costs in million euros.

The difference in total costs between the different control strategies is given in a cross table (Table 3.2). The average total costs for example of the EU strategy are €507m higher than for the cul1 strategy.

Table 3.2	Differences in mean total costs of different control strategies in the case of an outbreak of CSF in a DPLA in the Netherlands, in million euros (excluding enforcement costs)							
	EU	**cul1**	**vac1_EU**	**vac1_av1**	**vac2_EU**	**vac2_av2**	**av1**	**av2**
EU								
cul1	*-507*							
vac1_EU	-602	-95						
vac1_av1	-612	-105	-10					
vac2_EU	-626	-119	-25	*-14*				
vac2_av2	-633	-127	-32	-22	-7			
av1	-594	-87	8	18	32	40		
av2	-638	-132	-37	-27	-12	-5	-45	

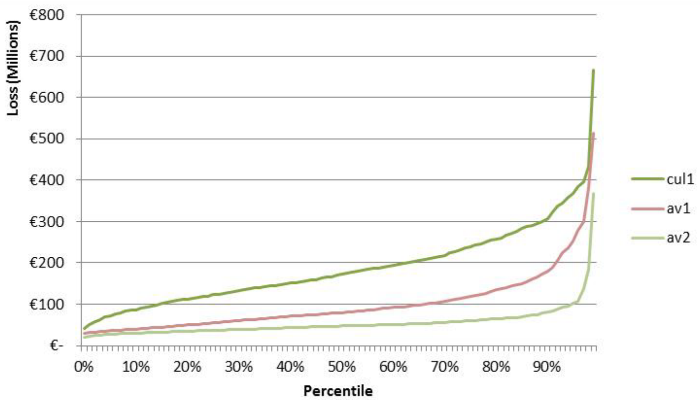
The EU strategy is likely to result in a very large, long-lasting epidemic, so it is not considered as a realistic option. To evaluate the potential benefits of a treatment with antiviral agents (excluding their costs), two scenarios are compared:

1. a scenario in which vaccination is not considered as a policy option and cul1 is the reference strategy for comparison (Figure 3.2); and
2. a scenario in which vaccination is considered as a viable policy option and vac1_EU/va2_EU are the reference strategies for comparison (Figure 3.3).

The cul1 strategy is thus the preferred option given a non-vaccination scenario and in the absence of antiviral agents. The total costs for cul1 are €87m higher compared to av1, and €132m higher compared to av1.

Figure 3.2 shows that both av1 and av2 have lower costs than cul1 over the whole domain of percentile values. The av2 strategy has lower costs than the av1 strategy.

Figure 3.2	Distribution of the outcomes: total cost for the cul1 strategy compared to the application of antiviral agents in a 1- or 2-km radius around infected farms, in million euros (excluding enforcement costs)



Results for the scenario where vaccination is considered a policy option or part of the contingency plan are presented in Figure 3.2. Because vac2_EU has €25m lower total costs compared to vac1_EU, vac2_EU is the benchmark to evaluate the economic effects of the strategies vac1_av1 and vac2_av2.

Figure 3.3	Distribution of the outcomes: comparison of vaccination strategies with or without the application of antiviral agents, in million euros (excluding enforcement costs)

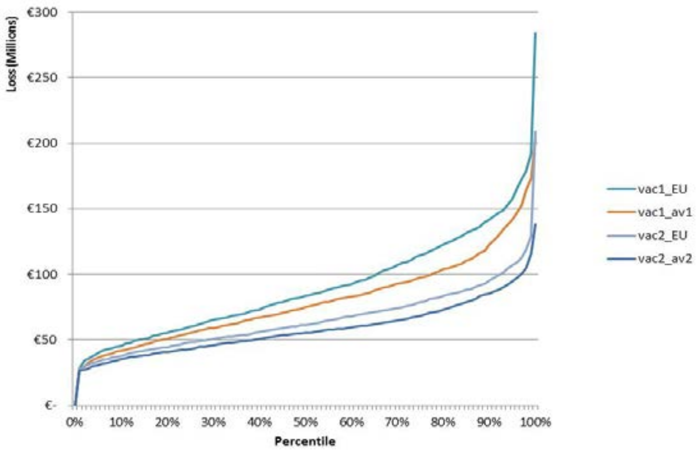


Figure 3.3 shows that adding antiviral drugs to the vaccination strategy lowers the average total costs compared to vaccinating in the same radius without the use of antiviral agents (excluding the costs of these agents and their application). However, the average total costs for vac1_av1 are higher than for vac2_EU.

Compared to vac2_ EU, the costs of vac1_av1 are €14m higher. So, if antiviral agents are available, vac2_EU is still preferred over vac1_av1. However, extending the radius to 2 km, the total direct costs for vac2_av2 are €7m lower than for vac2_EU.

The ranking of the strategies based on their economic impact does not change for the whole range of potential outbreak outcomes since the lines of the presented results never cross as shown in Figures 2 and 3.

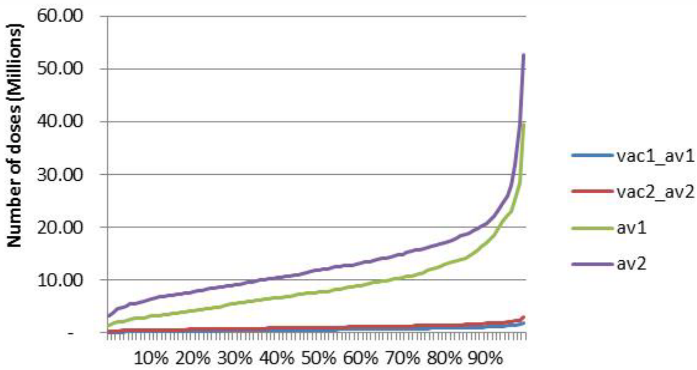
In a situation where there is no preference for eradication with or without vaccination, the *vac2_av2 strategy* is the most cost-effective strategy (under the condition of no costs for antiviral agents).

3.2 Application of antiviral agents: What is the 'price tolerance'?

The numbers of doses needing treatment with antiviral agents differ substantially between the evaluated strategies (Table 3.3 and Figure 3.4). In strategies that include vaccination, only sows are treated whereas the av_1 and av_2 strategies also include piglets and finishers. The numbers of doses differ substantially between the av_1 and av_2 strategy, whereas the variation between the two vaccination strategies vac1_av1 and vac2_av2 is much smaller. As shown in Figure 3.5a and Figure 3.5b, the number of doses used in an outbreak varies substantially also within a strategy.

Table 3.3	**Number of doses applied per strategy**		
	# doses		
Strategy	**Average**	**5% percentile**	**95% percentile**
vac1_av1	664,501	217,684	1,315,910
vac2_av2	1,089,853	446,008	2,001,753
av1	7,653,543	2,410,521	21,135,858
av2	12,947,618	5,197,441	24,588,548

Figure 3.4	Number of doses of antiviral agents depending on the size of an outbreak



As previously stated, the total costs for the strategies exclude the price for antiviral agents or their application. The differences in costs between strategies with and without treatment are the maximum tolerated prices for the antiviral agents or their application to break even. Dividing this difference by the number of doses needed gives the maximum price per dose applied (Table 3.4).

Table 3.4	Maximum price per dose			
Strategy	**Price per dose (euro)**			
	vac1_av1	**vac2_av2**	**av1**	**av2**
EU	921	581	67	49
cul1	158	116	10	*10*
vac1_EU	15	29	-1	3
vac2_EU	-22	*7*	-4	1

When evaluating the maximum price per dose for the treatment with antiviral agents, the following two situations are of interest:[1]

- A scenario in which vaccination is not considered a policy option with cul1 as reference strategy.

[1] In the other situations a strategy without application of antiviral agents is the preferred policy option. For strategies without vaccination this is cul1 and for strategies with vaccination this is vac2_EU.

In this situation av2 is the preferred option (Table 3.2), since it has the lowest average total direct costs (excluding enforcement costs). Despite the large number animals to be treated and therefore the large number of doses which are needed, the *maximum price per dose for av2 is €10.*

- A scenario in which vaccination is considered a viable policy option with vac2_EU as reference strategy.
  In this situation vac2_av2 is the strategy with the lowest average total cost (excluding enforcement costs) and the *maximum price per dose for vac2_av2 is €7*.[1]

To evaluate whether the maximum price per dose for antiviral drugs or for their application depends on the number of doses needed in a control strategy (hence defined as price elasticity), iterations were ranked according to the total outbreak costs. Subsequently, per iteration the maximum price per dose was calculated by comparing a treatment strategy with its benchmark strategy. The results are given in Table 3.5 and in Figure 3.5 for the comparison of the strategy av2 versus cul1 and in Figure 3.6 for the comparison of vac2_av2 versus vac2_EU.

Table 3.5 Price per dose: statistics and regression analysis

Alternative	**Statistics**			**Regression analysis a)**			
	Mean	**5%**	**95%**	**Constant**	**B**	**sig**	**R^2**
av2 (vs cul1)	10.41	5.74	15.49	11.4	7.4 E-8	0.00	0.025
vac2_av2 (vs vac2_EU)	6.70	4.19	10.05	7.4	6.5*E-7	0.00	0.011

a) Number of doses as independent variable.

[1] As shown in the Appendix, in the case the enforcement costs are included in the calculations the maximum price per dose is €11/dose for av2 and €12/dose for vac2_av2 .

Figure 3.5a	(av2 versus cul1) Price per dose of antiviral agent related to the total direct costs of an outbreak. Strategies were ranked based on outbreak costs

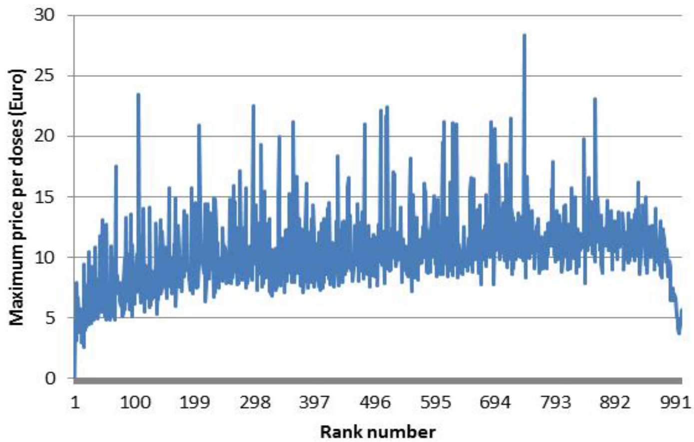


Figure 3.5b	(av2 versus cul1) Price per dose of antiviral agent related to the number of doses needed to control the outbreak. Strategies were ranked based on number of doses required

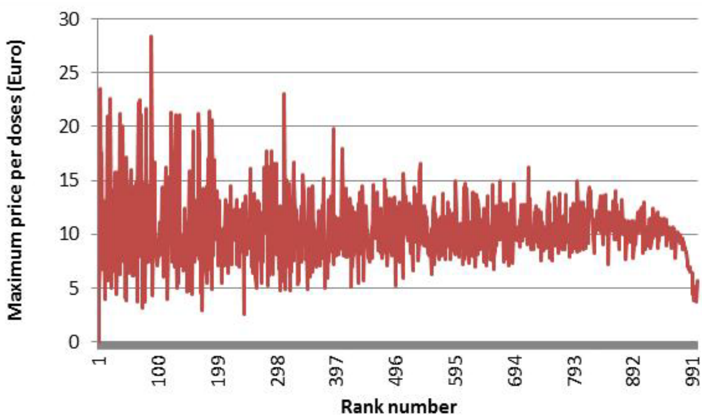


Figure 3.6a	(vac2_av2 versus vac2_EU) Price per dose of antiviral agent related to the number of doses needed to control the outbreak. Strategies were ranked based on number of doses required

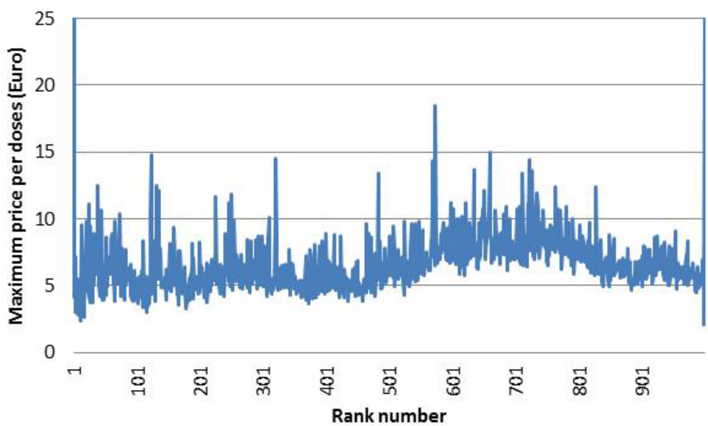
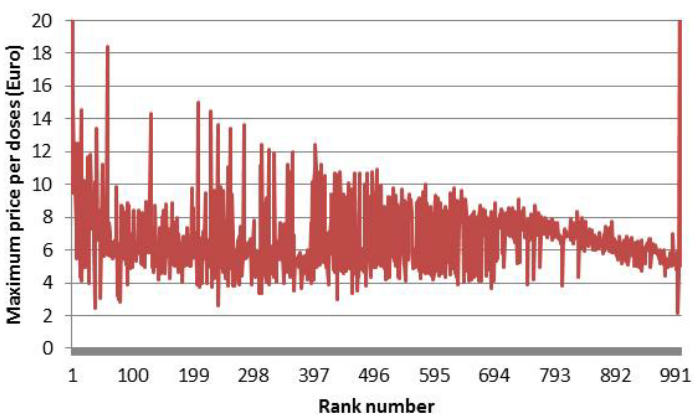


Figure 3.6b	(vac2_av2 versus vac2_EU) Price per dose of antiviral agent related to the number of doses needed to control the outbreak. Strategies were ranked based on number of doses required



There is a large variation in the maximum price per dose (Table 3.5). A regression analysis was performed to obtain insight into the relation between total direct costs of the outbreak and the maximum price per dose. Although a significant relation was estimated, this relation was weak for both evaluated alternatives, as expressed by the small variance explained (R^2) and the very small B-value.

Conclusion
There is large uncertainty in the maximum price per dose, although this variation only to a very small extent results from either the size of the outbreak or the number of doses of antiviral agents needed to control an outbreak. This variation is mainly caused by stochastic processes in the epidemiological model.

4 Discussion

In this discussion the following issues will be addressed: the impact of enforcement costs on the maximum price per dose and export losses in relation to the control strategy.

The impact of enforcement costs

- Enforcement costs are mainly affected by the duration of the outbreak and not by the size of the outbreak. These costs can be substantial. In previous outbreaks enforcement costs were estimated to be as high as 335 k€ per day. However, these costs are heavily influenced by policy decisions on how extensive the enforcement effort should be. It is expected that in future outbreaks farmers' cooperation will increase, especially when a vaccination-to-live strategy will be applied. Furthermore, cooperation will increase if the price of culled animals has been communicated beforehand, and transport of animals to slaughter houses is made possible after a relatively short period. So the incentives to move animals from infected to non-infected areas might decrease. The amount of enforcement measures and hence the costs per day may also decrease.
- The impact of including or excluding enforcement costs on the maximum price of antiviral agents is more profound in alternative strategies in which these enforcement costs are a larger part of the total costs. When an outbreak is characterised by a relatively small number of culled farms as in those strategies that include vaccination (i.e. vac2_av2), the share of enforcement costs is larger. This results in a price difference of €5/dose (€12/dose versus €7/dose) for calculations including enforcement costs in the evaluation. In the strategies that involve large-scale preventive culling, the share of enforcement costs is relatively smaller; hence a smaller difference of €1/dose in the maximum price per dose is seen when enforcement costs are included in the calculations (€11/dose versus €10/dose).

Export losses and costs related to trade restrictions

- As a result of an epidemic, national and international market access for animals of susceptible species and their products is restricted. An epidemic of CSF will result in trade restrictions that are mostly related to the epidemic per se and do not depend on the specific characteristics of the control strategy chosen. After the last outbreak it takes at least 6 weeks until the first movement restrictions are lifted. However, it can take up to 6 months until all trade restrictions in the EU are lifted and the 'normal' situation is resumed. Trade restrictions to third countries when applying a vaccination-to-live strategy take 6 months to be lifted.

- Total effects are determined by the size and duration of the outbreak, the control strategy applied and especially the country/area affected. For a country exporting mainly to third countries the present difference in export ban between a strategy with or without applying a vaccination-to-live strategy might be substantial.
- Can the av2 strategy be an alternative for vac2_EU or vac2_av2? The maximum price per dose when comparing vac2_av2 with av2 is only €1 (Table 3.4). So to make av2 a feasible alternative either the production price should be below €1/dose or the expected benefits from reduction in the duration of the export ban should be such that a higher price per dose is justified.

5 Conclusions

The differences in total costs between eradication strategies with and without treatment with antiviral agents, in case the costs of antiviral agents are excluded from the calculations, are substantial. Implementing antiviral agents as part of the control strategies against CSF should be seriously considered.

Compared to the reference strategy of 1-km preventive culling the maximum price per dose (including application costs) is around €10 in case only treatment with antiviral agents in a 2-km radius around infected premises and no vaccination is applied as eradication strategy. In the case of a combination of vaccination (of finishers and piglets) and treatment with antiviral agents (of sows) in a 2-km radius around infected premises, this maximum price is about €7 per dose when 2-km emergency vaccination (of finishers and piglets) is taken as the reference strategy. A price per dose below the above values makes a control strategy with treatment of antiviral agents the preferred eradication strategy in the case of a CSF outbreak in a densely populated livestock area in the Netherlands. The maximum price per dose can be higher when export losses, ripple effects, spill-over effects and/or enforcement costs are also accounted for.

- The maximum price per dose depends only to a limited extend on the size of an outbreak. However, there is substantial uncertainty which is mainly caused by variations stemming from the stochastic model used to estimate the epidemiological impact (Backer, 2011).

Literature

Backer, J. et al. 2009. *Vaccination against Foot-and-Mouth Disease; Differentiating strategies and their epidemiological and economic consequences*. Den Haag: LEI. p. 158.

Backer, J. 2011. *Antiviral agents to control Classical Swine Fever epidemics evaluation of control strategies*. Report number: 11/CVI0253.

Huirne, R.B.M. et al. 2002. MKZ: *Verleden, Heden en Toekomst; Over de preventie en bestrijding van MKZ*. Den Haag: LEI. p. 183.

Appendix 1

Huidige strategie bestrijding KVP in Nederland

Uitgangspunten
Uitgangspunt in de draaiboeken KVP is dat er in een cirkel van 2 km rondom besmette bedrijven gevaccineerd gaat worden.

Op varkensbedrijven worden op de bedrijven die in de vaccinatiecirkel liggen alle dieren behalve de dieren die drachtig kunnen zijn gevaccineerd. Het betreft vleesvarkens, fokberen, opfokzeugen en zuigende en gespeende biggen.
De zeugen worden bij KVP *niet* gevaccineerd. Een bedrijf wordt in principe maar één keer gevaccineerd. Indien een bedrijf meerdere keren in een vaccinatiecirkel komt te liggen worden alleen nieuwe/pasgeboren dieren die nog niet gevaccineerd waren gevaccineerd.

Maatregelen tijdens de uitbraak
In de gebieden rondom uitbraken gelden onder andere restricties voor vervoer van en naar locaties met gevoelige dieren en wordt ook ander vervoer van agrarische voertuigen zoveel mogelijk beperkt. Zodra een besmetting is bevestigd zullen de maatregelen die in de EU-richtlijn genoemd zijn uitgevoerd worden. Dit betekent het ruimen van het besmette bedrijf, maar ook het instellen van een beschermingsgebied met een straal van ten minste 3 km om het besmette bedrijf. Daarnaast wordt een toezichtsgebied met een straal van ten minste 10 km om het besmette bedrijf ingesteld. Indien besloten wordt om te gaan vaccineren zal er een vaccinatiegebied ingesteld worden. In het vaccinatiegebied zijn, op basis van de richtlijn, dezelfde maatregelen van toepassing als in het beschermingsgebied en toezichtsgebied.

In de draaiboeken worden drie zogenaamde fases onderscheiden. De maatregelen die voor het vaccinatiegebied in aanvang van kracht zullen zijn (fase 1: geldt van het begin van vaccinatie tot 30 dagen na de laatste vaccinatie), zijn identiek aan het maatregelpakket van het beschermingsgebied en toezichtsgebied. In de afbouw van de maatregelen worden de maatregelen van fasen 2 en 3 van kracht. Fase 2 gaat in na fase 1 en is geldig tot een gunstige uitslag van de screening bekend is, fase 3 gaat in na de screening en is geldig tot Nederland door de EU vrij wordt verklaard.

De maatregelen in fase 2 zijn gelijk aan de maatregelen in fase 1: vatbare dieren mogen met een ontheffing vervoerd worden rechtstreeks naar een slachthuis binnen of buiten het vaccinatiegebied. In fase 3 is het vervoer van vatbare dieren, met ontheffing, toegestaan tussen bedrijven *binnen het vaccinatiegebied*. Het vervoer van vatbare dieren naar een locatie buiten het vaccinatiegebied is verboden, tenzij de dieren met ontheffing rechtstreeks naar een slachthuis gaan.

Samenvattend: gedurende de uitbraakperiode (fase 1 tot en met fase 3) is er sprake van kanalisatie in zowel het vaccinatiegebied, beschermingsgebied en toezichtsgebied van alle gevoelige dieren en hun producten uit het gebied (figuur A.1). Kanalisatie houdt in dat de producten afzonderlijk herkenbaar bewerkt en separaat opgeslagen moeten worden (separaat opslaan zal naar verwachting zulke grote consequenties hebben dat VWA heeft aangegeven dat duidelijke identificatie voldoende is).

Maatregelen na de uitbraak

Ook na de uitbraak gelden er nog steeds beperkingen voor de afzet van gevaccineerde dieren en hun producten. De duur van deze periode met beperking na de uitbraak is afhankelijk van de dierziekte. De interpretatie van de richtlijnen is hieronder weergegeven[1] (Persoonlijke Mededeling: Akkerman, 2009).

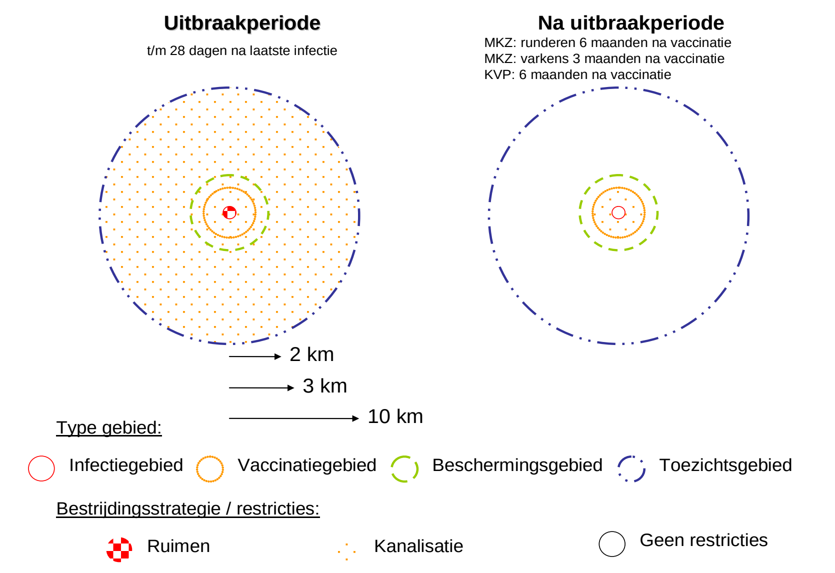
Voor KVP geldt dat hier onderscheid gemaakt wordt tussen gebruik van levend en marker vaccin. Bij levend vaccin geldt dat het vlees gedurende 6 maanden (na laatste vaccinatie) een *hittebehandeling* moet ondergaan. Bij gebruik van een marker vaccin (art 19 lid 9 Richtlijn 2001/89/EG) gelden andere procedures. In art 19 lid 8 9 Richtlijn 2001/89/EG staat vermeld dat, in afwijking van lid 5 en 6, de maatregelen zoals genoemd in art 4 kunnen worden ingetrokken onder genoemde voorwaarden. Door dit laatste artikel kan de periode van 6 maanden worden verkort.

Bij vaccinatie tegen KVP worden op de vermeerderingsbedrijven in de vaccinatiegebieden de aanwezige biggen met markervaccin gevaccineerd (en de zeugen niet dit in tegenstelling tot MKZ). De tijdshorizon met beperkingen voor afzet van producten van gevaccineerde dieren is begrensd tot de levensduur van de gevaccineerde dieren. Er zijn maar een relatief korte tijd gevaccineerde dieren op het bedrijf aanwezig. Na ongeveer 70 dagen (de gemiddelde afleverleeftijd van een big naar het vleesvarkenbedrijf) na de laatste vaccinatie

[1] Eén van de speerpunten binnen het EU project 'Animal Health Strategy' betreft de herziening van de wetgeving met betrekking tot dierziektebestrijding. Hierbij zal zeker de mogelijkheid van vaccinatie als bestrijdingsinstrument, maatregelen tijdens vaccinatie, vermarkten van producten en vlees van gevaccineerde dieren herzien worden (meer gericht op de praktijk).

zullen, bij afwezigheid van verdere vervoersbeperkingen, geen gevaccineerde dieren meer op het zeugenbedrijf aanwezig zijn. Op een vleesvarkensbedrijf worden in de vaccinatiegebieden alle aanwezige dieren eenmalig gevaccineerd. Dit betekent dat binnen ongeveer drie maanden deze dieren aan het slachthuis geleverd zullen zijn. De maximale duur met beperkingen is dus circa een half jaar (duur van big tot met aflevering vleesvarken).

Figuur A1.1 Bestrijdingsstrategie/restricties per gebied gedurende en na een MKZ-/KVP-uitbraak



Appendix 2
Enforcement costs

Table A2.1	Enforcement costs (price level 2012)	
RDW	2,907	€/day
Army	41,281	€/day
Customs	17,443	€/day
Police	204,081	€/day
Agricultural inspection (AID)	69,771	€/day
Enforcement (total)	**335,484**	€/day

Appendix 3

Tables with results for enforcement costs INCLUDED

Table A3.1	**Costs of the different control strategies in the case of an outbreak of CSF in a DPLA in the Netherlands, in million euros (including enforcement costs)**		
	Total costs (in million €)		
	Mean	**(5%**	**95%)**
EU	*949*	195	1574
cul1	254	105	465
vac1_EU	168	80	286
vac1_av1[1]	151	74	260
vac2_EU	117	65	187
vac2_av2*	*105*	60	164
av1*	190	76	438
av2*	110	60	196
a) The cost of the antiviral agents are not included in this calculation.			

Table A3.2	**Differences in average total direct costs of different control strategies in the case of an outbreak of CSF in a DPLA in the Netherlands, in million euros (including enforcement costs)**							
	EU	**cul1**	**vac1_EU**	**vac1_av1**	**vac2_EU**	**vac2_av2**	**av1**	**av2**
EU								
cul1	-695							
vac1_EU	-780	-86						
vac1_av1	-798	-103	-18					
vac2_EU	-831	-137	-51	-33				
vac2_av2	-844	-149	-64	-46	-13			
av1	-759	-64	21	39	72	85		
av2	-839	-144	-59	-41	-8	5	-80	

Table A3.3	**Maximum price per dose, based on total costs (including enforcement costs)**				
Strategy	**Price per dose**				
	vac1_av1	**vac2_EU**	**vac2_av2**	**av1**	**av2**
EU	1201		775	85	65
cul1	156		137	7	11
vac1_EU	27		59	-2	5
vac1_av1	0	50	42	-4	3
vac2_EU		0	12	-8	1
vac2_av2			0	-10	-0.40
av1				0	6
av2					0

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