THE ROLE POPULATION DYNAMICAL MODELS IN RISK-ASSESMENT

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ABSTRACT

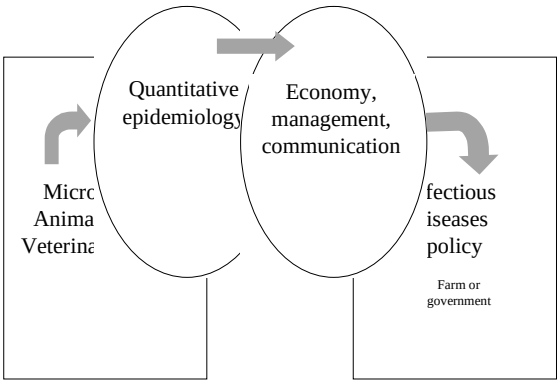
Risk-assessment is a structured way of studying risks. This approach will also be applied to risks resulting from infections in animals. However, risk assessment cannot replace the investigation of infections is animal populations. It is necessary to estimate correctly the parameters relevant to the risks and to study the dynamics of these infections in order to be able to correctly assess risks.

SAMENVATTING

Risk-assessment is een gestructureerde wijze om risico's te bestuderen. Deze benaderingswijze zal ook worden toegepast op de risico's veroorzaakt door infecties bij dieren. Risk-assessment kan echter niet in de plaats komen van de studie van infecties bij dieren. Het is noodzakelijk om op juiste wijze de parameters te schatten die van belang zijn voor dergelijke risico's en om de dynamica te bestuderen om de risico's correct uit te kunnen rekenen.

1. INTRODUCTION

Veterinary science has developed as a means to manage the risks that result from infections in animals. Risk management was the motivation to open the first veterinary schools like for example Alford in France.. Therefore risk-assessment, which is part of risk-management, is not foreign to the veterinary field. However, since the establishment of Alford much has changed and other scientific disciplines than the strictly veterinary science have become involved in dealing with the risks posed by infections in animals (Fig. 1). On the one hand the role of molecular biology has increased in the study of animal infections. On the other hand there is more emphasis on quantitative methods: statistical methods and dynamic modelling.



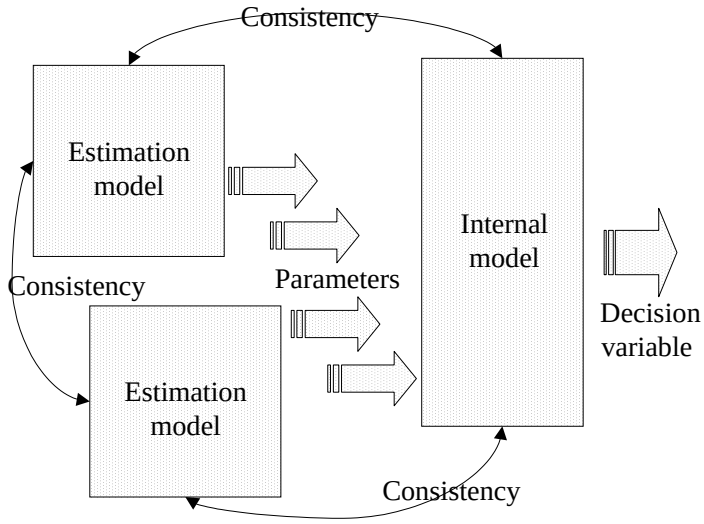
Presently a more formal methodology of risk-assessment is proposed as another tool in doing risk management for animal infections. Policy makers have quickly embraced this new tool of risk-assessment because it offers to provide direct answers to the policy maker's questions without the necessity to further investigate the infectious agent's behaviour. In structuring the risk problems with focus the risks as perceived by decision makes and in directly answering the policy makers questions risk-assessment is indeed useful. However, there is also the trap that analysis is always possible without further analysis. Those of us that believe in Popperian falsification will quickly see that cannot be true. It remains to be shown that particular risk-assessments without further investigations will indeed lead to better policy decisions.

It is true that not everything has to be known before existing knowledge can be used to make an assessment of the risks. Therefore focussing the risk-assessment on the risk, that the policy makers need to know, helps. However, to improve decisions the manner in which information is combined to assess risks and answer questions has to offer some additional benefit. To explain this I will focus on quantitative risk assessment. For quantitative risk assessment mathematical models are the key element that connects estimated parameters to the risks that are to be assessed. The model gives the relationship between the quantitative information that is used and the output variable on which the decision is made. Thus the validity and usefulness of the risk assessment methods depends on the validity and usefulness of the mathematical model.

In this paper presented today I will argue that the mathematical model on which to base the risk assessment does matter and that a wrong choice of model can lead to wrong results. (Fig. 2)
There are three ways in which the model can be wrong:

- the parameters as estimated do not meet the model specifications and/or cannot be estimated
- the model formula do not mimic the process that is studied
- the calculated output is not the variable to base decisions on.

Therefore for improving risk-assessment insight and cooperation in parameter estimation, studies of underlying dynamic processes and insight in the decision process is needed.



2. CORRECT PARAMETER ESTIMATES?

The parameter estimates have to be estimates of the parameters that are used in the model. In general we want to base decisions on as simple a model as possible. The limiting factor is the possibility to estimate the parameters included in the model. Designing an intervention strategy for FMD outbreaks we need to know what the impact will be eventually for the national budget. However as we cannot estimate that directly by repeatedly using other control measures in subsequent outbreaks we need to make a more complex model with more parameters. Often the actual parameter estimates are not available and the estimates that are used are actually of other parameters.

For example in controlling FMD or CSFV with vaccines one needs to know the effect that these vaccines have on transmission (1) not the protection that they offer to disease or to virus excretion. Modelling is needed to

model what happens when the animals are still building up immunity when the virus is introduced (4).The timing of effective protection against transmission could be much quicker than what is expected from individual experiments.

Another set of parameters often used in models is the sensitivity and specificity of diagnostic tests. The estimates that are published are mostly based on scoring “difficult” sets of test sera with different tests. This is a good practice in the research for the development of new tests. However, the values for sensitivity and specificity given in those publications cannot be used as estimates. For example these values do not tell us what is the probability that a random sample from an infected animal from the target population is indeed scored as positive. Currently, there is an increased interest in estimating sensitivity and specificity for the target population.

3. CORRECT MODEL?

The internal structure has to represent reality in a manner compatible with the goal of the modelling: i.e. the internal algorithm (formula’s or calculation rules) has to result in sufficiently correct calculation of the output variables when the correct parameters would have been estimated. Recently my colleague Hans Heesterbeek and I have explained in our joint inaugural lecture how all models are lies but nevertheless or rather “just because” they can be very useful. Models are not necessarily wrong but they are necessarily different from reality. We used in this lecture the example of Margritte how wrote under a picture of a pipe: “this is not a pipe”. If you can remember your first response to that picture or when you see it now for the first time you will understand that it shows how we tend to see representation of reality as the reality itself. Therefore there two incorrect responses to models: one group discards everything as a lie or whereas others see everything as being the truth. We argue that a critical appraisal in the light of the goal of the modelling is to be preferred.

One example is the way mass action is modelled in infection chain models. Take S to be the number of suceptibles and I the number of infectious individuals. Decision models have been based on models that assume that new cases are proportional to SxI whereas it should be SxI/N (2). This wrong model formulation is sometimes not important but for particular decisions it can lead to totally wrong outcomes.

Recently the production of food from animals has been modelled as a simple linear chain where in each link multiplication or reduction can occur. Such models can be applicable if certain measures as decontamination at the end of the chain is considered. Comparison of decontamination to measures taken on the farms cannot be performed, as measures of the chain will influence also other animal groups than the group to which measures are applied. For example fighting *Campylobacter* in the production of poultry meat. Measures reducing the incidence in broiler groups will lower the probability of introduction to other such groups either subsequently or present at the same time.

4. CORRECT OUTPUT VARIABLES?

Decision-making can only be carried out when the relevant output variables are known. Often formulating the correct output variables is either complex or it is politically complicated. For example the question how to declare a country or an area free of a certain disease has provoked some discussion. The point here is that the area should not pose more of a risk to other area’s than these area’s pose for each other. The risk that area’s pose for each other depends on their surveillance stem, i.e. the system with which they detect a new introduction of an infection and prevent further transmission within their own country. In general it could be said that the surveillance system could be evaluated by the number of countries a country would infect when it itself would become infected. If this number would be below one for all countries with respect to a certain infection, than that infection could never spread among countries. This is not yet the case for most List A diseases in most countries. Declaring a country free after an outbreak should be done when the country (area) would not pose an additional risk. (compare 3).

5. CONCLUSIONS

A structured approach to risk assessment is useful but cannot replace the research regarding the dynamics of infections. The knowledge about the dynamics is needed for defininig and estimating parameters of the risk-assessment model. Furthermore the extrapolation to assess the risk of unobserved situations makes it necessary

to systematically study the model structure. Finally for defining the output variables the dynamic character of infectious diseases should also be taken into account.

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RISK ASSESSMENT FOR CLASSICAL SWINE FEVER INTRODUCTION INTO THE NETHERLANDS

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ABSTRACT

Introduction of classical swine fever virus (CSFV) is a major risk for the pig production sector in the Netherlands. A spreadsheet model was constructed to obtain more quantitative insight into the main factors determining the probability of CSFV introduction (P_{CSFV}) into the Netherlands. The scenario pathway approach was used as most probabilities in the model are very small. The model contained pathways of CSFV introduction including the import of pigs and pork products, returning livestock trucks and contacts with wild boar. All European Union member states were included as possible sources of CSFV. Results showed a mean overall annual P_{CSFV} of approximately 0.06. Almost 65% of this probability could be attributed to the pathway returning livestock trucks. The most likely sources of CSFV introduction were Germany, Belgium and the United Kingdom. Although the calculated probabilities were rather low when compared with expert estimates and recent history, the most likely causes of CSFV introduction indicated by the model were considered to be realistic.

SAMENVATTING

Insleep van klassieke varkenspestvirus (KVPV) is een belangrijk risico voor de varkenssector in Nederland. Om meer kwantitatief inzicht te krijgen in de belangrijkste factoren die bijdragen aan de kans op KVPV insleep is een spreadsheet model ontwikkeld. De scenario pathway approach is gebruikt omdat de meeste kansen in het model zeer klein zijn. De insleeproutes voor KVPV in het model zijn: import van varkens en varkensprodukten, terugkerende veewagens en contact met wilde zwijnen. Als mogelijke herkomstlanden van het virus zijn alle lidstaten van de Europese Unie in het model opgenomen. De resultaten laten een gemiddelde insleepkans van 0.06 per jaar zien. Deze kans kan voor bijna 65% toegeschreven worden aan de insleeproute terugkerende veewagens. De meest waarschijnlijke herkomstlanden van het virus zijn Duitsland, België en het Verenigd Koninkrijk. Hoewel de berekende kansen klein zijn in vergelijking met expert schattingen en het recente verleden, zijn de belangrijkste oorzaken die het model aangeeft realistisch.

1. INTRODUCTION

The introduction of classical swine fever (CSF) is a major risk for the pig production sector of the Netherlands. Its potentially disastrous consequences were illustrated by the 1997/98 epidemic that started in February 1997 in an area with one of the highest pig and herd densities in Europe (10). In total 429 farms got infected, while more than 10 million pigs were destroyed preventively and for welfare reasons (2). The costs of this epidemic (i.e. direct costs and consequential losses to farms and related industries) were estimated at US$ 2.3 billion (17). The probability that CSF virus (CSFV) is introduced is an every-day-threat for the Netherlands. International transports of pigs are abundant while CSF epidemics still occur sporadically in the domestic pig population of the European Union (EU), with the most recent examples in Luxembourg, Spain and Germany (20). In addition, CSF occurs in an endemic form in wild boar populations in some areas of Germany, France, and Italy (15). In recent years infected wild boar were also found in Belgium and Luxembourg (20).

Risk is defined as the likelihood and magnitude of the occurrence of an adverse event (1). The process of risk assessment can be subdivided into three steps: release, exposure and consequence assessment (25). Accordingly, the risk of CSFV introduction consists of (i) the probability that the virus is introduced into the country (release assessment), (ii) the probability that susceptible animals get infected (exposure assessment) and (iii) the epidemiological consequences and economic losses induced by the resulting epidemic (consequence assessment). In this paper emphasis will be on the probability of CSFV introduction (P_{CSFV}) comprising both the release and exposure assessment.

The P_{CSFV} is determined by many factors, e.g., presence or absence of CSFV in neighbouring or trade-partner countries, number of contacts with other countries (trade, tourism, etc.), presence of infected wild boar, and preventive measures in force. To reduce the P_{CSFV} by risk management strategies the major causes of CSFV introduction have to be known. A pathway diagram presenting all factors that possibly contribute to the P_{CSFV} and their interactions is given by De Vos *et al.* (6). Based on this diagram, a spreadsheet model was constructed in order to calculate the P_{CSFV}. The main aim of this model is to analyse which pathways (i.e. carriers and mechanisms that can transmit the virus from an infected to a susceptible animal) contribute to the P_{CSFV} into the Netherlands and from where these pathways originate. The model can be used as a decision-support tool in setting priorities for the prevention of CSFV introduction.

In this paper the modelling approach used to calculate the P_{CSFV} into the Netherlands is described and some results are presented.

2. MATERIAL AND METHODS

2.1. Modelling approach

The model calculates the P_{CSFV} into the domestic pig population of the Netherlands by exogenous and endogenous pathways. Exogenous pathways are linked with virus sources outside the Netherlands, whereas endogenous pathways reside within the Netherlands. Examples of exogenous pathways include legal and illegal imports of pigs, genetic material, and pork products, returning livestock trucks, tourists, and air currents. Examples of endogenous pathways are laboratories working with CSFV and infected wild boar populations (6). The countries where exogenous pathways may come from are called countries of origin. Exogenous pathways only contribute to the P_{CSFV} into the Netherlands during CSF epidemics in the countries of origin.

Most probabilities calculated in the model are very low, as they are calculated per epidemic for each country of origin and separately for each exogenous pathway. Therefore, the scenario pathway approach was used as a modelling technique, and not simulation, because the scenario pathway approach requires relatively little computing time and can easily calculate extremely low probabilities (23). In the scenario pathway approach, the probability of each possible scenario leading to CSFV introduction is explicitly calculated, whereas in simulation the possible outcomes, i.e., is CSFV introduced by a certain pathway-unit[1] or not, are generated as a natural consequence of the random simulation.

Using the scenario pathway approach, the sequence of events that would ultimately lead to CSFV introduction into the Netherlands is determined, starting with the event of a pathway-unit being infected or contaminated with the virus and ending with the event of an infective viral dose being transmitted to a susceptible pig in the Netherlands. These events are ordered in a scenario tree (7, 19, 22). Only those events that are decisive in terms of whether or not a pathway-unit will transmit virus to susceptible animals are included in the scenario tree (23). Each event in the scenario tree is assigned a probability that it will occur. These are all conditional probabilities, i.e. the probability of occurrence given that all previous events have occurred.

For each pathway in the model, a scenario tree was constructed (7). To calculate the P_{CSFV} for a certain pathway, all probabilities along its scenario tree were multiplied. The scenario trees for the exogenous pathways were calculated separately for each country of origin. Combining the outcome of all scenario tree calculations gave insight into the relative contribution of countries of origin and pathways to the P_{CSFV} into the Netherlands.

The annual P_{CSFV} into the Netherlands is not a single or constant value, because it depends on the occurrence of CSF in the countries of origin, the contacts (e.g. trade) with these countries and the presence of infected wild boar populations in the Netherlands, all of which are not constant over time. To take into account the variability

[1] Unit in which a pathway is measured, e.g., a batch of animals, a metric ton of animal products or a returning livestock truck.

of some of these input parameters, probability distributions were used and model calculations were iterated using Latin Hypercube sampling (24), resulting in a range of possible output values for the P_{CSFV} into the Netherlands.

The model was constructed in Microsoft Excel 97 with the add-in programme @Risk 4.5.2. (21).

2.2. Model contents

2.2.1. Countries of origin
All EU member states except the Netherlands were included in the model as possible countries of origin. No third countries were included for two reasons: (i) import of live pigs and pork products from third countries was marginal compared to import from EU member states (less than 5% of total imports) and (ii) information available on the occurrence of CSF in third countries was not sufficiently detailed.

2.2.2. Pathways
A selection was made of all pathways that possibly contribute to the P_{CSFV} for inclusion in the model (5). Two selection criteria were used: (i) expected importance for CSFV introduction on the basis of historical data and scientific literature and (ii) availability of knowledge and data to quantify the underlying probabilities. The model structure is, however, such that additional pathways can easily be incorporated.

The major routes for CSFV introduction within the EU - since the cessation of preventive mass vaccination - were the feeding of improperly heated swill, direct or indirect contact with wild boar and animal movements (4, 12). Therefore, the exogenous pathway import of domestic pigs and the endogenous pathways direct and indirect contact with wild boar were included in the model. Furthermore, the exogenous pathway import of pork products was included, as it is one of the routes that might contribute to CSFV introduction due to illegal swill feeding. The exogenous pathway returning livestock trucks was included in the model because data could be derived from the total number of animals exported and experts considered it to be an important risk factor for CSFV introduction into the Netherlands (13). The pathways were divided into subgroups according to pig or product type in order to perform the model calculations (7).

2.3. Model structure
In Fig. 1 the general structure of the spreadsheet model is given. The model consists of four input spreadsheets, two calculation spreadsheets and one output spreadsheet. The four input spreadsheets contain all data, probability distributions and basic calculations that are required to determine the probabilities of the events in the scenario trees. In the two calculation spreadsheets the probabilities of the events in the scenario trees are computed, after which the P_{CSFV} by each pathway and from each country of origin can be calculated. In the output spreadsheet, figures and graphical representations are given of:

1. the P_{CSFV} into the Netherlands from each country of origin per epidemic and per year, and the relative contribution of exogenous pathways, the high risk period (HRP, i.e. the period between first infection and first detection), and the remainder of the epidemic (PostHRP) to these probabilities;
2. the annual P_{CSFV} into the Netherlands by exogenous pathways and the relative contribution of exogenous pathways and countries of origin to this probability;
3. the annual P_{CSFV} into the Netherlands by endogenous pathways and the relative contribution of endogenous pathways to this probability;
4. the overall annual P_{CSFV} into the Netherlands.

2.4. Calculations

2.4.1. Exogenous pathways
The P_{CSFV} by exogenous pathways is calculated in four steps. In the first step (step 1), the probability that a single pathway-unit will cause CSFV introduction into the Netherlands is calculated, given a CSF epidemic in the country of origin. The scenario trees described in section 2.1. are used in this step. The starting point in the scenario trees is that CSFV is present in the country of origin. The three main events that can be distinguished in all scenario trees are:

- is the pathway-unit infected or contaminated with CSFV?
- if so, is the infection or contamination detected or eliminated by preventive measures?
- if not, does the infected or contaminated pathway-unit come into contact with susceptible pigs in the Netherlands and transmit an infective viral dose?

The probabilities used in the scenario tree are different for the HRP and the PostHRP as control measures will be put in place in the country of origin as soon as CSFV infected pigs are detected. The Netherlands will then also take additional measures in order to prevent CSFV introduction from this country of origin.

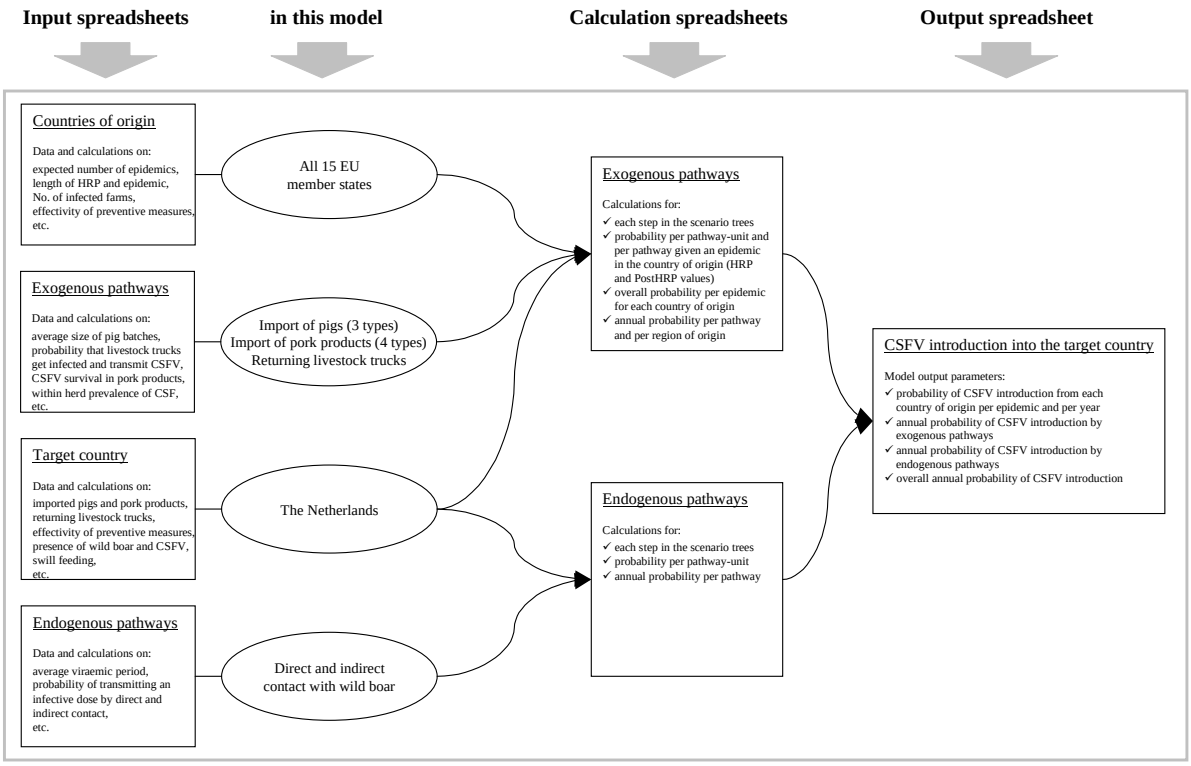

Fig. 1. General structure of the spreadsheet model for CSFV introduction.

In the second step (step 2), the probability that CSFV is introduced by a particular pathway is calculated using a binomial distribution (24):

$$P_{\{pathway\}} = 1 - (1 - P_{\{pathway\text{-}unit\}})^{n} \quad (1)$$

with $P_{\{pathway\text{-}unit\}}$ is the P_{CSFV} per pathway-unit and n = number of pathway-units going from the country of origin to the Netherlands during the period that CSFV is present. This number will also differ for the HRP and PostHRP. Therefore calculation (1) is performed separately for the HRP and PostHRP. At the end of step 2 the probabilities for the HRP and PostHRP are added as shown:

$$P_{\{pathway\_epidemic\}} = 1 - (1 - P_{\{pathway\_HRP\}}) * (1 - P_{\{pathway\_PostHRP\}}) \quad (2)$$

Steps 1 and 2 are performed for all exogenous pathways in the model. Then, in the third step (step 3), the probability of CSFV being introduced into the Netherlands during an epidemic in the country of origin is calculated by adding together the probabilities of all n exogenous pathways:

$$P_{\{epidemic\}} = 1 - \prod_{i=1}^{n} (1 - P_{\{pathway\_epidemic\}i}) \quad (3)$$

In the fourth step (step 4), the annual P_{CSFV} into the Netherlands from this particular country of origin is calculated by:

$$P_{\{year\}} = 1 - (1 - P_{\{ epidemic \}})^{N} \quad (4)$$

with N = simulated number of CSF epidemics for one year in the country of origin. This whole procedure is repeated for all countries of origin (i.e. all EU member states except the Netherlands) in the model. Hence, in total 224 scenario tree calculations are performed for the exogenous pathways (8 pathways * 2 epidemic phases * 14 countries of origin) and combined.

2.4.2. Endogenous pathways

For the two endogenous pathways, i.e. direct and indirect contact with wild boar, the P_{CSFV} is calculated in two steps. In the first step, the probability that an individual wild boar will cause CSFV introduction into the domestic pig population of the Netherlands is calculated using a scenario tree. The three main events in this scenario tree are:

- is an individual wild boar infected with CSFV?
- if so, does this wild boar come into contact with susceptible domestic pigs?
- if so, is an infective viral dose transmitted to those pigs?

In the second step, the annual probability of CSFV being introduced for each of the endogenous pathways is calculated using a binomial distribution (24):

$$P_{\{pathway\}} = 1 - (1 - P_{\{boar\}})^n \quad (5)$$

with $P_{\{boar\}}$ is the P_{CSFV} by either direct or indirect contact per individual wild boar per year and n = total number of wild boar in the Netherlands.

3. RESULTS

The model was run with trade figures from 1999. The number of iterations required was determined by the auto-stop simulation convergence option in @Risk (21). The simulation was terminated when the distribution statistics (i.e. mean, standard deviation and percentiles (in 5% increments)) of all output variables changed by less than 1%. A total of 6900 iterations were needed in order to stabilise all output distributions. The output variables selected were (i) the P_{CSFV} into the Netherlands from each country of origin per epidemic (both HRP and PostHRP) and per year, (ii) the annual P_{CSFV} by exogenous pathways and the relative contribution of each exogenous pathway to this probability, (iii) the annual P_{CSFV} by endogenous pathways, and (iv) the overall annual P_{CSFV}.

3.1. Overall annual probability of CSFV introduction

In Fig. 2 the cumulative distribution function (cdf) for the overall annual P_{CSFV} into the Netherlands by the pathways included in the model is shown. This cdf represents uncertainty about the overall annual P_{CSFV} into the Netherlands due to yearly changes in the occurrence and course of CSF epidemics in the countries of origin. In years with few and small CSF epidemics in the countries of origin, the probability is at its minimum level and in years with many and large CSF epidemics in the countries of origin, the probability is at its maximum level. The median value for the overall annual P_{CSFV} is 0.038, indicating that for 50% of the years the overall annual P_{CSFV} will be lower than this value. The 0.95 percentile is 0.17, indicating that – if the current situation remained the same – then the overall annual P_{CSFV} would only exceed 17% for five years in every century. The mean value for the overall annual P_{CSFV} is 0.056, indicating that the Netherlands can expect CSFV introduction on average once every 18 years from the pathways and countries of origin included in the model.

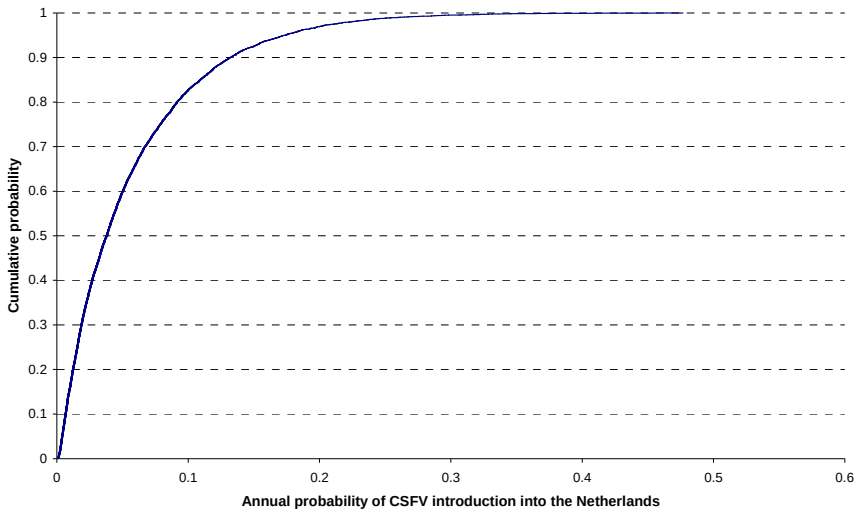

Fig. 2. Cumulative probability distribution for the annual probability of CSFV introduction into the Netherlands by 10 studied pathways.

The mean, median, 0.05 and 0.95 percentile values of the overall annual P_{CSFV} were used as the expected value (i.e. λ) in a Poisson distribution. The probabilities of 0, 1, 2, and 3 or more CSFV introductions per year for each output value are given in Table 1. Using the mean value, CSFV will not be introduced into the Netherlands in 94.56% of the years concerned. CSFV will, however, be introduced once in 5.29% of the years in question and twice in 0.15% of the years involved.

Table 1. Probability of 0, 1, 2, and 3 or more CSFV introductions into the Netherlands per year when using different model outputs for the overall annual probability of CSFV introduction

	Output used			
CSFV introductions per year	mean	0.05 percentile	median	0.95 percentile
0	94.56%	99.63%	96.31%	84.05%
1	5.29%	0.37%	3.62%	14.60%
2	0.15%	0.00%	0.07%	1.27%
3 or more	0.00%	0.00%	0.00%	0.08%

The overall annual P_{CSFV} into the Netherlands is equal to the annual P_{CSFV} by exogenous pathways. The annual P_{CSFV} by the endogenous pathways direct and indirect contact with wild boar is zero, as no CSF infections have occurred in Dutch wild boar populations in recent years (9).

3.2. More detailed results for exogenous pathways

The countries of origin and the exogenous pathways included in the model determine the annual P_{CSFV} into the Netherlands by exogenous pathways. Figure 3 gives insight into the main countries of origin contributing to this probability. Both the average probability per epidemic and the average probability per year are shown. For some countries of origin, i.e. Greece, Portugal, Austria, Finland, and Sweden, the probability that they cause CSFV introduction into the Netherlands is very small (probability per epidemic < $1.4*10^{-5}$) and could not therefore be displayed in the figure. Germany, Belgium and the United Kingdom are the countries of origin that contribute most to the annual P_{CSFV} into the Netherlands. The P_{CSFV} into the Netherlands during a single epidemic in Germany is much lower than the annual probability, which is explained by the high number of expected epidemics per year in Germany (on average 8.8 epidemics[2] per year in the period 1990-2001) (7). The annual P_{CSFV} from Belgium and the United Kingdom is smaller than that from Germany. During an epidemic in these countries, however, the probability is three to four times the annual level. This means that although the annual P_{CSFV} from Germany is higher, the Netherlands should pay more attention to the prevention of CSFV introduction from Belgium and the United Kingdom as soon as CSFV is present in one of these countries of origin. For Germany, preventive measures should be in place continuously in order to prevent CSFV introduction from this country of origin.

Figure 4 presents an overview of the relative contribution of exogenous pathways to the annual P_{CSFV} into the Netherlands. On average, returning livestock trucks contribute most to the P_{CSFV} with 64.8%. Import of breeding pigs contributes next with 17.6%. The high contribution of returning livestock trucks to the annual P_{CSFV} is mainly due to the large number of pathway-units present: the Netherlands is a major exporter of pigs ($5.14*10^6$ pigs exported versus $5.40*10^5$ pigs imported in 1999). The majority of imported pigs consist of fattening pigs (89% in 1999). Nevertheless, they contribute less to the annual P_{CSFV} than breeding pigs. This is explained by (i) the P_{CSFV} per pathway-unit, in general being highest for pigs imported for life (piglets and breeding pigs) and (ii) batch size, in general being quite small for imported breeding pigs (on average 28 pigs/batch in 1999). Hence, although the number of breeding pigs imported is only 5% of total pig imports, they account for 23% of the total number of batches imported. Import of pork products only contributes marginally to the P_{CSFV} into the Netherlands and this can for 95% be attributed to fresh/chilled and frozen pork products. 73% of the total amount of pork products imported by the Netherlands in 1999 consisted of fresh/chilled and frozen pork products. Furthermore, the probability of CSFV survival is much highest for these product types (8, 11).

[2] An epidemic is defined as one primary outbreak and all secondary outbreaks linked with this primary outbreak. The definition of a primary outbreak was derived from EU Council Directive 82/894/EEC: 'an outbreak not epizootiologically linked with a previous outbreak in the same region of a member state, or the first outbreak in a different region of the same member state'.

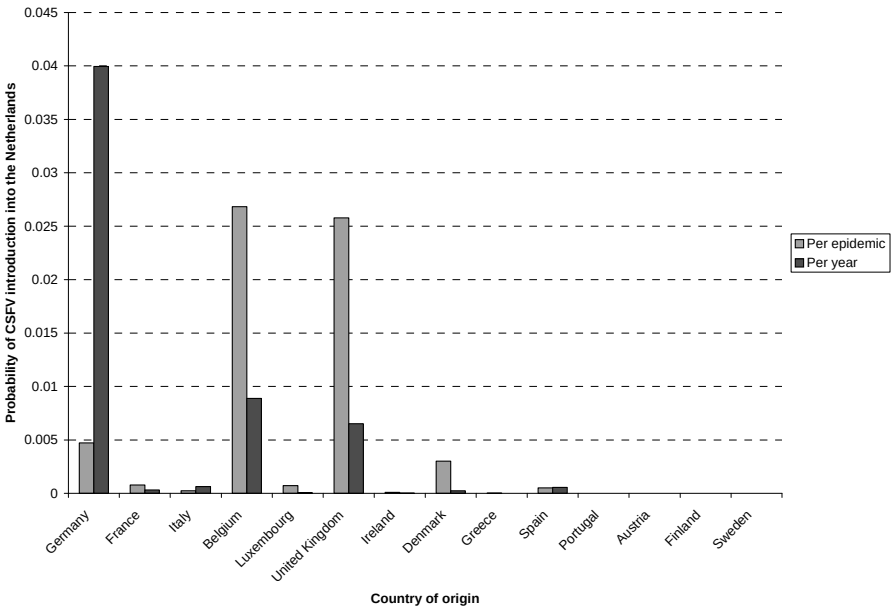

Fig. 3. Probability of CSFV introduction into the Netherlands per epidemic and per year from each country of origin in the model (all EU member states) by 8 studied exogenous pathways.

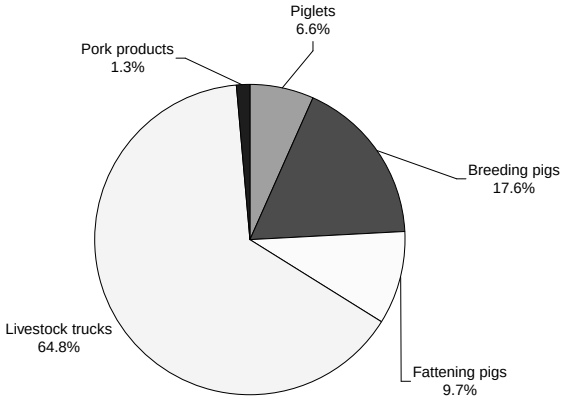

Fig. 4. Relative contribution of the exogenous pathways in the model to the overall annual probability of CSFV introduction into the Netherlands.

4. DISCUSSION

The spreadsheet model described in this paper was developed in order to obtain more quantitative insight into the main factors determining the P_{CSFV} into the Netherlands. As such, it shows which countries of origin and which pathways contribute most to the overall annual P_{CSFV}. This information can help policy makers in setting priorities for strategic preventive measures. Furthermore, the probability of CSFV being introduced into the Netherlands during a single epidemic in each country of origin has been calculated, indicating in which circumstances additional tactical preventive measures are required. The model can estimate the impact of both strategic and tactical preventive measures as well by changing relevant input parameters. Current model calculations were performed for the Netherlands. Calculations can, however, easily be performed for other member states of the EU. Only the values of the input parameters in the input spreadsheet ‘target country’ should be changed for this purpose.

4.1. Modelling approach

The scenario pathway approach was used to calculate the annual P_{CSFV}. It was assumed that, as long as this probability is small (say $p \leq 0.2$), it could be used as the expected value (i.e. λ) in a Poisson distribution in order to estimate the expected number of CSFV introductions per year (see Table 1). A simulation model would have led directly to this result. Simulation, however, would have required many iterations to get only a few 'hits', i.e. virus introductions, because the probabilities calculated by the model are very small. The scenario pathway approach, on the other hand, made it possible to perform model calculations rather quickly (23) (6900 iterations in less than five minutes).

A general property of the scenario pathway approach is that the more events in a scenario tree, the smaller the calculated probability of occurrence of the adverse event, since the probabilities assigned to the events in the tree are all ≤ 1. Therefore only those events that are decisive in whether a pathway-unit will transmit CSFV to susceptible pigs in the Netherlands were included in the scenario trees. The number of events in the scenario trees for the exogenous pathways differed. It was least for the import of piglets and breeding pigs and most for returning livestock trucks. This resembles reality: CSFV introduction by pigs imported for life only requires a few steps, whereas CSFV introduction by returning livestock trucks is a more indirect transmission route, requiring that the livestock truck visited an infected farm in the country of origin and got contaminated, that the virus was not removed by cleansing and disinfecting either in the country of origin, or in the Netherlands, that the virus survived the journey from the country of origin to the Netherlands, that the livestock truck came into contact with susceptible pigs in the Netherlands and that an infective viral dose was then transmitted. Despite this, the pathway returning livestock trucks contributed most to the annual P_{CSFV} into the Netherlands due to the high number of pathway-units present.

Using the scenario pathway approach implied that the complex reality of CSFV introduction was reduced to a set of scenario tree calculations. Model limitations should be kept in mind when interpreting its output. Each iteration of the model resembles one year. In every iteration one value is sampled for the length of the HRP, the length of the epidemic, and the number of infected farms in each country of origin. Hence, when the simulated number of epidemics for a country of origin exceeds one, all epidemics are described by the same characteristics. For most countries of origin in the model, i.e. for most EU member states, the expected number of CSF epidemics per year is, however, less than one (7). Another limitation is that the model treats each country of origin as a homogenous entity, without taking spatial variability into account. Hence, the calculations assume that CSF epidemics are evenly distributed over a country of origin and that exogenous pathways originate from all over the country. In reality, however, it might be that epidemics occur mainly in those parts of a country of origin where most pathway-units are exported from to the Netherlands. The model then underestimates the annual probability that CSFV is introduced into the Netherlands from this country of origin. The annual probability will, however, be overestimated when epidemics occur mainly in areas different to those from where most exogenous pathways are exported.

4.2. Results

The ultimate aim of the model was not to give exact estimates of the P_{CSFV} into the Netherlands, but to gain more insight into which pathways and countries of origin contribute most to this probability. Model results as presented in Fig. 3 and 4 gave clear insight into this matter for the Netherlands. If necessary, model results can be analysed in even more detail to reveal the major causing pathways from a specific country of origin.

The annual P_{CSFV} into the Netherlands calculated by the model is quite low when compared with expert estimates (13, 18) and recent history (the Netherlands experienced one or more primary CSF outbreaks in 1990, 1992 and 1997 (4, 10)). The model most probably underestimates the overall annual P_{CSFV} as not all pathways contributing to the P_{CSFV} were included in the model, nor were third countries (see section 2.2.). Absolute values of model outcome can therefore not be considered as 'true' values for the P_{CSFV}.

Only exogenous pathways contributed to the annual P_{CSFV}, as no CSF infections have occurred in Dutch wild boar populations in the recent past (9). This is, however, not a guarantee that Dutch wild boar populations will remain free of CSFV in future. Contacts between Dutch and German wild boar populations cannot be excluded in the southern part of the Netherlands, while CSFV is endemic in parts of the German wild boar population (9, 15). Assuming a 10% seroprevalence for CSFV in the Dutch wild boar population increased the average annual P_{CSFV} by approximately 60% (results not shown). This indicates that it is worth the effort to ensure that the wild boar population remains free of CSFV.

In general, the P_{CSFV} into the Netherlands was highest during the HRP of epidemics in the countries of origin. To give some examples, the mean P_{CSFV} into the Netherlands during an epidemic in Germany can for 88% be

attributed to the HRP. For Belgium this is 93% and for the United Kingdom as high as 97%. It is, however, impossible for the Netherlands to take additional preventive measures during the HRP of epidemics in the countries of origin because the presence of CSFV has not yet been detected in this phase of an epidemic, i.e., nobody knows it is there. Reducing the length of the HRP in the countries of origin is thus an important tool in terms of diminishing the P_{CSFV}. What-if analysis showed that a short HRP in the countries of origin indeed led to a considerable reduction of the P_{CSFV} into the Netherlands (results not shown) (7). Early detection of CSF infections is thus important, even more so as a short HRP will in most cases go with a shorter total length of the epidemic and fewer infected farms, hence decreasing the total economic losses for the country experiencing the epidemic.

4.3. Concluding remarks

Model behaviour was verified by what-if analysis (results not shown). Outcome of the different scenarios resulted in a reasonable change of the mean annual P_{CSFV} in the most likely direction (7). Therefore model structure and calculations were considered adequate. A comparison between model output and data from the real system in order to validate the model was impossible. Only few CSFV introductions occurred in recent years in the Netherlands and since such introductions are largely determined by chance (Poisson process), the number of observations is far too few to determine the annual P_{CSFV} or to draw conclusions on the main causing factors (pathways and countries of origin). Face validation of model output was considered impossible either, because of the small probabilities calculated. The annual P_{CSFV} into the Netherlands calculated by the model varied between $2.5*10^{-4}$ and $4.8*10^{-1}$. Changes in such small numbers are difficult to interpret, especially for people not familiar with quantitative risk analysis.

Only limited data was available to quantify all input parameters. Furthermore, data obtained from CSF epidemics in the past, experiments or simulations might already be outdated due to rapid changes in, for example, trade patterns, preventive measures, and control strategies applied. Hence, the model contains many uncertain input parameters. For these parameters point estimates were used. The next step will be to perform an extensive sensitivity analysis to investigate the impact of these uncertain input parameters on model output (see e.g. Kleijnen (14)). Such an analysis will also indicate priorities for further empirical research in the epidemiological field of CSF. Furthermore, it can support model validation by showing whether input parameters have effects that agree with expert's prior knowledge (14).

The model described only contains the first two steps distinguished in risk assessment, i.e., release and exposure assessment. It calculates the P_{CSFV} into the Netherlands, i.e. the probability of a primary outbreak. Only when also the third step, i.e. consequence assessment, is performed, the risk of CSFV introduction into the Netherlands can be estimated. Mangen et al. (16) calculated the epidemiological and economic consequences of CSFV introduction in the Netherlands. Simulations were performed with the primary outbreak herd located in either a sparsely or a densely populated livestock area (SPLA or DPLA) (4). They concluded that epidemics in an SPLA were smaller in size and length than epidemics in a DPLA, especially when only the minimum EU control strategy was used (16). A regional approach directing measures to prevent CSFV introduction especially at DPLAs might thus yield a higher reduction of the risk of CSFV introduction. Decreasing the P_{CSFV} by preventive measures is only one way to reduce the risk of CSFV introduction. More adequate control measures to reduce the size and length of the epidemic, once CSFV has been introduced, is another approach to diminish the risk of CSFV introduction. Further research is needed to determine which approach is most cost-effective.

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RISK-MAPPING OF BOVINE HYPODERMOSIS IN BELGIAN CATTLE HERDS

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ABSTRACT

The objective of this study was to map the presence or absence of *Hypoderma* spp. according to local climatologic, geographic and demographic risk factors.
This survey was carried out on herds of all types from December 1997 to March 1998, which were included in a national infectious bovine rhinotracheitis and paratuberculosis survey. All animals over 24 months of age were blood sampled in the selected herds and an ELISA test was carried out on pooled serum samples of ten animals.
The association between various environmental risk factors and the occurrence of positive serological reactions in cattle was evaluated using a logistic regression model. The resulting model was used to produce a risk map of serological reactivity in cattle.
Mixed-type and beef cattle herds have a more than four-fold and two-fold increase in the odds of being *Hypoderma*-positive, respectively compared with dairy herds, after adjustment for herd size and environmental factors. The latter included as significant factors daily minimum temperature and daily mean rainfall, as well as land cover type.

SAMENVATTING

Het doel van deze studie was de aan- of afwezigheid van *Hypoderma* spp. in kaart te brengen volgens locale klimatologische, geografische en demografische risico factoren.
Deze survey werd gedaan op runderbeslagen van alle types die enkele jaren geleden, van december 1997 tot maart 1998, bemonsterd waren voor een infectieuse boviene rhinotracheïtis en paratuberculose survey. In deze toevallig geselecteerde beslagen werden van alle dieren van minstens 2 jaar oud bloedstalen genomen. Op de mengstalen komende van 10 individuele sera werd een ELISA test uitgevoerd.
De associatie tussen verscheidene omgevings-risico factoren en het voorkomen van serologische reacties bij runderen werd geëvalueerd door een logistisch regressie model. Het uiteindelijke model werd gebruikt om een risico kaart te maken van seropositiviteit bij runderen.
Beslagen van het gemengde type alsook vleesvee beslagen hadden een meerkans van respectievelijk meer dan vier en meer dan twee om *Hypoderma* positief te zijn, vergeleken met melkvee beslagen. Dit na het in aanmerking nemen van de beslag grootte en de omgevings-factoren. Significante omgevings-factoren waren de dagelijkse minimum temperatuur, de dagelijkse gemiddelde regenval, alsook het type bodembedekking.

1. INTRODUCTION

Warble flies (*Hypoderma* spp.) are common parasites of cattle in the northern hemisphere. Their economic importance is reflected in the different eradication schemes undertaken with success in several countries, especially Belgium's neighbouring countries (The Netherlands [22], France [6], Germany [14], Great-Britain [25, 19, 20]). Belgium discontinued its control plan in the early 80's and since then has been under increasing pressure to control hypodermosis.
Very few data are available about hypodermosis in Belgium. Only one localized survey done by Lonneux *et al.* (16) showed a high seroprevalence in two provinces.

The spatial distribution of vector-borne and parasitic diseases is restricted by the habitat preferences of the vector and the parasite and/or the host's geographical range. The ecology of the vector or the parasite and the environmental determinants of their distribution are of prime importance in the transmission, surveillance and control of vector-borne and parasitic diseases (11).
But only in vitro studies investigating the relationship between the presence of warble flies and potential risk factors are reported in the literature (18, 17, 10, 2, 3).

2. MATERIAL AND METHODS

2.1. Survey design

The survey was carried out on herds of all types during the winter 1997-1998 (4, 5). A stratified one-stage cluster sample design, with province as the stratification variable and proportional allocation of the number of herds amongst province according to total number of herds was realized (24). The sampling frame consisted of all cattle-keeping holdings in Belgium which are included in the SANITEL-Cattle database.

All animals over 24 months of age were blood sampled in the selected herds and their sera were aggregated into pools of maximum 10 animals. A herd was defined as *Hypoderma*-positive if at least one positive pooled serum sample was detected. The pooled serum samples were tested for antibodies against *Hypoderma* spp. with a commercially available ELISA test kit (Calfcheck-hypodermose®, Vétoquinol, France). All samples were tested according to the manufacturer's instructions.

Information about climatic risk factors was provided by the Royal Meteorological Institute of Belgium (3 Avenue Circulaire, 1180 Brussels, Belgium) for the years 1996-1997. Only data from April 1st to November 30th were used, the longest period while flies could be found in Belgium. Data obtained from the ground stations were minimum and maximum daily temperatures, daily rainfall in mm and daily relative air humidity in %. The mean daily minimum, maximum, average and range of temperatures were calculated for each station over the above period as well as the mean daily rainfall and mean daily relative air humidity.

The National Geographic Institute of Belgium (13 Abbaye de la Cambre, 1000 Brussels, Belgium) provided the Belgian CORINE (Co-ordination of Information on the Environment) database on land cover information. The data is recorded at a resolution of 1:100,000 for 44 different land cover types, of which 32 are present in Belgium. Homogeneous cover of one single class is digitized down to a smallest area of 25 ha. The land cover type covering at least 75% of the cell was assigned when mixed land cover types were present in a 25ha cell.

2.2. Data analysis

The distribution of the herds was displayed over a map of Belgium, using the geographical information system software ArcView 3.2 (ESRI, Redlands, CA, USA). The herd location data was converted into continuous surfaces using the kernel-density interpolation function of ArcView, showing the case occurrence as intensity per square kilometres. The kernel density was estimated using a bandwidth (τ) of 15 km and a cell size of 1500 m.

Disease clustering was investigated using the spatial scan statistic (SaTScan 2.1, National Cancer Institute, MD, USA) based on 999 Monte Carlo iterations and a maximum spatial cluster size set to 50% of the total population at risk.

The kriging technique was used to generate raster surfaces from the various climatic variables with the ArcView add-in software Kriging Interpolator 3.2 (http://www.nieuwland.nl). The kriging estimates were converted into vector contour data (contour interval .05 °C, .05 mm or .05 %). The spatially relevant environmental and land

cover data were linked to each herd record using GIS overlay functions.

The occurrence of the warble fly exposure in cattle was then evaluated using a logistic regression model (Stata 7.0, Stata Corp., TX, USA). Continuous scale variables (herd size, minimum temperature, maximum temperature, average temperature, average temperature range, rainfall, relative air humidity) were categorized by quintiles. The 32 land cover types present in Belgium were grouped into 6 classes (urban, agricultural, pastures, forests, waste land, and wet land). The likelihood ratio test was used to assess model fit in a backward variable selection procedure. Independent variables measured on a continuous scale were tested for departure from a linear trend. The variables included in the final model were tested for interaction effects. Spatial dependence between observations was taken into account through use of the robust variance estimator for clustered data (26, 7, 12, 13). Administrative boundaries (provinces) identified the subgroups or clusters.
The predictive accuracy of the model was assessed using a receiver operating characteristic curve (ROC) (8).
The most important environmental factors were determined using logistic regression, from subsequent analyses including only climatic and land cover variables.
This final model regression equation was used to generate a GIS raster layer expressing disease probability based on local environmental conditions. This was done using the map calculator function of ArcView based on the following equation (24):

$$p_i = \frac{\exp(\alpha + (\beta_j \times riskfactor_j))}{1 + \exp(\alpha + (\beta_j \times riskfactor_j))}$$

where α is the intercept and β_j is the variable's coefficient in the logistic regression model

3. RESULTS

A total number of 844 herds were sampled. Of those, 454 herds were withdrawn as insufficient serum was available for testing, being used as part of a national IBR and Johne's disease survey, or because the test gave erroneous results. Also, some herds had to be excluded because no geographic location information was recorded in the SANITEL-Cattle database. As a result, a total of 390 herds remained in the analysis, of which 362 had geographic information, 361 had data about size and 349 about herd type.

The map of positive and negative herds is shown in Figure 1 as well as a kernel density map of positive herds. A clear pattern can be seen with respect to the disease distribution. The Walloon region in the south of the country has mainly positive herds while in the northern part of the country, Flanders, the number of positive herds is lower but not evenly distributed. There are three large areas with a high proportion of positive herds across the country but the Provinces of Antwerp and Limburg along the border with the Netherlands are mainly free.

The spatial scan statistic applied to the dataset showed that the most likely cluster represents negative herds (relative risk of 0.29, p = 0.001) in the provinces of Antwerp and Limburg. There are three significant secondary clusters which are (ordered according to their likelihood ratio):
- East of Belgium (province of Liège, Herve, German border) with a relative risk (RR) of 1.88 (p = 0.001) compared to the surrounding area, 45 cases (23.96 expected) out of a population of 49
- Province of Hainaut, RR = 1.84 (p = 0.001), 35 cases (19.1 expected) out of 39
- Eastern province of Flanders, RR = 0.20 (p = 0.006), 3 cases (15.2 expected) out of 31

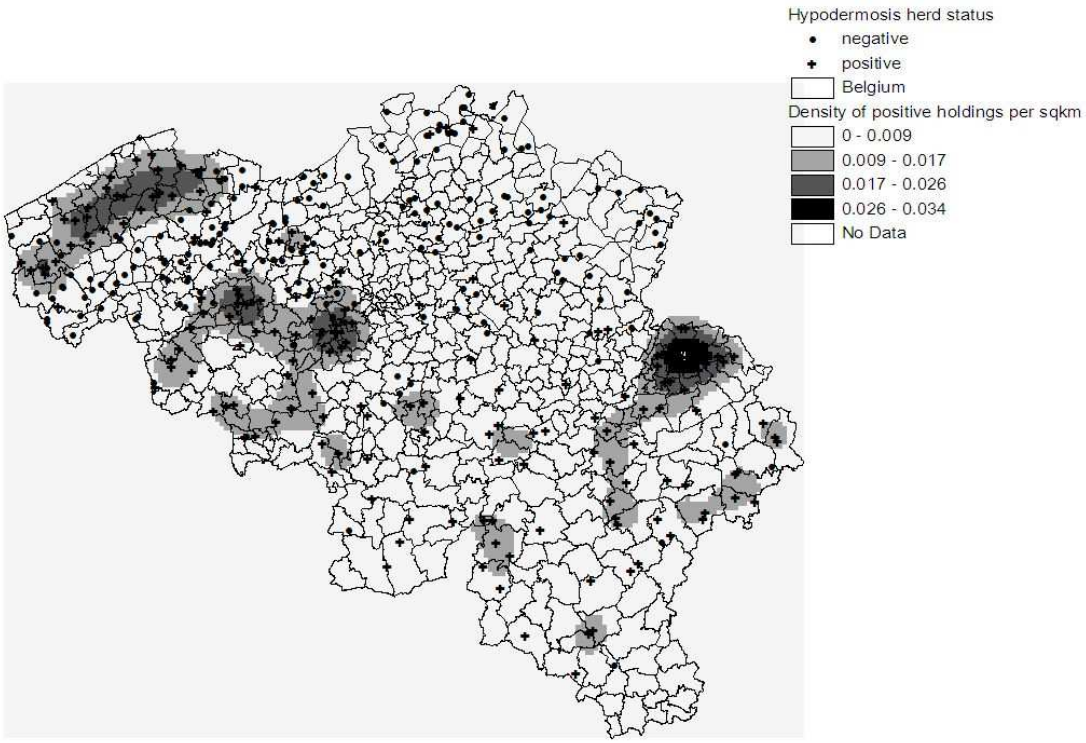

Figure 1 : Serological hypodermosis herd infection status and kernel estimate of positive density of infected holdings

A logistic regression model was developed ignoring the dependence in the data structure and representing continuous variables as categorical variables derived from quintiles of size and climatic variables. This model included the variables mixed herds (vs. dairy herds), minimum temperatures, maximum temperatures, rainfall and pastures landcover (urbanized area being the baseline) (Table 1). No statistically significant association was found between serological *Hypoderma* herd status and the potential risk factors average temperatures, range of temperatures and relative air humidity. Taking account of dependence between observations in the model changed the output to some extent (Table 2). The variable beef herd now becomes significant whereas maximum temperature is not anymore.

Table 1: Logistic regression model of risk factors (without robust estimator) (* = standard error)

Variable	Odds ratio	SE*	P-value	95% confidence interval	
Mixed herd	4.32	1.76	<0.001	1.94	9.59
Beef herd	1.97	0.75	0.074	0.94	4.14
Quintiles of herd size	1.42	0.17	0.003	1.12	1.78
Quintiles of mean daily minimum temperatures	0.68	0.08	0.001	0.55	0.85
Quintiles of mean daily maximum temperatures	0.60	0.07	<0.001	0.48	0.76
Quintiles of mean daily rainfall	1.32	0.15	0.016	1.05	1.66
Agricultural land	0.74	0.23	0.320	0.40	1.35
Pastures	0.35	0.18	0.043	0.13	0.97

Table 2: Logistic regression model (with robust estimator)

Variable	Odds ratio	SE	P-value	95% confidence interval	
Mixed herd	4.32	1.16	<0.001	2.55	7.31
Beef herd	1.97	0.65	0.040	1.03	3.77
Quintiles of herd size	1.42	0.15	0.001	1.15	1.74
Quintiles of daily minimum temperatures	0.68	0.07	<0.001	0.55	0.84
Quintiles of daily maximum temperatures	0.60	0.19	0.111	0.33	1.12
Quintiles of mean daily rainfall	1.32	0.18	0.041	1.01	1.73
Agricultural land	0.74	0.27	0.402	0.36	1.51
Pastures	0.35	0.14	0.007	0.17	0.75

A ROC curve was produced, showing sensitivity and specificity for this last model (Figure 2). The area under the curve was 0.83.

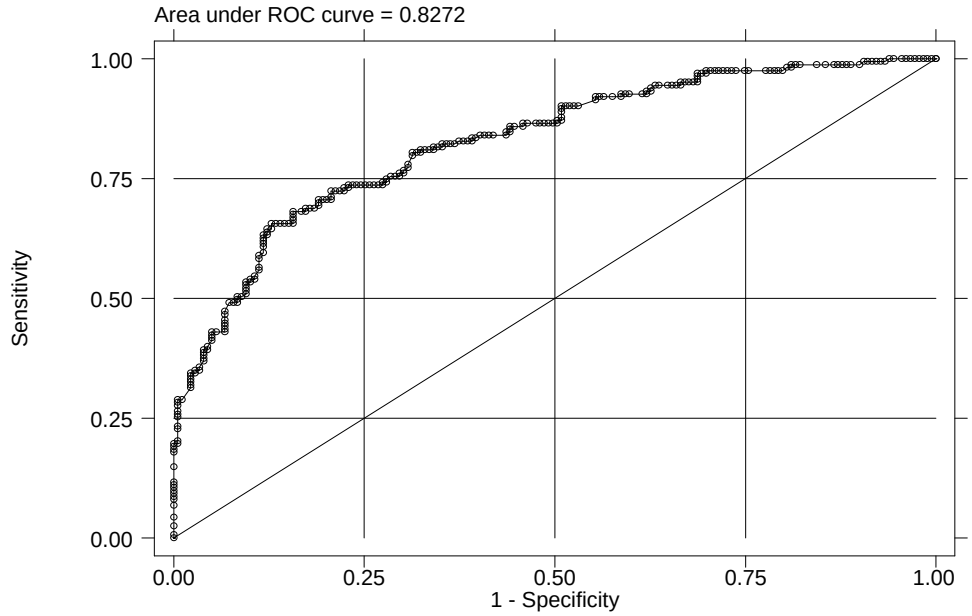

Figure 2: Receiver operating characteristic curve

The pasture variable was the only significant land cover risk factor. All land cover types other than pasture were used as the reference category and a new logistic regression model including only climatic variables and this binary land cover variable was produced. The coefficients expressed at a log odds scale were used to produce a disease risk map based on the most important environmental risk factors (Figure 3).

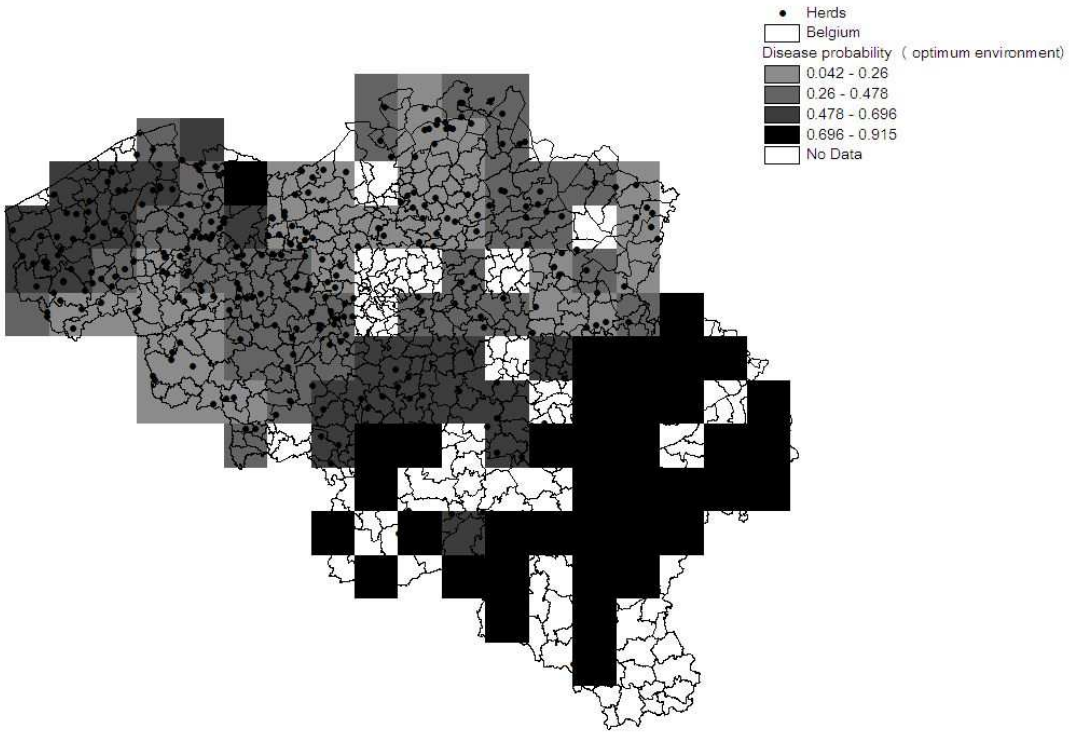

Figure 3: Predicted hypodermosis risk map based on environmental data

4. DISCUSSION

Hypodermosis is endemic in Belgium but its distribution is not homogeneous across the country. While the southern part of the country has a very high prevalence, the northern part can be divided into two zones, one positive along the coast and one negative elsewhere.

Logistic regression can be used to model a dichotomous (presence/absence) dependent variable, as a function of a series of independent variables, either continuous or categorical. Under this assumption of independence any event has an equal probability of occurring at any position in the study region (no first order effects) and the position of any event is independent of the position of any other: events do not interact with one another (no second order effects) (1). But it is very likely with spatial data that events will vary over the study region (heterogeneity) and/or that occurrences of events will be correlated between neighbouring regions (spatial dependence). Therefore it is important to control for spatial autocorrelation in the disease pattern, if present. Not allowing for this autocorrelation violates the rules of independence for parametric data analysis and this may lead to underestimates of the errors of model parameters and to overestimates of the level of significance (21).
The method used in the current study was the robust variance estimator for clustered data. This method gives consistent estimates of the regression parameters and a robust estimation of the variance when dependence among observations from the same cluster is present (26, 7, 12). This method usually results in larger standard errors and p-values. With the current data analysis five variables out of eight have smaller standard error and p-value after adjustment for clustering. This can happen when the intra-cluster correlations are negative.

The final logistic regression model indicates that mixed and beef herds had an increased odds of being *Hypoderma*-positive compared with dairy herds of more than four fold and about two fold respectively. It is generally acknowledged in the literature that dairy breeds are at a particular risk (2, 3) due principally to their management. Avermectin and milbemycin are not allowed in dairy cattle, only eprinomectin can be used which make dairy cattle less likely to be treated against hypodermosis. Treatment of hypodermosis is much easier in beef cattle and the larvae are very susceptible to modern drugs. But the treatment has to be applied at the appropriate time in order to eradicate hypodermosis from the herd. It is also important to note that modern

management of dairy cattle involves keeping animals inside and less time is spent outside on pasture. The cost of treating heavy beef cattle should also be taken into account as normal dosage of ivermectin given to adult animals can be very expensive for some holders.
Herd size appeared also as a risk factor after controlling for herd type and environmental factors. It appears that larger herds are at increased risk of being *Hypoderma*-positive than smaller ones. Management of parasites control in a large herd could be more difficult and also more expensive.

The significant climatic factors in the model were daily minimum temperatures and daily rainfall. Heavy rainfall increased the risk of disease, contrary to what has been found in the literature (23, 17, 15, 10). Minimum temperature was a protective factor in Belgium but the risk increases as the temperature increases. However, the upper limiting temperature might not be reached in the country as maximum temperature was not a significant factor.

The observed effect of the different land cover types was unexpected at first sight. Compared to the baseline urban area, agricultural land was not significantly different and pastures were at decreased risk. The baseline consisted of continuous or discontinuous urban areas, industrial zones, and sport and leisure equipments. Cattle are more likely to be present on agricultural land, especially on pasture, but not in urban zones. This would have given an odds ratio greater than one for these areas. But Belgium is a densely populated country and a large part of the countryside is considered as a discontinuous urban area, according to the CORINE database which codes landcover types according to a European standard. In fact, according to this classification most of the farms were considered to be in an urban area and this resulted in the above result. A more accurate analysis using landcover classification data would require a higher spatial resolution but this is not currently available for Belgium.

The risk map shows that the south of the country is largely suitable for the fly. The situation in Flanders is less uniform and the risk according to environmental data is lower. But we can observe that the region along the coast can be linked to the Walloon region in the south. This situation can cause problems during an eradication campaign if it is not implemented at the national or regional level due to possible re-infestation from neighbouring regions.

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Draft MEMORANDUM OF UNDERSTANDING

for the implementation of a European Concerted Research

designated as

COST Action 920

"Foodborne Zoonoses: a Co-ordinated Food Chain Approach"

A.H. Havelaar and H.J. van der Fels-Klerx

www.cost920.com

The Signatories to this Memorandum of Understanding, declaring their common intention to participate in the concerted Action referred to above and described in the Technical Annex to the Memorandum, have reached the following understanding:

1. The Action will be carried out in accordance with the provisions of document COST 400/94 "Rules and Procedures for Implementing COST Actions", the contents of which the Signatories are fully aware of.
2. The main objective of the Action is to better control foodborne zoonotic infections.
3. The overall cost of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at Euro 30 million in 2000 prices.
4. The Memorandum of Understanding will take effect on being signed by at least five Signatories.
5. The Memorandum of Understanding will remain in force for a period of five years, unless the duration of the Action is modified according to the provisions of Chapter 6 of the document referred to in Point 1 above.

Draft Technical Annex

A. Background

Microbiological food safety in Europe and the rest of the developed world is assessed in terms of acceptable levels of risk of humans contracting food-related illnesses. For certain pathogens such as Verocytotoxigenic *Escherichia coli* (VTEC) the acceptable level of risk may be as low as zero. Our food-supply chains whether international, national or local provide numerous opportunities from farm to fork for the contamination of food and water for human consumption.

Given the enormous number and variety of potential contamination sources along the food processing chain, it is unrealistic to imagine that all food can be kept free from contamination throughout the process. However, it is now recognised that the most appropriate way to enhance food safety is to identify the critical contamination points affecting the safety of the final product. It should then be possible to introduce the most effective measures to minimise or eliminate the possibility of contamination from food production and processing to distribution, preparation and consumption. Advances in the twentieth century such as pasteurisation, refrigeration and more recent improvements in hazard analysis and control along the foodchain have contributed to improvements to the microbiological safety of most foods. Nevertheless, foodborne disease remains a significant cause of morbidity and mortality in Europe and the rest of the developed world. A recent national surveillance study in England and Wales revealed that one in five people developed infectious intestinal disease each year, and that *Campylobacter* and *Salmonella* were the most common bacterial pathogens isolated (1). In the United States it has been estimated that foodborne diseases may cause up to 76 million illnesses, 325,000 hospitalisations, and 1800 deaths each year (2). In the same study *Campylobacter*, nontyphoidal *Salmonella* and VTEC accounted for the vast majority of bacterial foodborne disease requiring hospitalisation. *Toxoplasma gondii* and Norwalk-like viruses accounted for the great majority of severe cases of parasitic and viral infections respectively. These two recent studies bear out the generally high estimated national and international human incidence of foodborne pathogens, especially *Salmonella* and *Campylobacter* in most parts of the developed world (Table 1).

Table 1. Estimated 1997/98 incidence of bacterial foodborne zoonoses

Incidence per 100,000 population

	Europe[a]	USA[b]	Australia[c]	Japan[d,e]
Salmonellosis	51	14	38	7
Campylobacteriosis	53	25	100	ND
VTEC infections	0.7	2.0	ND	1.7
Listeriosis	0.3	0.5	0.4	ND
Yersiniosis	4.0	1.0	1.5	ND
Brucellosis	1.2	ND	ND	ND

a) European Commission, 1999 (3), b) Anon, 1999 (4), c) O'Brien et al., 1999 (5), d) Anon, 1997 (6), e) Anon, 1998 (7)

Taken together this data confirms the continuing importance of food as a source of human illness and, in particular, of foodborne zoonotic diseases arising from the infection of farmed livestock throughout Europe with these microbial pathogens.

Estimates for economic loss covering health costs, lost production and family-related expenses are imprecise due to the paucity and non-standardisation of data and approaches to provide the estimates. However, in England and Wales *Salmonella* cases alone could cost in excess of £100 million each year and in the US in 1996 it has been estimated that *Campylobacter* spp., *Salmonella*, VTEC O157 and *T. gondii* cost the public purse 0.8-5.7; 0.9-3.6; 0.16-0.3 and $3.3 billion respectively (8).

As surveillance systems and epidemiological tools have developed and improved, increasing numbers of foods, and in a number of cases the source of contamination, can be traced and linked to major food poisoning outbreaks. For example, *S. enteritidis* in poultry and in particular egg products, *Campylobacter* in poultry meat products, and *E. coli* O157 in ground and sliced beef and contaminated dairy produce. Many of these outbreaks could have been avoided through correct hygiene procedures in the handling of foods. However, only a co-ordinated farm to fork approach is likely to achieve permanent and significant reductions in foodborne infections in the future. Countries in the European Union operate within the framework of the 1992 Zoonoses Directive 92/117/EEC to monitor and control *Salmonella* in poultry flocks (9). The strategy focuses on the poultry breeding and layer sector and has, to a greater or lesser extent, demonstrated that an integrated and co-ordinated approach to controlling *Salmonella* in domestic livestock is feasible and leads to a sustained reduction in human incidences. This is best exemplified by examining the relative effectiveness of the Danish control programmes via the published estimated food sources of human salmonellosis in Denmark 1988 - 1998 (Fig. 1)(10).

Although admitted to be a rather crude assessment it clearly shows the dynamics in the changing sources of human salmonellosis over a 10-year cycle. Denmark experienced three waves of human salmonellosis, where the majority of cases were attributed to three different food sources. In the late 1980s broilers were the major food source, whereas in the mid 1990s pork products increased in significance and from the mid 1990s to the end of the century eggs and egg products predominated.

At each of the peaks of human salmonellosis new control programmes in animals were implemented and resulted in a reduction of human cases attributable to that particular food source. This is the clearest evidence to date that intensive and co-ordinated *Salmonella* control programmes in animals can effect a reduction in human salmonellosis from that food source. It also provides sound evidence that controlling foodborne pathogens in animals is a very important control point in the entire foodchain.

However, some successes in reducing *Salmonella* infections should not detract from other real challenges for the future. *Campylobacter* infections are now the commonest cause of bacterial foodborne infections and in a recent study in the UK, ranked second in the list of organisms isolated from cases of infective diarrhoeal infections. Human VTEC O157 cases have continued, implicating a variety of contaminated food sources and direct animal to human contact. *Cryptosporidium* continues to cause large outbreaks through contamination of the water supplies. Increase and emergence of antibiotic resistance and multiply resistant bacterial strains, some of which have arisen from animals and their environment, highlights the immediate requirements for improved surveillance methods and alternative strategies for controlling infections. Emergence of new *Salmonella* epidemic strains e.g. *S. typhimurium* DT104 and continued evolution of VTECs highlights the need for robust early-warning systems and greater understanding of the mechanisms of genetic mutation and adaptation (11).

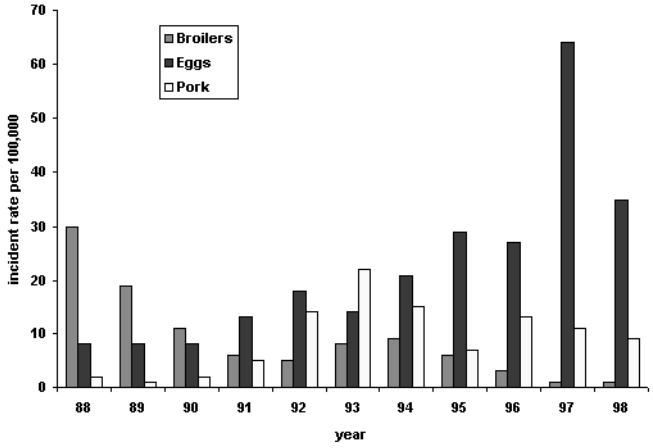
The farm to fork concept has encouraged closer co-operation between all sectors of the food industry and as stated above achieved some considerable successes in reducing *Salmonella* in livestock. However, it is likely that the most cost effective way within limited resources in targeting longer term strategies to control foodborne zoonotic infections in animals, is to focus on emerging trends in human infections caused by the major foodborne zoonotic pathogens, since most of these organisms are asymptomatic in animals. Thus integrated research and surveillance of animal and human foodborne zoonotic infections is crucial to future strategies. For example, rapid dissemination of changing trends between veterinary and medical sectors to improve response to emerging pathogens, changes in antimicrobial resistance patterns, co-ordination of surveillance systems that can accurately identify results of intervention methods implemented along the food chain and co-ordination and integration of research objectives. Thus the original farm to fork approach often ignored the key component along the food chain which should help to formulate future strategies i.e. seamless and co-ordinated foodchain strategy. It is also now recognised that many of the most effective solutions will not be pathogen specific but focus on factors common to many different organisms in the foodchain. At present there are some Europe-wide initiatives such as CAMPYNET for the harmonisation of subtyping schemes for campylobacter, a Concerted Action project on VTEC and an EC research project on risk assessment on *Cryptosporidium parvum*. COST Action funding is a very efficient means of linking research and surveillance activities across Europe. In particular, by drawing together specific pathogen –based information from various European and national initiatives this COST Action will facilitate real generic discussions and studies in the control of foodborne zoonoses. Thus, this COST Action seeks to complement and build upon COST Action 97 (Pathogenic Microorganisms in Poultry and Poultry Products) to cover the major livestock species and to include all stakeholders along the foodchain. This will provide a framework for the rapid transfer and dissemination of information between veterinary, food and medical sectors; opportunity to develop generic, integrated research and surveillance proposals through future EC proposals; exchange of workers between key veterinary and medical organisations and to develop new relationships across Europe. These activities will be addressed in the various activities described below.

B. Objectives and benefits

The main objective of the Action is to better control foodborne zoonotic infections.

This will be achieved by focusing on four key secondary objectives that are closely inter-linked and will be implemented through Working Groups (WG). Firstly, there will be continued emphasis on the development and harmonisation of diagnostic and typing methods. Meeting this objective is crucial to the inter-comparability of surveillance data along the foodchain and between countries and regions in Europe. Progress has been made in areas such as *Salmonella* and VTEC O157 detection but much more effort is needed, in particular, to harmonise

Fig.1. Estimated important food sources of human salmonellosis in Denmark, 1988-1998



molecular typing techniques and methods for measuring antimicrobial resistance. Secondly, the emergence of new foodborne pathogens such as VTEC (O157 & non O157), pandemic *S. typhimurium* DT104 strain and multi-resistant organisms highlight the need to provide early warning or alert surveillance systems for potential emerging pathogens. The development of Salmnet and Enternet are contributing to developments. However, they need to be developed throughout Europe and along the whole foodchain so that changing trends of foodborne pathogens anywhere along the processing chain can be identified and the information disseminated to the rest of Europe. Thirdly, by applying a quantitative risk assessment to the foodchain, critical intervention points and areas requiring further surveillance and/or research can be identified and contribute to improved cost-effective control programmes that also offer new opportunities to countries in which control methods have hitherto been considered too expensive. Lastly, a greater understanding of the mechanisms of survival of zoonotic pathogens along the foodchain will aid risk assessment. For example, techniques are now emerging whereby one can link the identification of the hazard (potential pathogen) with a detailed molecular profile of the organism including presence or absence of key survival and virulence genes. This has tremendous potential in the application of likely risk associated with the isolation of new pathogens along the foodchain.

C. Scientific Programme

The scientific programme focuses around working groups:

Working group 1. Harmonisation of diagnostic and typing methods.

The task of this group will be to improve the standardisation and comparability of diagnostic and typing methods for the major zoonotic foodborne pathogens encountered in Europe
Key objectives of the WG will be:

a. To review current diagnostic and typing methods used in Europe.
b. To prioritise methods for improved harmonisation
c. To provide a focus for dissemination of inter-comparability ring trials
d. To facilitate standardisation and quality across Europe through training and exchange of methods

The expected benefits will be improved standardisation and comparability of surveillance data across Europe

Working Group 2. New and emerging foodborne pathogens

The task of this group will be to augment existing frameworks in Europe such as the Enternet system for human bacterial pathogens to provide a comprehensive early warning process for the rapid dissemination of information on new and emerging foodborne pathogens.

The main objectives of this WG will be:

a. To instigate a network within Europe to rapidly transmit details of rare and unusual foodborne pathogens.
b. To provide opportunity to present detailed case definitions to other partners
c. To rapidly exchange strains to aid research and surveillance

The expected benefits will be a more proactive approach to the identification of new and emerging foodborne zoonoses.

Working Group 3. Quantitative foodchain risk assessment

The task of this group will be to co-ordinate the development of quantitative foodchain risk assessments based on agreed priorities and inform other WGs on the outcomes and actions arising from these assessments.

The main objectives of this WG will be:

a. To review currently available foodchain risk assessments carried out in Europe and elsewhere.
b. To identify priority areas for formal quantitative risk assessments
c. To facilitate discussion of risk assessments carried out in Europe

d. To inform other WGs on the outcomes of these risk assessments so as to inform future surveillance and research priorities.

The expected benefits will be the continued integration of risk assessment into research, surveillance and policy initiatives.

Working Group 4. The Survival of zoonotic pathogens through the foodchain.

The aim of this group will be to gather all available knowledge on the molecular and phenotypic profiles of the major pathogens with special emphasis on those genes implicated in the virulence and survival of the organism through the foodchain.
The main objectives of this WG will be:

a. To review current knowledge of virulence and survival genes in foodborne pathogens
b. To facilitate presentation of novel research findings
c. To seek to apply genomic chip technology to specified pathogens
d. To facilitate exchange of techniques and staff through short-term scientific missions.
e. To regularly update other WGs on any new findings.

Expected benefits will be the integration of hazard and risk and a greater understanding of the likely human and animal importance of new and emerging strains arising in the foodchain.

D. Organisation, timetable and dissemination

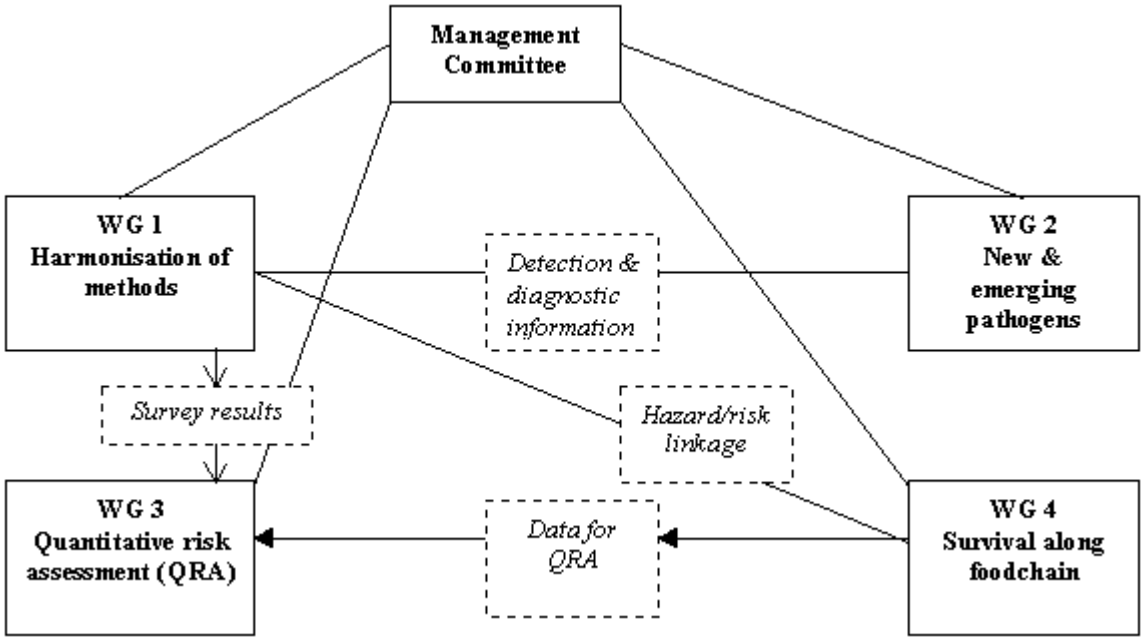
The organisation and co-ordination of the COST Action will be assumed by a Management Committee (MC). Ideally, members from each participating country will represent the whole foodchain from farm to fork.. At the first meeting the MC will established the general frameworks and remit of the WGs.

In each WG, workshops (2-3 days) will be organised at least annually in one of the participating countries and the proceedings will be published. Scientific exchanges will be considered throughout the year and recommendations transmitted to the MC by the WG Chair. Reports of the scientific exchanges will be presented at the workshops. The MC will hold an annual management meeting to review progress. Consideration by the MC will be given to the production and maintenance of an Action Web Site to facilitate the dissemination of information about the Action.

One of the most important outcomes of this Action is to facilitate sustainable and new collaborative networks in the field of foodborne zoonoses and to apply these to improve the co-ordination of research and surveillance activities across Europe, through much closer co-operation between the veterinary, food and medical sectors. This is particularly relevant to generic solutions to control foodborne zoonoses. Thus, to help achieve and assess progress the duration of the COST Action should be five years. During this period it is envisaged that the COST Action will combine with at least three International meetings. One such meeting could be the International meeting on Salmonella to be held in Ploufragan, France in 2002. There will also be at least two workshops representing all the WGs most likely at the beginning and end of the Action. External experts from outside COST member states will be invited to participate in several meetings. Industry will also be encouraged to participate fully in all the WGs. Details of the leading participants in each of the workgroups is presented in Annex 1.

Dissemination of achievements will be either by using the OPOCE publication scheme or through publication with renowned publishers. A web site will be developed for fast dissemination of intermediate information and results to participants and other stake holders. A person from the MC will be appointed to develop the website and to co-ordinate the dissemination of data. Besides the periodic dissemination via the internet, a final report will be written, including an executive summary, final financial statement, and a summary of the results achieved in comparison to initial and updated COST-action plans. Identified stakeholders including potentially interested enterprises and policy makers will be specifically informed about the Action. They will be asked to attend, if appropriate. Dissemination of specific technical knowledge between scientists will be further stimulated by short term scientific missions.

Relationship between the Management Committee and the Workgroups



Timetable of activities

Activity	Year 1		Year 2		Year 3		Year 4		Year 5	
Management committee	•		•		•		•			•
Working group 1		♦		♦		♦		♦		♦
Working group 2			♥		♥		♥		♥	
Working group 3		♠		♠		♠		♠		♠
Working group 4			♣		♣		♣		♣	
International meeting			J						J	

E. Economic dimension

The following COST countries have actively participated in the preparation of the Action or otherwise indicated their interest:

Belgium, Czech Republic, Denmark, France, Germany, Hungary, Ireland, Italy, the Netherlands, Spain, Sweden, the United Kingdom.

A number of international bodies and industrial companies will also be interested and support the Action in some form.

On the basis of national estimates provided by the representatives of 12 of these countries the overall cost of the activities to be carried out under the Action has been estimated, in 2000 prices, at roughly Euro 30 Mio.

This estimate is valid under the assumption that 12 of the countries mentioned above, but no other countries, will participate in the Action. Any departure from this will change the total cost accordingly

COST 920 Working Group 3: Quantitative risk assessment

Draft plan of work

Objectives

The stated objectives of the working group are:

a. To review currently available foodchain risk assessments carried out in Europe and elsewhere;
b. To identify priority areas for formal quantitative risk assessments;
c. To facilitate discussion on risk assessments carried out in Europe;
d. To inform other WGs on the outcomes of these risk assessments so as to inform future surveillance and research priorities

In the Management Committee meeting of July 26-27, 2001 in Brussels, Belgium it was agreed that these objectives would be met by organising two kinds of meetings.

1. Meetings of risk assessment specialists, who present and discuss ongoing work on QMRA in Europe. These meetings will require detailed insight in modelling and statistics and aim at exchange of knowledge at a specialised level.
2. Meetings between risk assessment specialists and scientists who perform observational and experimental studies that provide data used in QMRA.

This memo further develops the plan of work by proposing specific subject areas for each workshop, and details on items for discussion.

Membership

The COST 920 action is open to all countries that have signed the agreement. However, it must be realised that risk assessment is a highly specialised field of work. For the interaction between participants to be productive, a high level of specialisation is therefore required. As the pace of implementation of microbiological risk assessment projects varies between COST countries, it is not expected that all countries will currently be able to delegate specialists to the meeting. One possible solution for this problem is to have a partly floating membership. Each country would delegate one permanent member to the WG. This would be a scientist who is currently engaged in risk assessment activities, or who is planning to start such activities within the timeframe of the action. In the latter case, the WG would also serve as a tool for technology transfer. A second representative from any COST country would not be a risk assessment specialist per se but would have a background that is relevant to the particular topic of the workshop. For example, in workshop 1 (see below), input from predictive microbiology, consumer sciences, food intake surveys etc. would be relevant. Permanent representatives to the WG would be confirmed by the MC and would assist MC members and WG3 chairs in finding appropriate candidates for specific discussions.

Format and output of meetings

Each meeting will be divided in half-day sessions. In each session, two speakers will introduce a particular topic. Subsequently, discussions in plenary or in breakout groups will be organised to further explore items under consideration, and to make recommendations. Well-respected experts from COST member states but also from other countries will hold introductory presentations on the specific themes. Extended abstracts (4-8 pages) will be made available by each speaker. Conclusions from group discussions will be summarised by rapporteurs and all information will be made available in booklets and on the COST 920 website.

Specialised workshops, tentative subjects of discussion

Year 1: Exposure modelling
Modelling primary production
Standardising the toolkit for a modular approach
From laboratory data to model parameters

Variability in predictive microbiological models
Modelling consumer behaviour
Food consumption data

Year 3: Dose-response modelling
The single-hit hypothesis and cell-to-cell signalling (quorum sensing)
Modelling dose-response relations for toxins, parasites and prions
Modelling the effects of acquired immunity
Dynamic models of the pathogen/host/matrix interaction
Animal and *in vitro* models as additional sources of information
The perspectives for volunteer studies and intensified outbreak investigations

Year 5: Risk characterisation
Accounting for uncertainty and variability when integrating exposure and dose-response models
Effects on mixed populations
Modelling secondary transmission
Units of risk (infections, cases of illness, fatalities, DALYs etc.)
General workshops; tentative subjects of discussion

Year 2: The interface between data and models
Performance characteristics of detection and counting methods
Distribution of pathogens on/in raw materials and food
Accounting for growth and death of pathogens
Accounting for phenotypic and genotypic variation of micro-organisms
Accounting for variability (e.g. seasonality) and uncertainty
Using expert opinion

Year 4: Interaction between risk assessment and risk management
Quality assurance of risk assessment modelling
Validity and credibility of risk assessment studies
Presenting risk assessment results
Risk based decision-making

THE MPA-CASE AND THE NATIONAL RESIDUE PROGRAMS

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ABSTRACT

The MPA-case (MPA=medroxy progesteron acetate) is described, which took place in the summer of 2002. It started with fertility-problems on a pig-breedingfarm and showed up to be one of the largest contaminations of animal feed. About 70% of the Dutch animal feed-industry was involved in the case. Public health concerns and trade-politics are shortly discussed. The national residue plans didn't show any signs of contamination. Only a private controlling-system in the veal-calve-industry detected a very low contamination of MPA in veal-calve feed. The Dutch Food and Non-food Authority (VWA) indicates that residue plans should not only be used for surveillance or monitoring. Especially in the MPA-case an early-warning program could prevent a lot of damage. In this case a smart monitoring/surveillance program, in which the national residue plans only take a (small) part, and a good working network of veterinarians and other 'field' workers has more benefits.

SAMENVATTING

De MPA-crisis van 2002 wordt beschreven, die begon met de vaststelling van vruchtbaarheidsproblemen op varkensbedrijven waar de hoogste voerbesmettingen werden vastgesteld. Ongeveer 70% van de Nederlandse mengvoederindustrie was erbij betrokken. Volksgezondheidszorg en handelsproblemen worden kort besproken. De nationale controlemechanismen konden geen besmetting aantonen, enkel een eigen bedrijfsonderzoek kon bij voer voor vleeskalveren een lichte MPA-besmetting terugvinden. De Nederlandse VWA wijst erop, dat residuonderzoek niet enkel voor bewaking en monitoring moet toegepast worden. Vooral de MPA-crisis heeft aangetoond, dat een vroegtijdig waarschuwingssysteem heel wat schade kan voorkomen. Dit laatste moet vooral steunen op een netwerk van dierenartsen en andere veldwerkers, complementair aan het residuonderzoek.

1. THE MPA-CASE

On the 11th June 2002 the Dutch Inspectorate for Health Protection and Veterinary Public Health got a phone-call from a veterinarian, who saw large health problems on a pigbreedingfarm (about 1600 sows) in the south of the Netherlands. Sows had problems to get pregnant, coming in labour (a lot of sows had to be delivered by caesarean section) and other fertility problems. Investigations on the farm by the local veterinarian and the Dutch veterinary Faculty, detected a problem with the feed. In the beginning of May the pig farmer got a new lot of feed, where after the problems started. The different components of the feed were: brewers' grains, C-Serena (a wheatmealcomponent), potato peeling and by-products from the mustard industry. There wasn't a clear conclusion of the contamination; and the diagnosis was that there was a contamination in the feed with a substance 'with anti-estrogenic action'. On the 28th of May the feeding of these feed components was stopped and the problems (i.e. the labour-problems) vanished. Because of the bad production-expectance of about 300 sows, the pig farmer asked the veterinarian to clarify if there were any objections on food safety, to slaughter these sows.

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[2]Commitee for Veterinary Medicinal Products, Medroxyprogesterone acetate, summary report, doc. nr. EMEA/MRL/0129/96-FINAL

In the Dutch Law there is nothing arranged to experimentally slaughter animals with some suspect or history. The use of experimentally slaughtering can be used to pay extra attention to the slaughtered animals. With the cooperation of the farmer we decided to slaughter 10 animals as normal slaughter animals and examine them especially on all hormonal and anti-hormonal substances, as mentioned in the Dutch Meat Inspection Law. On the 14th June the animals were slaughtered and on the 20th June the results of the extra investigation on hormones were released. In all animals Medroxyprogesteronacetate (MPA) was found in kidney fat in the content of 2.5 – 8 µg/kg (ppb).

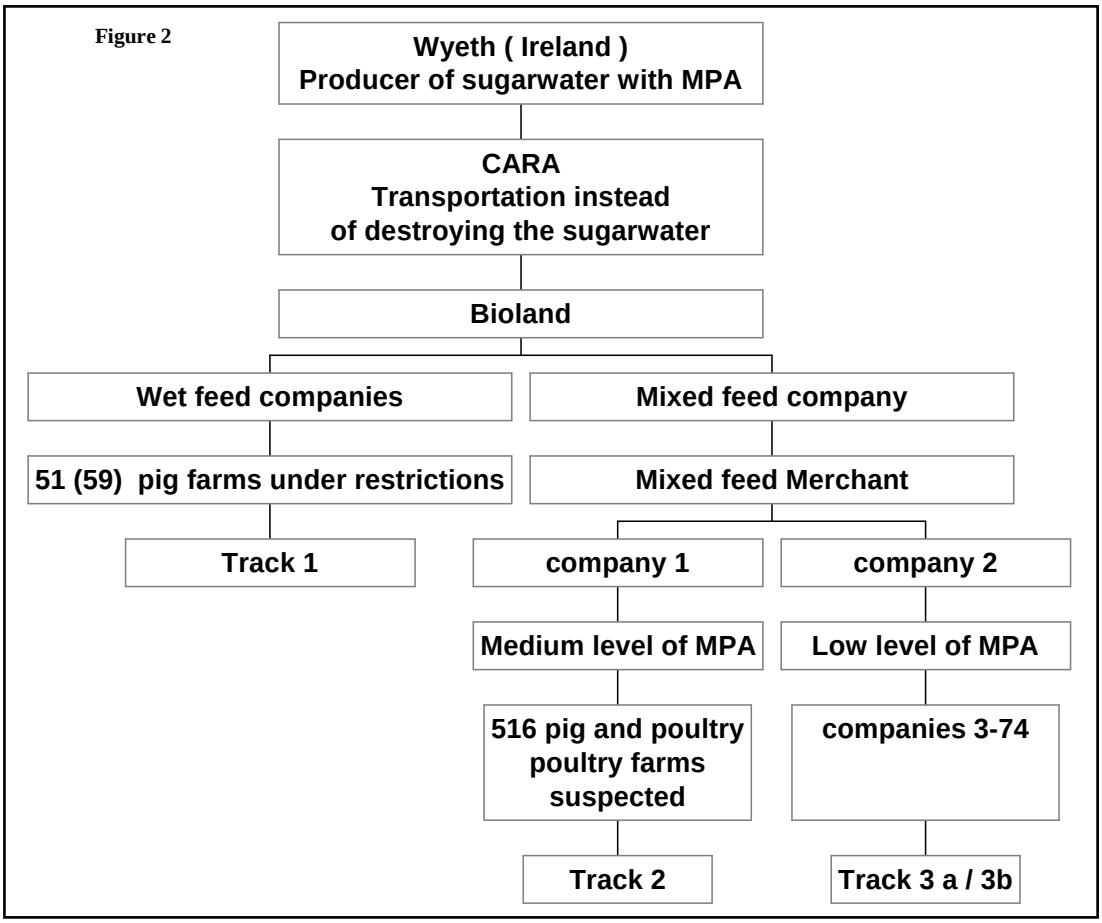
Figure 1 ***Medroxyprogesterone-Acetate (MPA)***

MPA is a syntheticial analogue of the natural seroidhormone progesterone. MPA is in human medicine used as a contraceptive, as cytostaticum in antitumour therapy and for the treatment of hormonal and gonadal disorders. MPA is a registered veterinary drug for sheep for the synchronisation and induction of oestrus. [2]
For other farm-animals MPA is supposed to be a forbidden growth-promoter.

For the executing services and the veterinarians it was a great surprise and decision was made to start a technical working group to discuss and work out the results and further actions. The farm was placed under restrictions because of the Dutch Veterinary Drug Law. In the meantime 2 more farms were noticed which had the same animalhealthproblems. One farm was related to the first farm, because it got mixed feed from farm 1. The other farm didn't have a relation with these 2 farms.
By the Dutch General Inspection Service of the Ministry of Agriculture tracing of the feed components was started. Little by little it became clearer that the wheatmealcomponent and the brewers' grain component were contaminated by MPA. About the wheatmealcomponent was known that it was red-coloured because it was mixed up with some lemonade syrup. This lemonade syrup (afterwards known as glucose syrup) was the malefactor. This glucose syrup was delivered by a Belgium company, Bioland. This company got via via pharmaceutical garbage from an Irish pharmaceutical company. This garbage was the sugarcoating of pills/medication for human use in which MPA was processed. An Irish trader delivered the syrup to the Belgium Company.
The material had to be destroyed but with false papers and/or declaration on the cans, it came available for the food- and feed industry. This started already in 2000. The syrup was delivered to the Belgium lemonade-industry. The Belgium-company went bankrupt in 2002 and in a short time the remaining stocks with syrup (totally 5 lots of about 38 tons each) had to be placed elsewhere.
As far as known at this moment, 2 lots were delivered at a large pig farmer in the south of the Netherlands. This pigfarmer also trades in by-products for feed. One lot was temporarily stored in a silo. In this silo also wheat meal was stored (track 1). The other 2 lots were delivered to a mixed-feed company on one hand (track 2) and a molasses-trading company (track 3) on the other hand. Molasses is used as an ingredient in the food industry and used by pelleting of feed.

1.2 The different tracks

Figure 2



Track 1
In this track the farms, which used by-products as feed, are situated. These farms have been contaminated by the use of contaminated wheat meal. On the other hand are (almost) all the farms of the large pig farmer contaminated by the mixing of glucose syrup with own by-products. In this track high amount of residues of MPA were in the feed as well as in the animals. Reason for this high amount is the high percentage of (high contaminated) glucose syrup that was used.

Track 2
A compound feed producer got a lot of contaminated glucose syrup and stored it after research in the silo of molasses. Because of the syrupy consistence of the molasses, the glucose syrup didn't mix very well. This showed very different levels of contamination in the different periods. At the end there were levels found up to 300 ppb in the feed. This was expected, because about 3 – 8% molasses was used in the compound feed.

Figure 1 ***Levels of MPA in syrup and feed***
(Source: Min. LNV, dir. VVA)

Glucose syrup	*up to*	*4.750.000 ppb*
Track 1	*up to*	*235.000 ppb*
Track 2 molasses	*up to*	*6.751 ppb*
Track 2 feed	*up to*	*286 ppb*
Track 3a molasses	*up to*	*4.487 ppb*
Track 3a feed	*up to*	*38 ppb*
Track 3b wyc	*up to*	*48 ppb*
Track 3b vinasses	*up to*	*193 ppb*

Track 3a
In the beginning there was only one track 3. It was the track caused by the contamination of a silo of molasses at one of the largest traders of molasses. This trader put one lot of molasses in one silo, especially used for deliveries to feed companies.
Out of this silo about 75 factories were delivered with molasses. These factories delivered feed to about 70% of the Dutch pig farms. It was low contaminated, with a maximum of about 40 ppb.
In other EU-member states compoundfeedfactories and farms were delivered with the contaminated molasses. And from the EU-member states some Dutch farms got contaminated.

Track 3b
After a big part of the tracing was completed, there seemed to be some deliveries of the molasses-trader to the food-industry. From the food-industry there was again a track of by-products going to the feed-industry, i.e. wheat-yeast concentrate and vinasses, by-products of the alcohol production. Nevertheless the low concentration in the molasses to the food-industry, because of some concentration steps in the process of the alcolholproduction, the level of contamination especially in the vinasses was higher than in the molasses. At the end the number of contaminated farms by this track were small.

1.3 MPA and Public Health

During the MPA-case, the RIVM (Bilthoven) made risk-analysis for the public health impact of the presence of MPA in pork. The European Committee for Veterinary Medicinal Products (CVMP) estimated for MPA a No Observed Effect Level (NOEL), based on the most sensitive effect (hormonal action). The NOEL was based on 30 µg per kg bodyweight daily. With a safety factor of 100 the Acceptable Daily Intake (ADI) was put on 0,3µg/kg BW (for a person of 60 kg means this 18µg daily). The highest levels of MPA in pork, as far as known at the time of the risk-analysis, were 65 µg/kg kidney fat. Based on a daily consumption of 50 g. fat (standard EU food pattern) the intake of MPA is (65 * 0.05) 3,25 µg. This is about 18% of the ADI and thus no public health problem.
Later on [3] it was confirmed that the glucose syrup also was contaminated with 17β-oestradiole. The RIVM also made a risk-analysis of the 17β-oestradiole. 17β-oestradiole is naturally present in human and animals (thus also in pigs) in various levels. It is a normal part of the human food. 17β-oestradiole is orally inactive. Even with very overestimated calculation of exposure, the intake is still 40-times below the NOEL for 17β-oestradiole, and thus no problem for Public Health. Thereby, 17β-oestradiole is (still) allowed for therapeutical and zootechnical use as a veterinary drug in all food-producing animals

1.4 MPA en 17ß-oestradiole in (trade) political way

The use of hormones as growth promoters in food producing animals in Europe is forbidden. On that part it differs from the approach in the United States of America. In the USA 6 hormones are allowed under strict authorisation for the way of administration. The hormones, used in the USA, are 17β-oestradiole, testosterone, progesterone, trenbolone and zeranol as implantation, and melengestrol-acetate as feed additive. Because of the opinion in the EU the detection of hormones is fully focused on illegal use. In this way there is continuing discussion about 'zero-tolerance'. For 17β-oestradiole investigation is very difficult. In the table below, there is an overview of the different levels in different products of animal origin.

Table 1. 17β-oestradiole (E2)-level (ppb) in different products of animal origin (Source: RIVM ARO/CRL)

Content (ppb)	E2 in pork (boars)	E2 in pork (sows & barrows)	E2 in eggs (hens)	E2 in beef (USA HQ HFC)	E2 in beef (USA MLQ domestic)
0% = minimum	0.2	< 0.01	0.06	< 0.01	< 0.01
50% = median	0.3	< 0.01	0.13	< 0.01	0.02
100%= maximum	2.4	< 0.01	0.38	0.04	0.27
number of samples	4	30	25	97	102

Table 2. Dietary intake of 17β-oestradiole (E2) (nanogram) in different products of animal origin, see also table 2 (Source: RIVM ARO/CRL)

Amount	in 250 gram of pork	in 250 gram of pork	in 50 gram of whole egg	in 250 gram of steak	in 250 gram of beef
median	75	< 2.5	6.5	< 2.5	5
Maximum	600	< 2.5	19	10	68

[3] Based on the clinical symptoms of farm 1, especially the presence of cysteous ovaria, there was a strong suggestion that there should also, besides MPA, be a contamination with an estrogenic substance.

Reading this tables the conclusion can be made, that with 'normal' consumption of pork (boars) a high amount of 17β-oestradiole will be consumed. Even the daily consumption of an egg gives almost a higher amount than the consumption of beef of 100 grams of hormone treated cattle.

Figure 2. Annex 1 of Directive 96/23/EC

Group A – Substances with anabolic action and prohibited substances
1. Stilbenes, derivates, salts and esters thereof
2. Antithyreogenic substances
3. Steroids
4. Resorcylic Acid Lactones (including zeranol)
5. ß-agonists
6. Substances mentioned in annex IV of Reg.. 2377/90

Groep B – Veterinary drugs and contaminants
1. Antibacterial substances including sulfonamids, quinolones
2. Other veterinary drugs: a. anthelmintics, b. coccidiostatics, including nitroimidazols, c. carbamates en pyrethroids, d. tranquillizers, e. non-steroidal anti-inflammatory drugs , f. other substances with pharmological action
3. Other in the environment existing substances and contaminants: a. organic chlorides including PCB's, b. organic phosphor, c. chemical elements, d. mycotoxins, e. colorants, f. others

With these figures the conclusion of the Scientific Committee on Veterinary Measures relating to Public Health: "*in the case of 17β-oestradiol there is a substantial body of recent evidence suggesting that it has to be considered as a complete carcinogen, as it exerts both tumour initiating and tumour promoting effects. The data available does not allow a quantative estimate of risk*"[4], could lead to a direct prohibition of the consumption of pork (from boars) and eggs. It isn't the time to do that.

2.1 National residue-plans

The juridical basis of the national residue plans can be found in the European Directive Directive 96/23/EC[5], in conjunction with Directive 96/22/EC[6]. Basis of this Directive is that the use of veterinary medicine for growth promotion in the farm holding is undesirable and should be prohibited. The Directive knows a total block for the administration to animals of stilbenes and substances with thyreostatic action. The use of other substances with hormonal action (substances as estrogenic, androgenic of gestagenic action) and of ß-agonists is allowed, for zootechical or therapeutical treatment. The prohibition of the administration of these substances is implemented in the Dutch Veterinary Medicine Act.
Directive 96/23/EC dictates control measures, when illegal substances are found in live animals and products thereof. In annex 1 of this Directive the substances and groups of residues are mentioned, where for control measures should be taken (figure 4).
As far as these measures are related to possession of and the trade of animals, treated with substances with growth promoting action, the rules are laid down in the "Regeling Verbod handel met bepaalde stoffen behandelde dieren en producten".

In Directive 96/23/EC there are also the basic requirements for the National Plans laid down.
These plans are set up for the reason to study the possible presence of residues in food of animal origin in the different stadia of production.
On the group A-substances the control should include the investigation on the administration of these forbidden substances and the illegal use of registered drugs. For the group B-substances the control should be focused on the residue levels. These levels should agree with the maximum levels as mentioned in the annexes I and II of

[4] Opinion of the SCVPH: Review of previous SCVPH opinions of 30 April 1999 and 3 May 2000 on the potential risks tot human health from hormone residues in bovine meat and meat products.
[5] Directive 96/23/EG of the Council of 29 April 1996 regarding control meassures to certain substances and residues thereof in live animals and in products thereof …
[6] Directive 96/22/EG of the Council of 29 April 1996 regarding the prohibition of the use, in the farm holding, of certain substances with hormonal action and of certain substances with thyreostatic action, also β-agonists….

the residue regulation 2377/90[7], and the maximum levels of residues of pesticides as in annex III of Directive 86/363/EEG. There should also be a control on the residue level of environmental contaminants.

2.2 National residue plans: monitoring-, surveillance- or early warning system?

The goal of Directive 96/23 is that national plans should be focused on the tracing of illegal use of forbidden substances and on the detection of exceeded residue levels of permitted substances. The results of the investigation should be used to explain the reason of presence of these substances. In the Netherlands the plans are mainly used, besides to agree with European regulations, to trace illegal use and start criminal investigation.
Comparing the Dutch residue plans with the definitions, as described in figure 5, it is hard to say under which term, monitoring / surveillance / early warning system, this plans can be placed.
The Dutch plans seemed to be a mixture of a monitoring- and surveillance-system. As early-warning system we should regard them as useless.
The plans only handle a small part of the Dutch production of animal products. According to Directive 96/23/EC 'only' at least 0,4% of de cattle population and 0,05% of the pig population of number of slaughtered animals in the previous year have to be examined. For The Netherlands means this that in the year 2000 for examination of the groups A and B (see figure 4), 8,850 cattle and 9,480 pigs should be examined[8].
For the different groups of substances it is again a percentage thereof (cattle: group A: 5520 / group B: 3330; pigs: group A 3980 / B: 5690). Group A substances are partly examined on the farm (cattle: 2760; pigs: 190) en partly in the slaughterhouse (cattle: 2760 / pigs: 3790). The number of the separate substances is even smaller (see also par. 3). It should almost be a miracle or accident when a contaminated pig was examined by the residue plan.

Figure 3. Definitions:

Monitoring: Monitoring describes ongoing efforts directed at assessing a prescribed status of a given population. This activity necessitates a system for collecting, processing, and summarizing data and disseminating information to appropriate agencies/stakeholders as well as individuals

Surveillance: Surveillance describes a more active system and implies that some form of directed action will be taken if the data indicate a level above a certain prescribed threshold level

Early Warning System: A process that provides timely information so that communities are not only informed, but sufficiently impressed, that they take preparedness actions before and during the anticipated hazardous event. (http://www.idndr.org/earlywarning.htm)

2.3 'Private' National Plans

Besides the Governmental plans, there are also plans executed as self-control plans by the companies / the sector. Two examples are the residue-plans of the SKV (Stichting Kwaliteitsgarantie Vleeskalversector (Foundation Quality-guarantee Vealcalve sector) and the KCR (Kwaliteits Controle Runderen (Quality Control Cattle). These Foundations check separate parts of the farms by a self-control system.
The SKV, for example, examines not only the presence of residues, but uses also visual controls to detect the use of illegal hormones. In 2000 the SKV executed 20.167 visual controls and took 19.660 urine samples, and 3.745 other samples, such as veal calve feed.

GECONTROLEERD
KWALITEITS
KALFSVLEES

3. THE MPA-CASE and THE NATIONAL PLANS

As mentioned in the introduction of the MPA-case, the National Plans didn't give the first signal of a problem in the pigfarm holdings. Despite that the problem already existed for more then a month (in the beginning only at a small number of farms), it was no surprise that none of the with MPA contaminated pigs was examined within

[7] Regulation nr. 2377/90 of the Council of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin
[8] Data from the National Plan residues in live animals and animal products, The Netherlands 2000

the National Plans. In this case one have to look at the number of examined pigs, the used detection limit and the place where samples are taken.
In the National Plan residues of 2002 yearly 'only' 100 samples of pigs (kidney-fat) have to be examined on MPA. In this case only in the slaughterhouse samples can be taken, because MPA cannot or very hard in excreta, such as urine or faeces be examined.
The used detection limit was till medio 2002 1 ppb and the action limit 2 ppb. The levels of MPA, found at the MPA-case, showed that at least in the 10 experimentally slaughtered sows, the detection and action limit were exceeded, and should be noticed as positive within the National Plans. Only in track 1 levels were found where the action limit was exceeded. Animals fed with the feed from the other tracks didn't show an exceeding of neither the action limit nor the detection limit. In medio 2002 the Ministry of Public Health deleted the detection and action limits in the regulations, in which a zero-tolerance was born.
For MPA it is very specific that this substance can't be examined in the living animal. With regards to the withdrawal time of MPA, which was estimated on about 7 days, it would be very hard to find MPA in the slaughterhouse.
At this moment it is not possible to clarify, what the chance would be if one of the animals of especially track 1 should be examined within the framework of the National Plan and give a positive result. The results of the National Plans of 2000 and 2001 never showed one MPA-positive or suspected (between detection and action limit) sample.

Then the SKV.
The SKV examines specifically in the vealcalve sector, in which MPA didn't play a role in the beginning of the MPA-case. Only later on, when compound feed was on a low level contaminated with MPA by molasses and vinasses, other sectors, as the poultry holdings and the vealcalve holding, get involved in the MPA-case.
An essential difference between the National Plans and the SKV-plans is that in the vealcalve sector also feed is examined. It wasn't a surprise during the MPA-case that the information was handed over that a sample vealcalve-feed, taken on 3 July 2002, showed a positive result on 15 July 2002. The level was very low: 5 – 10 ppb. Tracing the origin of the feed, it showed to be a compound feed out of track 3a. It was produced with contaminated molasses. This molasses was of Dutch origin, but traded to Germany. In Germany it was used in compound feed and traded back to the Netherlands.

4 CONCLUSIONS

The MPA-case shows that the National Plan residues have a limited value as an earlywarning system. The number of examinations on specific substances is limited. From the total number of samples on pork-products of 9480, 'only' 100 should be examined on MPA.

For some substances, such as MPA, the National Plans have no value as earlywarning system. These substances can't be tested on the place where the administration or intake of these substances takes place. At least not on or in the animals. Further on one should notice the dilution of the substance by feeding it. A special note to the tracks 2, 3a and 3b where still a mediate level of MPA was present in the feed, and no residues could be found in the animals. Another point is the elimination of the substance by the animal. The withdrawal time of MPA was estimated on 7 days. With low or even mediate levels of MPA in the feed, and the use of clean feed, MPA couldn't be found after a short period. A substance, which can't be detected on the living animal, gives disadvantage for the control of residues, when you keep looking at the animal.
The SKV-results shows us that the National Plan Residues should be extended with the examination of feed. The Directive 96/23/EC doesn't give a possibility or obligation for it. The Government and/or the Sector has no obstacles, perhaps only financial, to take his own responsibility.
The Food and Non-food Authority (VWA), independent authority on the area of food safety, plans to reconsider all monitoring- and surveillance systems. These systems should be judged on the function of the system, the overlap of all the systems, and the goal of the total system. At the end there should be at least an overview of all the systems and black holes of the system. The systems should become smart and function in a way that food safety (starting even with feed safety) is taken care in the best way. Research programs should be tuned and the goal of the system (monitoring/surveillance/early warning) should be clear at the start. Tuning National Plan Residues and National Plan Feed should be done as soon as possible.

The MPA-case also shows, that there is no good functioning earlywarning-system. On the area of residues we depend too much (or only) on the National Plan Residues. Especially in the MPA-case, these Plans turned out to

be useless as earlywarning. Not only National Plans should be used as earlywarning system, but also results of examinations made by companies or other participants.
The MPA-case made clear, that clinical symptoms are very important as a first signal of problems. In this case the network of veterinarians plays (or can play) a valuable or even essential role. Contaminations leading to animalhealthproblems are first in sight by the practitioner. Sometimes these problems are only in sight of the practitioner and will never become visible on a countrywide level, and stay on the farm level.
The VWA attaches much value on this role of the veterinary practitioner. Not only the VWA, but also the veterinary sector plays an important role in achieving a high value of food safety (by visible risk-reduction). The veterinary sector should introduce a structure, in which veterinary practitioners are able to report signals very quickly. The Central Government or Authority should be helpful to realise such a structure or network.
At the end it is very hard to understand, that the announcer/reporter of the first signal stands all alone with the problems and doesn't get the right solutions.

FINANCING LOSSES OF INFECTIOUS LIVESTOCK DISEASES IN EUROPE: AN ECONOMIC RISK ANALYSIS

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ABSTRACT

Financing losses of infectious livestock diseases by means of an insurance or levy system is very complex because of rating difficulties. This study focused on Classical Swine Fever (CSF), Foot and Mouth Disease (FMD), and Avian Influenza (AI) in Europe. An economic model is developed, based on an epidemiological model. Data needed for both models are not readily available in individual countries, so they were collected though a questionnaire sent to the CVOs of the 'European' OIE countries. In total 21 questionnaires were mailed back and 14 of them were used for our analysis. Based on the responses in the questionnaires, the expected size of an epidemic and the expected economics losses were calculated. The level of the rates (i.e, levies or premiums) turned out to be extremely different in each country. The paper demonstrates the importance of the availability of a reliable and complete epidemiological and economic data set.

SAMENVATTING

In Europa is de financiering van schade veroorzaakt door uitbraken van besmettelijke dierziekten (in deze bijdrage Klassieke Varkenspest, Mond- en Klauwzeer en Vogelpest) via een verzekerings- of heffingensysteem erg moeilijk vanwege inschattingsproblemen van de precieze schade. Daarom is een economisch model ontwikkeld, voortbouwend op een epidemiologisch dierziektemodel. Aanvullende epidemiologische en economische invoergegevens zijn verzameld via een enquête onder 21 CVO's (Chief Veterinary Officers) uit 'Europese' OIE-landen. Hiervan konden er 14 in de analyses worden gebruikt. Resultaten laten zien dat schadebedragen (c.q. premies voor verzekeringen en heffingen) zeer uiteenlopen voor de diverse landen en regio's. Voor de financiering van de schade is een complete en betrouwbare epidemiologische en economische dataset onmisbaar. Vele Europese landen kunnen deze dataset (nog) niet aanleveren.

1. INTRODUCTION

The recent outbreaks of Classical Swine Fever and Foot and Mouth in the UK and the Netherlands drew attention to the costs of outbreaks of epidemic livestock diseases. Farmers do not need to bear all of these losses themselves. If a country that is faced with an epidemic takes appropriate control measures and provides appropriate compensations to farmers involved, the European Union compensates part of the direct losses incurred. The veterinary budget of the European Union refunds 50 percent of the costs of compulsory and pre-emptive slaughter, 70 per cent of the costs of welfare slaughter, and 50 per cent of the organizational costs. The financing of the non-compensated part of the direct losses differ between the EU member states. In general, only the value of the animals that are compulsorily slaughtered are compensated. Consequential losses are not eligible for compensation (3, 12).

While some member states finance the direct losses from the national budget, most member states have set up some form of statutory system to co-finance the direct losses. The co-finance contract is than in the form of a compulsory program in which all farmers pay an up front or assessment levy. Both risk-financing instruments are based on pooling over time within the sector. The levy varies between species, but more importantly in case of the assessment program, the levy is varied according to the needs of the fund. After an outbreak of a disease, the levy usually increases to cover these costs. These latter systems have no no annually fixed levies while the Government guarantees to partly finance the losses in advance. The compensation payments are made from the

available funds and the Government will pay for the costs if the fund runs out of money. The input of the Government will however be repaid over the following years and this is usually why the levy increases after a disease outbreak. A comparison of the past or current levies paid between the member states is arbitrary to estimate the future levies of a certain country on. This also because the risks between the countries differ.

In contrary to an assessment levy system, a standard insurance scheme is financed through fixed advance payments (e.g., premiums). Insurance capacity is provided through various layers of own retention and reinsurance. However, in the case of an assessment mutual, the company has the right to assess insureds for losses and expenses via initial premiums, or after a loss occurs (additional premiums), or both. Few private insurance schemes exist to cover the risk of consequential losses as a result of epidemics in livestock. Those that do exist are either extensions of general livestock insurance policies or specific policies of stock insurers and mutual insurers. Many standard livestock insurance policies indemnify farmers for animal losses as a result of illness and accidents, but some have been extended, sometimes as an option, to cover at least a part of consequential losses from epidemics.

Premium or up front levy setting (hence both called rates) is very complicated and should be based on a profound knowledge of all factors included. With knowledge of the most important risk factors, the probability of an outbreak and the economic consequences, the level of the premium or levy can be estimated. In this paper the basis of the economic analysis is introduced. Our approach starts with the epidemiological description of the potential spread of a contagious disease. The economic analysis is based on these epidemiological results by placing them in the specific economic context of the country in which the outbreak occurs.

Such epidemiological analyses typically require many epidemiological (e.g., disease spread, herd structure and animal intensity) and economic (e.g., income per animal, output prices, import/export position of country) data on the outbreak. In most countries, these basic data are not available. Therefore, a questionnaire to collect the epidemiological and economic data, including the importance of different risk factors, about introduction and spread of the infectious diseases CSF, FMD and AI was developed, and sent to the CVOs of the participating OIE-countries. These questionnaires were used to provide a first insight into epidemiological and economic consequences of CSF, FMD and AI epidemics in the participating countries. The paper finishes with the discussion and conclusions.

2. RISK CLASSIFICATION OF THE EUROPEAN AREA

The European area can be divided into various regions that differ with respect to the risk of livestock epidemics. A risk classification can be based on various criteria, such as country borders, herd density, animal density, the amount of import/export and natural borders (4, 12).

Livestock epidemic disease risks considerably differ across countries. Table 1 gives an overview of the estimated number of FMD and CSF epidemics (primary outbreaks) for different (groups of) countries, originating from different sources of literature. Considering the estimations from (2), the table shows large differences in the most likely and fractile values across groups of countries. For instance, the number of expected primary outbreaks is 20 for eastern Europe, while only 0.5 for the 'Islands'. Also Ryan and Gallagher (11) found considerable differences, although their numbers are much lower. Meuwissen et al. (9) only considered the Netherlands.

Table 1. Expected number of primary outbreaks of FMD and CSF per 5 years for different (groups of) countries in Europe. Data originate from three different sources.

	Horst et al. 1999 (most likely, 25%, 75%)		Ryan and Gallagher 2000 (mean, 5%, 95%)	Meuwissen et al. 2002 (most likely)	
	FMD	CSF	FMD	FMD	CSF
Netherlands	1 (0.5, 2)	2.7 (1, 5)		1	2
Belgium, Luxemburg, Germany	3 (1.5, 5)	15 (10, 25)	1 (0,3)		
Austria, France, Switzerland	2.5 (1, 4.5)	5 (3.5, 10)			
Greece, Italy, Portugal, Spain[1]	7.5 (3.5, 12.5)	13 (10, 21)	3 (1, 7)		
Eastern Europe	20 (15, 24)	21 (18.5, 25)	4 (1, 10)		
'Islands'[2]	0.5 (0.5, 1)	0.5 (0.5, 1.5)	1 (0, 2)		
Balkans			7 (3, 14)		

[1]Ryan and Gallagher include Malta and exclude Greece (part of Balkan).
[2]Great Britain, Ireland, Scandinavia. Ryan and Gallagher also include Iceland.

A higher herd density is likely to indicate more animal contacts and transports and thus a higher risk. Herd density can be expressed per km2 'total land' (includes cities, roads etc.) and per km2 'agricultural land'. As with herd density, a higher animal density is likely related to a higher risk from animal contacts etceteras (see previous point). Animal and herd density are, however, not completely interchangeable parameters since a region with less but larger farms may represent a lower risk than a region with more but smaller farms. Within densely populated regions, animal densities can highly fluctuate across municipalities. Although data at the level of municipalities provides useful inside into the differences within regions, we base our epidemiological analysis (next chapter) on more aggregated, i.e. practical, useful and simple approach, namely on country level.

The higher the amount of animals imported and/or exported, the higher the risk related to the imported animals and returning trucks. Natural borders, such as rivers and mountains, may be a barrier for disease spread since they are likely to lead to more controlled contacts between regions.

3. MATERIALS AND METHODS

3.1. Control measures

In countries in which preventive vaccination is prohibited (i.e. in the whole European Union), outbreaks of CSF, FMD and AI are controlled with a number of severe control measures. The basis for these measures in the EU originates from EU Council Directive 80/217/EEC, 85/511/EEC and 92/40/EEG respectively. Measures include (3): (1) stamping-out of infected herds, (2) pre-emptive slaughter of contact herds, and (3) the establishment of protection (> 3 km) and surveillance zones (> 10 km). In the remaining of this paper, these zones are called 'restriction zones'. Depopulated farms may repopulate 30 days (CSF) 21 days (FMD and AI) after the cleaning and disinfecting of the farm (7-10 days after diagnosis), or, after the lifting of restriction zones (lifted only after clinical and serological tests). The latter generally takes much longer than 21-30 days. As an example, during the 1997/98-epidemic of CSF in the Netherlands many pig farms were in restriction zones for more than 6 months.

Depending on the severity of the epidemic, national governments can take *additional control measures*, such as the pre-emptive slaughter of all herds within a certain radius (for example 1 km) of infected herds. In the 2001 FMD-epidemic in the Netherlands, the Dutch government decided on a temporarily complete movement standstill in the whole of the Netherlands, including also horses and poultry, and the transport of feed and animal products, such as manure and milk. Also, herds within a 1-km radius of contact herds were pre-emptively slaughtered. Furthermore, all susceptible animals within a large area around the infected herds were vaccinated (emergency vaccination, 'ring vaccination') and slaughtered afterwards.

If restriction zones lead to severe *animal welfare problems* on the farms (possible on farms with 25-kg pigs, hogs and broilers), so-called welfare slaughter is generally applied. With stamping-out and pre-emptive slaughter, buildings are completely emptied (i.e. depopulated). With welfare slaughter, buildings may only become partly empty. All animals in stamping-out, pre-emptive slaughter, and welfare slaughter programs are destroyed and rendered. A further 'welfare measure' (taken during the 1997-1998 CSF-epidemic in the Netherlands) includes a breeding prohibition. With sows this only starts to have an effect after about 115 days.

3.2. Financial losses and compensation

Losses related to the control measures described can be subdivided into *direct losses* on the one hand and *consequential losses* for the various parties of the production chain on the other hand. *Direct losses* refer to the value of destroyed animals and the costs of organizational aspects such as the monitoring of farms in restriction zones. Governments (national and European) generally cover direct losses. *Consequential losses* are completely borne by the farmers. They include one or more of the following five categories (see also 7):

(1) *Business interruption* occurs because farm buildings become (partly) empty due to stamping-out, pre-emptive slaughter, welfare slaughter or breeding prohibition, and stay empty until restriction zones are lifted. On farms that are completely empty losses from business interruption may be limited if farmers renovate their stables, temporarily seek another job, etc.

(2) *Losses related to established restriction zones*: farms in restriction zones face (long) periods in which animals (such as finishing pigs, culled sows, broilers) and manure can not be transported from the farm. These periods are characterized by animal welfare problems, extra feeding costs, and emergency measures for housing of pigs and storage of manure. Milk from dairy farms in restriction zones is (mostly) collected (taking into consideration strict hygienic measures). However, milk prices may be lower than normal.

(3) *Insufficient compensation for animals*: although governments compensate infected herds, pre-emptively slaughtered herds, animal welfare slaughtered rather generously (to stimulate co-operation of farmers), compensation may be insufficient in some cases.
(4) *Repopulation of the farm*. These losses include losses due to extra weeks with empty buildings (for example because new dairy cows are not readily available) and extra costs of animal health problems. These losses thus do *not* refer to the costs of buying a new herd; government compensation for the slaughtered herd is generally sufficient to buy back a herd of equal quality.
(5) *Price effects*. Livestock epidemics can have a rather severe impact on prices, especially on those of pigs. The size and duration of the impact depends on aspects such as the size of the epidemic (duration, size of restricted area), reactions of other countries (closure of borders, increased production) and whether vaccination is applied (which generally leads to long periods of export limitations). As explained in the previous section, note that the price effects depend to a large extent on the fact whether a country in which an outbreak occurs is an importing or exporting country with respect to products (e.g., meat, milk, eggs) involved in the export limitations.

Due to data availability requirements, this study focuses on the direct losses and the first two categories of the consequential losses. Note that other parts of the agricultural supply chain (e.g., breeding organizations, feed mills, slaughter houses, milk processing industry, transportation companies) are also affected economically (sometimes positively, mostly negatively), just as other sectors such as tourism. Due to the limited space available, we do not address these losses in this paper.

3.3. The questionnaire: eliciting expert opinions on CSF, FMD, and AI epidemics per country

Historical data about the chance of introduction of CSF, FMD and AI is very limited in most countries. Since outbreaks of CSF, FMD and AI occur irregularly in time and place it is difficult to derive general properties and predictive values. Also the probability distribution describing the possible (future!) spread of CSF, FMD and AI is difficult to ascertain.

Because there is not enough data available on FMD, CSF and AI in the different European member states of the OIE, the model used in this research is based on elicited subjective expert knowledge. Tree-point estimates that completely specify the so-called triangular probability distribution (asking for minimum, most likely, and maximum values) were elicited to derive information concerning the chance of an outbreak, the number of infected farms, duration and radius of restriction zones. Solely on basis of these numbers an estimation of the outbreak can be calculated.

As explained before, the above data for this research were collected by a questionnaire that was sent to all Chief Veterinary Officers (CVOs) of the member states of the regional Commission Europe of the OIE. The response rate was about 44% (i.e. 21 questionnaires). 36% of the returned questionnaires (i.e., 7 questionnaires) could not be used for the analysis because they were only partly completed and therefore not useful for calculations. So, we used the questionnaires of 14 countries. Because some of these questionnaires had a few missing values, a few assumptions had to be made to enable the economics calculations. For instance if economic values were not provided the average value of the other questionnaires were used.

3.4. Monte Carlo simulation as basis of epidemiological and economic models

A Monte-Carlo simulation model is constructed in order to obtain insight into the annual loss-distribution (1). Monte Carlo simulation is considered an appropriate and very flexible method of investigating aspects that are stochastic of nature, such as livestock epidemics. Including the possibility of these types of events in a simulation model is an important technique in risk analysis. Risks are thereby incorporated as probability distributions. In this study, the problem situation is analyzed by creating a stochastic simulation model with @Risk, which is manipulated by input modification with respect to the different scenarios or decisions. The applied sampling technique is Monte Carlo sampling in which random numbers are sampled from a priori specified distributions, i.e. stochastic simulation. At each iteration, randomly drawn numbers from specified distributions are used representing a possible combination of values that could occur. Combining the results of each iteration will lead to a distribution of output values, reflecting a realistic aspect of chance.

In the Monte-Carlo simulation model, a Poisson distribution reflects the uncertainty about the introduction of an epidemic in a specific year. Epidemic and ultimately economic consequences are reflected by triangular distributions, with parameters referring to the most likely, minimum and maximum values derived from the experts through the questionnaire (see previous paragraph). Results (next section) are based on 5000 iterations.

For calculating the economic consequences the following additional assumptions had to be made:
(1) For each infected farm, three farms are slaughtered pre-emptively.
(2) All affected farms (i.e. all farms that are infected, pre-emptively slaughtered, and/or located in a restriction zone) face restrictions for the whole duration of the epidemic (i.e. there are no temporarily removals of restrictions for part of the farms).
(3) For the ratio sows-to-finishing-pigs on farrowing-to-finishing farms the ratio 1:7 was used.
(4) Piglet production per sow per year, litters per sow per year, hogs (110 kg) turnover per place per year and broiler turnover per place per year were respectively rated at 22.6, 2.2, 3.18 and 7.3.

More details of the epidemiological and economic models used for our analyses are published (2, 3, 4, 5, 6, 8, 10, 12) .

4. RESULTS OF QUESTIONNAIRE-BASED EPIDEMIOLOGICAL-ECONOMICS ANALYSIS

4.1. Epidemiological results

The CVOs were asked about the expected occurrence and size of a CSF, FMD and AI-epidemics in their country for the next five years (i.e., 2003–2008). Table 2 shows the averages of the most likely, minimum and maximum estimated values of the occurrence of an outbreak (using all 14 questionnaires). It also shows the two extreme countries for each disease (called 'optimistic' and 'pessimistic'). A complete overview of the responses is given in Appendix I and II. The table shows that CSF is most likely to occur, on average, 2.93 times per country in the next 5 years. FMD is likely to occur, on average, 0.74 times and AI 0.86 times per country in the next 5 years. The most optimistic situation was estimated for FMD with the most likely, minimum and maximum number of outbreaks at 0. The most pessimistic scenario was estimated for CSF with most likely, minimum and maximum number of outbreaks of (respectively) 25, 10 and 100.

Table 2. Expected number of CSF, FMD and AI outbreaks per country for 2003 to 2008

	Average (all countries; n=14)	Optimistic	Pessimistic
CSF most likely	2.93	0	25
CSF minimum	1.04	0	10
CSF maximum	11.15	1	100
FMD most likely	0.74	0	2
FMD minimum	0.25	0	0
FMD maximum	2.46	0	5
AI most likely	0.86	0	2
AI minimum	0.23	0	0
AI maximum	3.08	1	5

In Table 3 the most likely, minimum and maximum estimations for the size of epidemic are shown. Included were the number of farms infected, the duration of an epidemic (expressed in days) and the radius of restriction zones (in km). The latter refers to the total area that is expected to be confronted with restrictive measures.

For CSF, the average most likely value of the number of pig farms that will be affected is 11 with a minimum of 2 and a maximum of 117 (during the 5-year period). The duration of the epidemic is estimated to last 66 days with a minimum of 28 days and a maximum of 153 days. The radius of the affected area is 26 km with a minimum of 9 km and a maximum of 56 km. Again the most optimistic and most pessimistic individual-country scenarios are shown. The values for FMD are comparable with CSF, while AI is expected to affect less farms with a lower duration and radius.

Table 3. Average expected size of CSF, FMD and AI-epidemics for the period 2003-2008 and the most optimistic and most pessimistic individual scenarios (most likely values, and the minimum and maximum values between brackets)

CSF	Average (n=14)	Optimistic	Pessimistic
No. of pig farms infected	11 (2-117)	1 (0-2)	50 (6-1200)
Duration of epidemic (days)	66 (28-153)	7 (5-30)	180 (60-365)
Radius of affected area (km)	26 (9-56)	3 (3-5)	100 (14-200)
FMD	Average (n=14)	Optimistic	Pessimistic
No. of pig farms infected	12 (3-63)	0 (0-1)	50 (20-500)
No. of cattle farms infected	21 (10-147)	0 (0-1)	100 (50-1000)
No. of sheep & goat farms infected	11 (2-104)	0 (0-1)	50 (5-1000)
Duration of epidemic (days)	55 (23-139)	10 (5-14)	150 (60-365)
Radius of affected area (km)	23 (9-83)	5 (3-10)	50 (14-300)
AI	Average (n=14)	Optimistic	Pessimistic
No. of poultry farms infected	4 (1-32)	1 (1-2)	15 (5-200)
Duration of epidemic (days)	33 (22-95)	5 (3-10)	90 (60-340)
Radius of affected area (km)	18 (8-50)	3 (3-10)	50 (10-200)

Table 4. Rating scores of the relative importance of risk factors and risk countries (average most likely value (n=14) and minimum and maximum values between brackets)

*Risk factors that cause the **introduction** of the virus*	CSF	FMD	AI
Import of livestock	19.33 (0-50)	23.81 (0-75)	25.32 (0-90)
Import of animal products	29.43 (0-94)	28.05 (0-90)	7.68 (0-40)
Swill feeding	8.86 (0-30)	6.43 (0-40)	1.27 (0-15)
Tourists	8.67 (0-30)	13.62 (0-60)	4.45 (0-25)
Returning empty livestock trucks	9.14 (0-25)	10.14 (0-30)	7.91 (0-30)
Air	0.62 (0-5)	6.48 (0-30)	5.55 (0-65)
Wildlife (birds, feral, boars)	20.00 (0-60)	2.71 (0-25)	43.82 (0-100)
*Risk factors that cause the **spread** of the virus*	CSF	FMD	AI
Movement of infected animals	34.50 (0-80)	37.05 (0-85)	37.82 (0-80)
Airborne spread	2.45 (0-25)	8.95 (0-25)	5.45 (0-25)
Products of infected animals	12.35 (0-40)	12.59 (0-34)	11.77 (0-35)
Vehicles (transporting animals)	16.15 (0-31)	14.82 (0-30)	18.55 (0-50)
Contacts by prof. people (vets)	7.65 (0-30)	6.55 (0-20)	5.55 (0-30)
Unknown / neighborhood	20.21 (0-65)	18.33 (0-80)	13.19 (0-42)
*Countries as a **source** of introduction*	CSF	FMD	AI
Turkey	3.17 (0-36)	22.47 (0-85)	4.25 (0-36)
Middle East	3.61 (0-34)	16.32 (0-70)	10.70 (0-70)
Caucasian / Central Asian Rep.	3.83 (0-15)	7.00 (0-25)	7.30 (0-30)
'Western' Europe	46.89 (0-100)	18.16 (0-80)	25.25 (0-90)
'Eastern' Europe	29.56 (0-70)	10.58 (0-50)	10.45 (0-50)
South / Central America	1.89 (0-12)	8.11 (0-40)	4.45 (0-25)
North America	0.72 (0-10)	0.68 (0-10)	4.85 (0-30)
Asia	7.17 (0-38)	8.21 (0-30)	19.00 (0-50)
North Africa	1.67 (0-11)	4.21 (0-15)	10.25 (0-78)
Rest of Africa	1.50 (0-10)	4.26 (0-15)	4.00 (0-30)

In addition, the questionnaire contained three questions about the importance of different risk factors for the introduction and spread of CSF, FMD and AI and the importance of different (groups of) countries as a source of introduction of the disease. The experts rated the relative importance of the different risk factors on a scale of 0–

100, with 0 meaning not important and 100 meaning very important risk factor (or an very important country to introduce the disease). In Table 4 the average rating scores over all the 14 countries are given. The results show that there is a substantial variation in expectations about the importance of different risk factors. The average rating is higher than 40 only in two cases (see the risk factor 'wild life' in case of AI and the risk country 'Western Europe' in case of CSF). In the rest of the cases there is no dominating risk factor or risk country.

4.2. Economic results

Given the estimated loss distribution, including part that is compensated by the EU, the rates can be evaluated with respect to the average rate but also the distribution of the rates. The rates are expressed in promille of the animal value, without a deductible, insurance premium tax and profit. The spread in rates originates from the number and severity of epidemics occurring. Table 5 shows the annual total distributions (direct losses and consequential losses) resulting from the simulation model (5000 iterations) for CSF, FMD and AI. Data per epidemic are aggregated into annual data at the country level by considering the number of epidemics in a certain year and the losses per epidemic.

The expected total rate for CSF varies from 0.12 promille to 117.15 promille per year. The total expected rate for FMD varies from almost 0 promille to 212.42 promille per year, and the total expected rate for AI varies from 0.51 promille to 194.61 promille per year. Again, substantial differences per country are observed. The 0.75 and 0.95 percentile values indicate that the distributions of the annual rates are skewed.

Table 5. Total losses per country per year resulting from CSF, FMD and AI in promille (mean value, 0.75 and 0.95 percentile

Country	CSF			FMD			AI		
	Mean	0.75	0.95	Mean	0.75	0.95	Mean	0.75	0.95
A	0.99	1.36	4.98	0.99	0.00	0.00	9.37	0.00	66.11
B	11.92	0.00	78.41	5.76	0.00	37.77	194.61	0.00	39.39
C	3.74	5.87	15.54	2.17	0.00	16.49	2.96	0.00	23.64
D	0.15	0.00	0.00	0.78	0.00	0.00	2.42	0.00	0.00
E	48.39	51.27	257.86	212.42	0.00	1568.40	22.27	0.00	159.70
F	40.80	0.00	308.81	1.56	0.00	11.18	1.54	0.00	10.28
G	0.20	0.00	1.50	0.01	0.00	0.00	0.85	1.60	3.84
H	63.69	89.42	163.37	50.34	57.86	262.40	4.44	8.17	19.23
I	0.12	0.18	0.58	28.08	0.00	214.12	0.20	0.00	0.82
J	0.33	0.00	0.00	0.59	0.00	0.00	0.77	0.00	0.00
K	0.32	0.00	1.94	0.12	0.00	0.84	1.07	0.00	0.86
L	117.15	0.00	752.45	141.22	0.00	951.82	0.51	0.00	0.00
M	6.67	0.00	47.06	5.25	0.00	40.07	4.75	0.00	0.00
N	63.24	0.00	448.05	89.43	0.00	689.66	84.00	0.00	617.09

5. DISCUSSION AND CONCLUSIONS

In this study, a detailed risk analysis is carried out for FMD, CSF and AI in the EU. These diseases often cause major epidemics that have an enormous impact on the countries involved, because of the high morbidity and mortality among the infected animals and the consequential economic losses.

Animal density is a very important determinant for the expected rate. The export/import situation of a country is also a very important economic parameter. Because most participating countries differ considerable in these variables, results showed that rates per country differ substantially.

It is important to note that outbreaks of notifiable animals diseases also have effects on the other parts of the economy as a whole because of side effects of disease control measures (e.g. the closure of footpaths harms the tourist sector) and interactions between economic sectors (e.g. price drops for livestock products favors consumers). These 'non-agricultural' effects have not been quantified in our analysis.

Epidemiological and economic analysis were limited by the very incomplete and inhomogeneous character of the underlying data (such as in our questionnaire and in for instance EUROSTAT). Statistical (data definitions, number and size and composition of herds, aggregation of data, etc.) harmonization of this database is urgent. For some member states there is not enough data of sufficient quality to perform analysis at all. Lack of detailed data on the location of animals hampers epidemiological calculations that are needed to further define the effects of regional concentration of animal densities. User-friendly software, linked to sound scientific methods are now available but their application is severely limited because of the poor quality of underlying data that is needed as input to these systems.

This study used available knowledge to model the epidemiological and economic consequences of an outbreak. Because of this reason, the model was restricted to specific CSF, FMD and AI strains. The role of the small ruminants (goats, etc.) and back yard birds remains uncertain in the introduction and spread of contagious diseases remains a risky and uncertain factor.

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APPENDIX I: Estimated number of CSF, FMD and AI outbreaks, per country, for the period 2003-2008 (most likely, minimum and maximum values)

	A	B	C	D	E	F	G
Estimated outbreak CSF	2 (0,10)	1 (1,2)	3 (-,-)	0 (0,1)	2 (0,6)	1 (1,3)	1 (0,2)
Estimated outbreak FMD	0 (0,3)	1 (1,2)	1 (-,-)	0 (0,1)	1 (0,5)	1 (1,2)	0 (0,0)
Estimated outbreak AI	1 (0,3)	1 (1,2)	1 (-,-)	0 (0,1)	1 (0,5)	1 (1,5)	2 (0,5)

	H	I	J	K	L	M	N
Estimated outbreak CSF	25 (10,100)	2 (1,10)	0 (0,1)	1 (0,4)	1 (0,2)	1 (0.5,2)	1 (0,2)
Estimated outbreak FMD	2 (0,5)	1 (1,5)	0 (0,1)	1 (0,4)	1 (0,2)	0.4 (0.2,1)	1 (0,1)
Estimated outbreak AI	2 (0,5)	1 (1,5)	0 (0,1)	1 (0,4)	0 (0,1)	0 (0,1)	1 (0,2)

APPENDIX II: Estimated size of CSF, FMD and AI epidemics, per country, for the period 2003-2008 (most likely, minimum and maximum values)

CSF	A	B	C	D	E	F	G
Number of pig farms infected	3 (1;20)	50 (5;100)	2 (1;3)	1 (1;2)	1 (1;5)	20 (1;1200)	1 (1;10)
Duration of epidemic (days)*	40 (40;150)	180 (50;360)	7 (5;40)	15 (10;30)	15 (7;60)	100 (20;365)	10 (5;30)
Radius of affected area (km2)	30 (10;90)	20 (10;25)	20 (10;50)	3 (3;5)	10 (3;50)	70 (10;140)	10 (10;30)

	H	I	J	K	L	M	N
Number of pig farms infected	3 (0;15)	5 (1;30)	5 (1;20)	2 (1;4)	20 (6;50)	30 (2;150)	15 (1;30)
Duration of epidemic (days)*	100 (40;240)	10 (5;50)	45(8;120)	60 (45;60)	90 (40;180)	100 (50;250)	150 (60;200)
Radius of affected area (km2)	20 (10;50)	15 (10;50)	20 (10;40)	5 (3;20)	19.5 (14;29)	20 (12;30)	100 (10;200)

FMD	A	B	C	D	E	F	G
Number of pig farms infected	3 (1;20)	50 (5;100)	1 (1;3)	3 (2;5)	3 (1;10)	1 (0;15)	0 (0;1)
Number of cattle farms infected	3 (1;20)	50 (20;100)	1 (1;3)	10 (5;30)	2 (1;10)	2 (1;10)	0 (0;1)
goat farms infected	3 (1;20)	50 (5;50)	1 (1;3)	10 (5;30)	2 (1;5)	0 (0;1)	1 (1;10)
Duration of epidemic (days)*	60 (40;150)	60 (30;120)	14 (7;14)	15 (10;40)	30 (21;90)	30 (14;120)	15 (10;20)
Radius of affected area (km2)	40 (10;100)	20 (10;25)	20 (10;100)	5 (3;10)	10 (3;100)	30 (10;70)	10 (10;30)

	H	I	J	K	L	M	N
Number of pig farms infected	30 (10;500)	5 (1;30)	5 (1;20)	2 (1;4)	50 (20;100)	10 (0;50)	1 (1;20)
Number of cattle farms infected	15 (1;200)	5 (1;30)	20 (1;200)	60 (45;60)	100 (50;300)	15 (10;100)	10 (4;1000)
goat farms infected	5 (0;50)	5 (1;30)	50 (1;200)	1 (1;2)	5 (2;20)	10 (5;40)	10 (4;1000)
Duration of epidemic (days)*	150 (40;365)	20 (5;90)	100 (10;240)	10 (5;30)	90 (40;180)	80 (30;180)	100 (60;300)
Radius of affected area (km2)	40 (10;150)	15 (10;100)	40 (10;80)	5 (3;20)	19.5 (14,29)	20 (12;50)	50 (10;300)

AI	A	B	C	D	E	F	G
Number of poultry farms infected	3 (1;20)	10 (5;20)	1 (1;5)	2 (1;6)	3 (1;10)	1 (1;10)	1 (1;5)
Duration of epidemic (days)*	40 (40;150)	90 (20;150)	10 (5;21)	20 (15;35)	21 (14;30)	14 (7;90)	5 (3;10)
Radius of affected area (km2)	20 (10;50)	3 (10;20)	20 (10;50)	3 (3;10)	10 (3;30)	10 (10;50)	10 (10;20)

	H	I	J	K	L	M	N
Number of poultry farms infected	15 (1;200)	3 (1;30)	5 (1;10)	1 (1;2)	1 (1;6)	5 (1;20)	3 (1;100)
Duration of epidemic (days)*	10 (40;340)	10 (5;30)	30 (20;60)	60 (45;60)	50 (30;90)	15 (3;60)	90 (60;200)
Radius of affected area (km2)	20 (10;50)	15 (10;50)	20 (10;40)	5 (3;10)	14(6;17)	50 (10;100)	50 (10;200)

ASSESSMENT OF RISK TO PUBLIC HEALTH FROM EXPOSURE TO BSE INFECTIVITY FROM A RENDERING PLANT

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ABSTRACT

To identify and quantify the risks to public health from the BSE infective agent arising from the activities of a rendering plant, a risk assessment study was performed. The flow of infectivity entering the rendering plant was modelled using an event tree approach. The model was evaluated using a probabilistic risk assessment approach to reflect the uncertainties in the input parameters. Selected variables were defined as a distribution of values and the result calculated multiple times using a Monte Carlo simulation tool. In 2001, in the Netherlands, a total of 20 animals were tested positive for BSE. It was assumed that all of these animals would have been processed at the rendering plant as part of the SRM processing, and that they had the infectivity of a fully infected animal. The median value of the infectivity entering the process was estimated to be 2860 human oral ID_{50} units per year. More than ninety-nine per cent of the infectivity entering the plant was estimated to be inactivated by the rendering process. Of the remaining infectivity, most was found to end up in the Meat and Bone Meal (MBM) product: 7 human oral ID_{50} units per year. All of this MBM was sent offsite for disposal by incineration. Infectivity from the plant could enter the environment through one of three routes, via sludge used in landfill or spread on the land as fertiliser, waste water discharged to a canal, or as particles released to the air. In all three cases the amounts of infectivity were found to be very small and could not pose any significant risk to public health.

Key words: BSE; risk assessment; rendering plant; public health; meat and bone meal; SRM
Running title: BSE risk assessment rendering plant

1. INTRODUCTION

Bovine Spongiform Encephalopathy (BSE) or 'mad cow disease' is a fatal neurological disease of cattle, first identified in 1986. Most known cases of the disease have occurred in Great Britain, but 26 cases have been identified in the Netherlands up to the end of 2001, with the first case identified in 1997. The disease reached a peak in the United Kingdom in 1992 when over 36,000 cases were reported (15). However, with the advent of control measures this number has now been reduced to 751 in 2001 with the trend continuing downwards.

The nature of the BSE agent remains unclear. However, it is known that the agent does not evoke an immune response in the host and is resistant to inactivation by heat, chemical disinfection or radiation. The dominant theory is that the agent is a distorted form of protein known as a prion protein. This molecule is believed to be able to incite the transformation of other similar proteins to the same distorted form, leading to a slow spread of infection, starting from its origin (e.g. the digestive tract), through lymph nodes in the gut wall, and finally into the central nervous system (9).

The condition known as new variant Creutzfeldt-Jakob disease (vCJD) is believed to be a human form of BSE (16) and evidence has been presented that vCJD is caused by the same agent as BSE (2). Variant CJD is a deteriorating mental condition, typically leading to death within 6 months. This condition differs from classical CJD in that it tends to occur in younger patients (aged 16–42), produces different symptoms, and produces a different pattern of lesions in the brain of patients.

The most likely source of human exposure to BSE is through consumption of beef product that included infected offal (brain and spinal cord), and therefore all bovine tissues that may contain detectable levels of BSE infectivity were designated as specified risk materials (SRM) and banned from human food in 1989. The infectivity of BSE for humans is believed to be lower than in cattle due to the species barrier. The species barrier in this context is defined as the factor by which the effective infectivity in one species is reduced when given to a second species.

All of the Specified Risk Material (SRM) produced in the Netherlands as well as any fallen stock are processed in one of two rendering plants. As inhabitants in the vicinity of one of these plants, had expressed their concern about the possible health risk from exposure to the BSE infective agent that may be present in waste products or accidental releases from the facility, a risk assessment study was ordered by Dutch local and national authorities.

The objective of the study was to identify and, as far as possible, quantify the risks to public health from the BSE infective agent arising from the activities of a rendering plant. The risk has been presented in terms of the expected discharge of infectivity into the environment expressed as human oral ID_{50} units.

2. MATERIALS AND METHODS

The risk assessment was conducted using a tiered approach whereby the quantities of potentially infective material entering the process were identified and then followed through either to inactivation or potential release to the environment. The risk assessment considered the sources of infectivity, the treatment of materials within the plant and the pathways whereby infectivity may be released to the surrounding environment. These pathways were modelled using event trees. In order to detail the processes of relevance to the study, a series of linked event trees was constructed describing three major areas: 1) The rendering process 2) The waste processing and 3) The Environmental Pathways. The boundary of this study was defined by the perimeter of the plant, and did not include the fate of incinerated material or other off site forms of waste disposal.

Where possible actual data were used in describing the process. However, for a number of activities precise data were not available and in those cases estimates were made. All data and estimates used, were reviewed by a project steering group of specialists in the field of BSE issues, and accepted as the best available information for the assessment.

The model was evaluated using a probabilistic risk assessment approach to reflect the uncertainties in the input parameters. Selected variables were defined as a distribution of values and the result was calculated multiple times using a Monte Carlo simulation tool (@risk from Palisade Corporation, Newfield NY, USA).

The risk was presented as the expected discharge of infectivity into the environment expressed in terms of human oral ID_{50} units. A worst case assumption would be that exposure to one human oral ID_{50} unit would result in a 50% chance of infection and similarly exposure to 0.1 of an ID_{50} would result in a risk of infection of 5%. This is based on the underlying assumption that there is a linear dose response relationship and that there is no safe threshold.

2.1 Infectious dose

The infectivity of tissue from an animal with BSE was expressed in terms of its Infectious Dose 50 (ID_{50}) value. This is the dose (a single person would need to consume) to cause infection in 50% of the exposed population.

This term acknowledges that some people may become infected from much smaller doses, while others may be uninfected after consuming much larger doses. We used estimates of the human oral infectious dose described by the Scientific Steering Committee (SSC) of the European Commission (Opinion adopted 13-14 April 2000 'Oral Exposure of Humans to the BSE Agent: Infective Dose and Species Barrier') which were based on an (incomplete) attack rate experiment carried out by the UK Ministry of Agriculture Fisheries and Food (MAFF) and the calculations using the results of published and peer reviewed experiments (5). This resulted in an estimated infectious dose of 50 cattle oral ID_{50}/g clinically infected brain. The infectious dose is generally assumed to follow a lognormal distribution. Consistent with previous studies, we assumed a distribution which has a median value of 50 cattle oral ID_{50}/g. The P95 value (95% of all values are less than this number) of the distribution was 100. A distribution was used with a mean value of 90 cattle oral ID_{50}/g, a standard deviation of 150 cattle oral ID_{50}/g and truncated at 10 and 1,000 cattle oral ID_{50}/g.

2.2 Species barrier

In their opinion, the SSC concluded that the size of the species barrier between BSE in ruminants and BSE in humans (vCJD) is not known. They considered that a worst case scenario considering no species barrier (i.e. = 1) should be included, although available evidence indicates that values greater than 1 are likely to be more realistic. They recommended that, until more scientific data are available, for risk assessments of human exposure to potentially BSE infected products, a species barrier of about 1 should be considered as a worst case scenario and that the range from 10^4 to 10^1 be considered. In previous risk assessments the species barrier was represented as a distribution using values of 10, 100, 1000 and 10,000 with equal probabilities, (24.75%) and a 1% probability of it being 1 (6, 7). The same distribution was used in this assessment. (Fig 1).

2.3 Specified risk material

Specified Risk Material has been defined by the Scientific Steering Committee of the EC to include all tissues that may contain detectable levels of BSE infectivity. It includes: the skull, including the brain and dura mater, the pituitary gland, the eyes, the tonsils, the intestines from the duodenum to the rectum, the vertebral column, including the dorsal root ganglia, spinal cord and dura mater, of bovine animals aged over 12 months, and ovine and caprine animals which are aged over 12 months or have a permanent incisor tooth erupted through the gum, plus the spleens of ovine and caprine animals (EU regulations EC 999/2001 amended by EC 1248/2001, 1326/2001 and 270/2002). For the purposes of this study it was assumed that all of the SRM produced in the Netherlands was processed at the rendering plant under study.

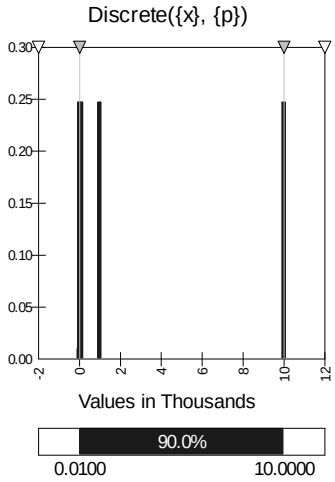

Figure 1. Plotted distribution of the cattle to human BSE species barrier (note that at this scale it is difficult to distinguish between 1, 10 and 100).

2.4 Infectivity input

The total infectivity entering the rendering process was obtained by combining the total number of animals for processing, the assumed prevalence of BSE in the cattle, and the estimated infectivity per infected animal. The data used in this assessment were for 2001 where possible. Where 2001 figures were not available for the study , less current information was used, and this was made clear in the text.
In 2001, the Netherlands, in line with other EU countries, started a programme of testing for the BSE infective agent, using the commercially available Prionics® assay which has been approved by the EU. Cattle in the Netherlands are tested for BSE if they fall into one of the following three groups:

- Animals over 30 months of age at the time of slaughter (This category includes animals over 24 months, not completely healthy at slaughter or emergency slaughtered)
- Fallen stock over 24 months of age
- Animals showing clinical signs of disease consistent with BSE.

All bovines over 30 months are tested at the slaughterhouse. Any positive cases are removed from the production line and sent to a rendering plant for processing.
Fallen stock are tested on arrival at the facility. These are animals that have died on the farm or have been put down by a veterinary surgeon. The complete carcasses are processed with other SRM. For the purposes of this study it was assumed that in all these cases the level of infectivity was the same as in a clinical case.
Of all animals diagnosed with clinical signs of BSE on a farm and tested positive at the laboratory, the carcasses are sent to the rendering plant for processing and subsequent incineration. In these cases, the complete herd is also slaughtered and tested for BSE. We did not assume any additional infectivity from the rest of the herd unless other BSE positive animals were identified.
Most of the infectivity in a clinically infected animal is found in the brain and spinal cord and some other CNS tissues. Residual infectivity associated with SRM products other than brain and spinal cord is assumed to constitute a small fraction of that contained in CNS tissues, which typically represents some 750 grams of infected material per infected animal. For the purposes of this study the weight of infective material was therefore taken as a total of 750g per animal. Thus the infectivity coming into the plant was the number of infected animals multiplied by the infectivity values given in Section 2 multiplied by the amount of infected material (750 g).
It was assumed that all cases had the infectivity of a fully clinical case, although particularly in cases detected early in the infection this is unlikely to be the case. It is generally accepted that the highest titres of infectivity are found in clinically affected animals in the terminal stages of the disease. The rapid BSE test used, may also detect cases several months (estimated 3 to 5) before the final stage of the disease, in which case the infectivity level will be lower (3). The difference is difficult to assess, but it could be in the range of 10-fold lower.
The total infectivity was defined by the following equation
TOTINF = NOC * WTINF * INFDOSE / SPECBARR where
TOTINF = total infectivity measured in human oral ID_{50} units per year
NOC = number of cattle processed per year (assumed to be 20)
WTINF = weight of infected material per animal (assumed to be 750 gm)
INFDOSE = infectious dose, measured in cattle oral ID_{50} units (variable, see M&M)
SPECBARR = species barrier (highly variable, see M&M)

2.5 Effects of rendering on infectivity

For the purposes of this study it was assumed that the only points in the rendering process where activity is reduced through treatment are during the sterilisation stage and where materials are burned in the boiler. Inactivation studies (10) using a laboratory scale simulation of the rendering process have shown that it will lead to a reduction in infectious load of at least 1 in 200 and probably 1 in 1000. The studies of Schreuder et al. are relevant to the rendering facility under study and their results were used here. We adopted a conservative estimate of a 200 fold reduction of infectivity in the MBM as the best estimate with a 95 percentile figure of 1000.
An important attribute of the prion protein is that it is hydrophobic, and will tend to attach to solids (8). Thus any infective material will tend to associate with the MBM as opposed to tallow (fat) or liquid effluent streams. This aspect of prion behaviour formed a fundamental assumption used in modelling how potentially infective material will behave within the rendering process and environmental pathways. In this study it was assumed that any suspended solids associated with the fat stream or liquid effluent had the same infectivity as the MBM, and that removal of suspended solids by effluent treatment will remove infectivity (14). For the purposes of this study it was assumed that rendering results in the production of MBM, fat and water in the ratio of 24:12:64 respectively (data supplied by the plant).

3. RESULTS

3.1 Infectivity input

The overall plant capacity was 600,000 tonnes per year, but the plant was not run at full capacity. In 2001 the plant processed some 580,000 tonnes of material, composed of slaughter-by-products, blood, feathers, pig hair and fats and oils. This study was only concerned with the slaughter by-products that are considered to include all the SRM and fallen stock.
The numbers of animals tested for BSE in the Netherlands and the resulting proportion found positive are shown in Table 1. for each category.

Table 1 Numbers of animals tested in 2001 and found positive for BSE in the Netherlands

Category	Number tested	Positive for BSE	
		Number	Percentage
Over 30 months*	500,000	11	0.002
Fallen stock (>24 months)	30,599	3	0.01
Clinical cases		6	

* This category includes animals over 24 months, not completely healthy at slaughter or emergency slaughtered

From Table 1. it can be seen that 20 BSE positive cases were identified in the Netherlands in 2001. It was assumed for this study that 100% of the infectivity from these 20 animals was sent to the rendering plant for processing together with other SRM.

We defined the total infectivity as TOTINF = NOC * WTINF * INFDOSE / SPECBARR (see 2.3). Because two of the parameters are highly variable there is no single calculated value for the total infectious material. The final answer can be as low as:
TOTINF = 20 * 750 * 10 / 10,000 = 15
or it can be as high as
TOTINF = 20 * 750 * 1,000 / 1 = 15,000,000 when the minimum and maximum values of species barrier and infectious dose are taken into account. A more realistic answer was obtained when all possible combinations were considered, and practical minimum (P5), practical maximum (P95), mean and median values were calculated. This was achieved by randomly selecting the paprameter values (but in a manner so that the characteristics of the input distributions are preserved), using the Monte Carlo method. The final output distribution is presented in Table 2.

Table 2 Total infectivity entering the rendering plant

Measures	Human oral ID_{50} units
P5	34
Median (P50)	2,860
Mean	53,000
P95	224,000

The median value is plotted in Figure 2. Note that only part of the graph is shown here. Maximum values can reach into the millions, as discussed above. Hence the curve has a very long ‘tail’; this accounts for the high mean or average values, and the fact that 50% of the values calculated are higher than the median value of 3110.
The median value was used as this was considered to be a good representation of the central tendency of the data, whilst remaining relatively conservative in relation to the vast majority of values generated. This is consistent with other studies in this area.

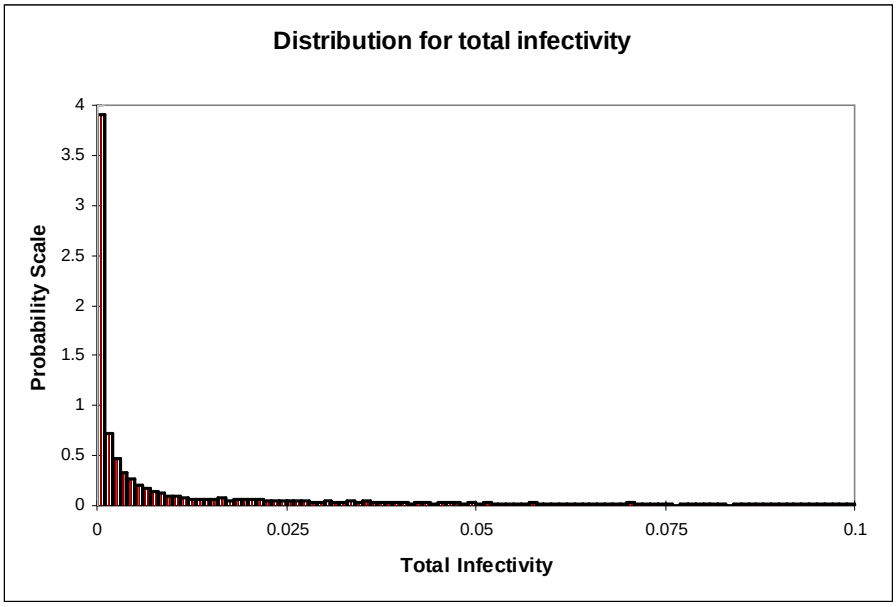

Figure 2. Distribution of total infectivity entering the rendering plant. Median value 2860.

3.2 Process description

The production process for SRM is geared to process the raw materials into MBM and fat. Raw materials are consecutively reduced, cleared of metal, ground, evaporated and sterilised, with all end product materials destroyed by incineration. SRM is processed via an independent line within the plant. This system has been designed to ensure segregation of this material from other processing streams that may be subject to lower levels of containment and disposal.

To model the proces for the purpose of this study, the rendering process was broken down into a number of steps, namely: reception, metal detection / size reduction hall, vaporisation, sterilisation and de-fatting, and milling and storage.

The flow of materials through the rendering process is relatively complex, with recirculation and reintroduction of materials at various points. However, in this study it was assumed that only materials entering or leaving the containment offered by the process are of concern

Table 3. summarises the stages in the process where materials are removed, either as part of a waste stream or as products.

Table 3 Products produced in processing SRM

Activity	Product					
	Waste water	Air	Vapour	Metal	MBM	Fat
Reception	○*	○				
Metal detection / size reduction		○		○		
Vaporisation	○	○	○			○
Sterilisation & de-fatting	○	○	○			○
Milling and storage		○		○	○	

*Material passed to sewage treatment only in the event of a spillage outside the reception building

As the distribution and flow of MBM through the process was central to modelling potentially infective material within the plant, values were assigned to product and waste streams to reflect the associated proportion of solid material (see figure 3.). The following sections describe each of the main process activities in detail, together with their associated waste and product streams.

3.3 Reception

Dedicated vehicles are used to collect SRM and these follow a defined route within the plant before being unloaded in a dedicated bay. The reception area is enclosed within a building and serviced by dedicated drains in order that any wash or spillage in this area is fed into the process. Drains outside this building feed to the plant's

own waste water treatment plant. Raw materials are deposited into bunkers, and afterwards the trucks are cleaned and disinfected. Waste material is mainly associated with wash water that is fed into the process via the dirty water tank, with any solid material entering the bunkers for processing.

3.4 Metal detection and size reduction hall

Raw materials are crushed by pre-breakers, and metal-free material is further reduced in fine breakers. Metal-containing material, divided from metal-free material by metal-detectors, is heated in a pre-cooker to 145^{o}C and 4 bar gauge for about 1 hour. The cooked material is then mixed with the metal free material and recycled fat, before being further reduced in disintegrators, to slurry that is transported to a three-stage evaporation installation. The metal material remaining in the pre-cooker is treated with a caustic solution and transported off site as production waste, with the wash solution fed back into the process.
For the model it was assumed that 1kg/tonne of raw material solids will be associated with the metal stream. It is likely that both the cooking and the caustic treatment result in some reduction in infective load, but this was not included in the model. There are no indications for concentration through evaporation or smearing of dried out material, during the cooking process. A resulting reduction of effectiveness of autoclaving (13), therefore was not included. The only other waste product from this stage is air.

3.5 Vaporisation

In the vaporisation stage reduced materials are separated into solids and fat. The solid portion is sent to the autoclave for further processing, and the separated fat is treated into a finished product or reintroduced into the process via fat recycling tanks, to act as a carrier for the MBM and maintain the consistency of the product.
Approximately 25% (200 tonnes) of the fat produced during vaporisation is burned in the plant's boilers. In the evaporator the slurry is further dried to the desired moisture content, and the vapour produced is transported to the second stage. The dried slurry is then passed to decanters, where it is separated into (coarse) fat and dry solids (half-product). During vaporisation half- product fat is produced and vapour driven off the mixture to form condensate. Vapour produced during vaporisation and sterilisation consists condensate and non-condensables. The condensate is cooled to produce waste water that is routed to the waste water treatment plant, whereas the non-condensate remains in the vapour phase and is washed before being sent to be burned in the boilers. It was assumed that 90% of the solid material associated with the condensate will be derived from the vaporisation stage, with the remaining 10% from sterilisation.

3.6 Sterilisation and de-fatting

Half-product from the decanters is transported to autoclaves, where it is sterilised and further dried. Sterilisation also results in the production of vapour and fat from the process, with the vapour fraction forming condensate and non-condensate fractions.
Sterilisation occurs under steam pressure where materials are heated to 133 ºC and 3 bar pressure for 20 minutes. After each batch, the contents of the autoclave are removed. Remaining fat is removed by gravity separation and extraction presses. The meal product, known as crackling, is then transported to the cool bunker.
Surplus fat from the decanters that is not brought back into circulation is purified in a decanter, with the separated solids transported back to the fat extraction presses. The fat produced at the sterilisation stage (3% of the total fat removed from the system) is pumped via precipitation tanks and a filter into storage tanks before incineration. The same proportion of the fat produced as in vaporisation (approximately 25%) is burned in the plant's boiler house.

3.7 Milling and storage

Crackling is transported from the cool bunkers and combined with blood meal. Any remaining metal is then removed from the coarse parts of the product before it is further reduced in hammer mills via dosage bunkers. The product is then brought up to the desired moisture content and transported via mixing silos to the storage silos, which feed two granule press installations. Any particles contained in the cooling air are extracted in cyclones and transported to the air treatment installation for purification. The granulated meal is transported off from separate silos via a loading bay.

3.8 Product and waste processing

Throughout the rendering process there are stages where materials are removed either as product or waste materials. Figure 3. shows the event tree that was used to model these events, which are described in the following sections.

3.9 MBM and fat

MBM and fat are the products of the rendering process and which normally be sold for incorporation into other products, including fertiliser and animal feeds. However, due to the nature of the material used to produce these products they are sent for disposal by incineration. The scope of this study does not include the fate of the products of incineration, although this will almost certainly further reduce the potential infectivity by several orders of magnitude.

3.10 Waste water treatment

All waste water produced on the rendering plant is treated in the dedicated treatment plant on site. Sources of waste water from the process were identified as condensate from vaporisation and sterilisation, together with wash water used to remove particulates from air and non-condensates. In addition, waste water is received from the other process facilities on the site. The flow of liquid into the sewage treatment plant is approximately 600,000 m^3 per year. Less than 40% of this amount is related to the processing of slaughter byproducts etc. and has a suspended solid content of 0.01-0.02%. The remaining liquid flow comes from cleaning water and rainfall. For the model an assumed value of 0.02% solid content in 600.000 m^3 was taken. Of this solid material the fat content has been measured to be approximately
150-300 mg/l (assumed value 150 mg/l). The difference between the suspended solid content and that accounted for by the fat fraction is therefore 30 tonnes per year. However, the total tonnage of solid material removed as sludge from the water treatment plant is approximately 1,000 tonnes per year. This discrepancy is accounted for by the addition of other materials including dust, leaves, solids from other processing lines (e.g. feathers and hair lines), and the products of microbial growth within the waste water treatment plant. Sludge from the treatment plant is removed by tankers and is normally fed into a deep well oxidation facility, where it is oxidised under conditions of high temperature and pressure. In times when the deep well oxidation facility is out of commission the material can be disposed of by dumping at landfill sites or spreading on the land as fertiliser in accordance with current legislation.
For the purposes of the study a simplified model of waste water treatment was adopted, where a series of filters remove a large portion of the solid material from the process with the remainder discharged to the canal at a suspended solid concentration of 5mg/litre

3.11 Air treatment

All activities associated with the rendering process involve the removal of air from the plant and surrounding areas. This measure has been designed both to remove potential aerosols and control odours. The total volume of air removed from the areas of the plant was estimated to be 1.3×10^9 m^3/yr.
Solid material is removed from the air by scrubbers and passing through a water bath. Removed solids are assumed to enter the water treatment process. For the purpose of this study these were included as a small unspecified part of the condensate fraction. The fraction of solids that is not removed from air is likely to be extremely low, and was estimated 1 $\mu g/m^3$. Fractions of this material were allocated to the air streams originating from different processes in accordance with the volumes of air processed, reflecting stages before and after sterilisation has taken place. All air is passed over a biofilter before being released to the environment. It was also assumed that 90% of the particulate matter will adhere to the biobed material. The biobed material itself is used for 2 –3 years before being buried in the grounds of the plant.

3.12 Combustion in boilers

Non-condensable gases produced during vaporisation and sterilisation are burned in the boiler, together with 25% of the fat produced. It was assumed that a reduction of one million fold will be achieved when material is burned in this way. Negligible quantities of soot were reported to remain in the boiler and it was assumed that all particulate material will pass up the stack.

3.13 Output of infectivity

The model indicates that approximately 99% of the infectivity associated with processing the material is inactivated as a consequence of the rendering process. This includes material inactivated in the sterilisation phase, together with further reduction that occurs as a consequence of burning fat and non-condensables in the boiler.
Table 4. shows the total amount of infectivity associated with the product and waste streams from the rendering plant under normal operation conditions, based upon the input data provided for this study. Values are shown as the median (P50), 5 percentile (P5) and 95 percentile (P95) values. Values referred to in the paper are median values unless otherwise stated.

Table 4: Summary of Infectivity Associated with Product / Waste Streams

	Human oral ID_{50} units		
Parameter	P5	P50	P95
Infectivity entering process	34	2,860	224,000
Infectivity removed			
Infectivity removed during rendering	34	2851	223,291
Infectivity removed in boilers	9.6×10^{-6}	8.1×10^{-4}	6.3×10^{-2}
Total infectivity removed	34	2851	223,291
Infectivity to offsite disposal			
Infectivity associated with MBM product	8.3×10^{-2}	7	568
Infectivity associated with fat product	1.3×10^{-2}	1	82
Infectivity associated with metal	7×10^{-6}	6.2×10^{-4}	4.9×10^{-2}
Total infectivity to offsite disposal	9.6×10^{-2}	8	652
Infectivity to environment			
Infectivity released to canal	2.3×10^{-7}	1.9×10^{-5}	1.5×10^{-3}
Infectivity associated with WTP sludge	8.3×10^{-3}	7.1×10^{-1}	55
Infectivity released to air	1.5×10^{-8}	1.3×10^{-6}	1.0×10^{-4}
Infectivity associated with biofilter	1.4×10^{-7}	1.2×10^{-5}	9.0×10^{-4}
Infectivity released with combustion gas	9.6×10^{-12}	8.1×10^{-10}	6.3×10^{-8}
Total infectivity released to environment	8.3×10^{-3}	7.1×10^{-1}	55

3.14 Infectivity to offsite disposal

The estimated levels of infectivity associated with MBM and fat were 7 and 1 human oral ID_{50} units per year, respectively. This would result in final concentrations based on the estimated quantities of product produced of 7×10^{-8} and 2×10^{-8} human oral ID_{50} units/kg. The infectivity associated with waste metal (total value 7×10^{-4} human oral ID_{50} units per year) was very low.

3.15 Infectivity to environment

The most significant source of infective material to be disposed to the environment was the sludge from the waste water treatment plant with 1 human oral ID_{50} unit per year. This was normally sent to deep well oxidation but could be put in landfill or spread on the land as fertiliser if the first option was not available.
The total amount of infectivity released to the canal was very small at 2×10^{-5} human oral ID_{50} units per year. This infectivity is released in a total discharge of 600,000 m^3 giving an extremely low concentration of 3×10^{-11} human oral ID_{50} units/m^3.

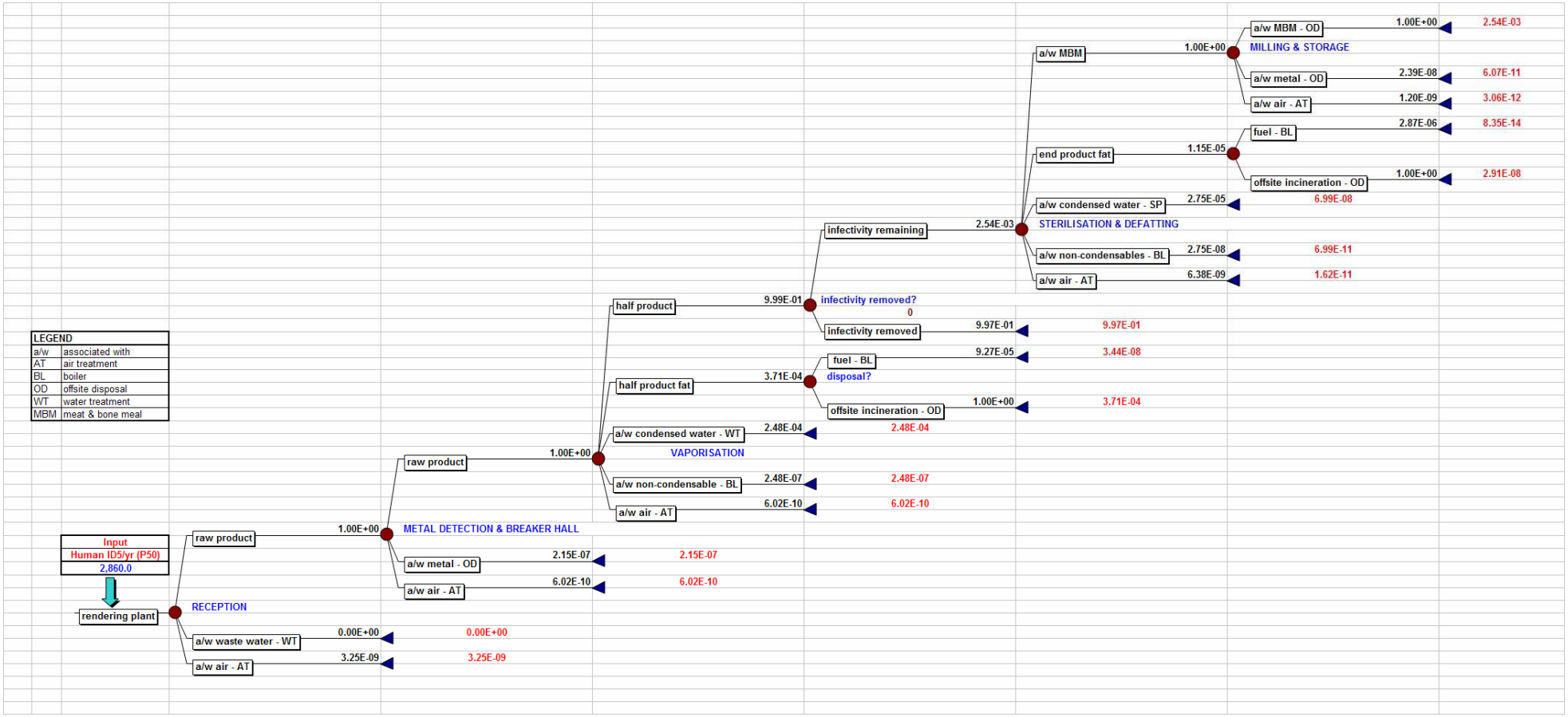

Figure 3: Event tree for rendering process

Very low amounts of material are associated with the biofilter (9×10^{-6} human oral ID_{50} units per year) and burial of this material is therefore considered to be of very low risk. Similarly the fraction released to the air (9×10^{-7} human oral ID_{50} units) is not considered to be significant, even before a massive dilution factor is applied.
Releases of infectivity associated with combustion gases were extremely small with a total emission value of 8×10^{-10} human oral ID_{50} units. This figure is largely due to the large reduction in infectivity through burning material in the boilers.

3.16 Risk associated with water treatment plant effluent

In order to put output values into context using an example, we can consider the risk to a person drinking the effluent from the waste water treatment plant before it is discharged to the canal, an unlikely eventuality in itself. Discharge to canal has 2×10^{-5} (P50) or 2×10^{-3} (P95) ID_{50} units per year in a discharge of 600,000 m^3.

1. A typical person drinks 2 litres water per day (730 l/year).
2. If a person were to have the discharge to the canal as their sole supply of drinking water, then their exposure would be:
   - P50: $(2 \times 10^{-5} / 600{,}000) * 0.73 = 2 \times 10^{-11}$ human oral ID_{50} per year.
   - P95: $(2 \times 10^{-3} / 600{,}000) * 0.73 = 2 \times 10^{-9}$ human oral ID_{50} per year.
3. This person's risk of infection would therefore be 2×10^{-11} per year, well below the negligible level of 1×10^{-8} per year, or 2×10^{-9} per year if the discharge was at the P95 level for the whole year (which is highly improbable).

4. DISCUSSION

The objective of this study was to identify and, so far as possible, quantify the risks to public health from the BSE infective agent arising from the activities at a rendering plant.
According to this study, after inactivation by the rendering process, most of the remaining infectivity, will be found in the Meat and Bone Meal (MBM) product: 7 human oral ID_{50} units per year. (6×10^{-8} human oral ID_{50} units per kg MBM). All of this MBM is sent offsite for disposal by incineration. Infectivity from the plant can enter the environment through one of three routes, via sludge used in landfill or spread on the land as fertilizer, via waste water discharged to the canal, or as particles released to the air. This results in emissions into the environment (P50 values) of 2×10^{-5} ID_{50} units per year in waste water, 7×10^{-1} ID_{50} units per year in WTP sludge, and 9×10^{-7} ID_{50} units per year released to air. Infectivity discharged to the canal is released in 600,000 m^3 /year, giving a concentration of 3×10^{-11} human oral ID_{50} units per m^3, and the amount of sludge produced per year is 1000,000 kg, giving a concentration of around 9×10^{-7} human oral ID_{50} units per kg. The dilution of infectivity in the air is unknown but definitely massive at all times. This means that in all three cases, according to this study, the releases of infectivity into the environment from the normal operation of the rendering plant were extremely small.
There are no universally applicable criteria to define whether or not risks are tolerable; this is a social and political judgement which can be guided, but not replaced by technical advice.
Risk criteria used in the Netherlands to assess the impact of hazardous installations have been set out in an Ordinance known as 'Besluit Risico's Zware Ongevallen' (BRZO) that was issued in 1988, amended in 1990 and 1992 (BRZO, Staatsblad 1988, 432; W-BRZO-I, Staatsblad 1990, 443; -BRZO-II, Staatsblad 1992, 291) and amplified in the report 'Omgaan met Risico's' (Tweede Kamer 1988-89, 21, 137, No 5). This report defines a Maximum Permissible Risk as being an individual risk of 10^{-6} per year for new situations and 10^{-5} per year for existing situations, with a Negligible Risk defined as 10^{-8} per year. An 'Individual Risk' was defined as the risk of fatality to a hypothetical individual exposed 24 hours per day at a given location. According to these criteria, the releases of BSE infectivity into the environment from the rendering plant under study would not pose any significant risk to people living in the vicinity, especially because intake by humans of large amounts of WTP sludge or effluent, is highly improbable.
For the purpose of the study, BSE infectivity was assumed to be exclusively present in SRM. If, as a result of future research other tissues may also appear to contain BSE infectivity, these tissues will be included in SRM processing and this may influence the outcome values of released BSE infectivity by rendering plants.
A major assumption for modelling the behaviour of the BSE agent in the rendering process was that the BSE prions are bound to particulate matter. This has been adopted Gale and cworkers, who studied the biophysical properties of the BSE protein (8). Another important assumption was that BSE infectivity will not be present in tallow. Taylor et al. (14) tested for the presence of infectivity in the fat stream. They tested unfiltered tallow from two processes and found no detectable infectivity. In one of the processes the level of infectivity in the MBM was similar to that in the raw material (i.e. there had been no significant reduction in infectivity) and yet

there was still no infectivity detected in the tallow. This is supported by the Scientific Steering Committee of the EC in their revised Opinion on the safety of tallow (12). In this Opinion the SSC concludes that 'There is no evidence that tallow derived from ruminant animals would constitute a TSE risk, although according to the SSC it is not possible to absolutely exclude any risk of BSE infectivity being present in tallow (12).

Since the study was conducted to assess the risk to public health, worst case assumptions were applied throughout the study. Input parameters were always chosen to be conservative, and it was assumed that there was a linear dose response relationship and no safe threshold. This is likely to be pessimistic especially for low exposures. The assumption that all detected animals are infected at the clinical level was also a conservative estimate. Based upon experimental work in hamsters (1) and pathogenesis studies in mice, sheep and cattle, it can be assumed that there are two stages in the 'BSE replication'. Initially there is a zero phase, during which the agent multiplies in peripheral nerves between gut and CNS, followed by a period of logarithmic increase when it reaches the CNS. This takes place roughly in the last 50% of the incubation period. The conservative assumption that all detected animals are infected at the clinical level addresses the issues that there may be low levels of infectivity associated with animals that fall below the detection levels of the test, false negatives, and any infectivity associated with peripheral tissues other than brain and spinal cord. To estimate the inactivation by the rendering proces, the conservative level of BSE inactivation found by Schreuder et al.(10), was used, and it was assumed that the only points in the rendering process where activity is reduced through treatment are during the sterilisation stage and where materials are burned in the boiler. This is considered to be a cautious assumption as there are other steps including vaporisation and microbial degradation processes within the sewage treatment plant, where there will very probably be a further significant reduction in infectivity.

An interesting finding was the fact that WTP sludge appeared to contain higher levels of BSE infectivity than MBM (9×10^{-7} human oral ID_{50} units per kg versus 6×10^{-8} human oral ID_{50} units per kg). The levels of infectivity associated with WTP sludge can be explained as the majority of suspended solid was assumed to come from condensate associated with the vaporisation phase, which occurs prior to sterilisation. It was assumed that the vaporisation process does not result in any inactivation of infectivity. Given that this infectivity will be distributed within 1,000 tonnes of sludge the final concentration was relatively low at around 9×10^{-7} human oral ID_{50} units/kg. According to current EU legislation MBM has to be incinerated whereas WTP sludge may be dumped at landfill sites.

Rendering plants are indispensible in animal production and extremely important to veterinary and public health, because numerous infectious agents are inactivated by the process. The heat stability of the prion protein has raised questions about possible releases of the agent into the environment but has also forced rendering plants to adjust their proceses. Quite a number of assumptions had to be made to assess the released BSE infectivity, because of the complicated processes.

This study has shown that the possible releases of BSE infectivity into the environment from the rendering plant under study, are extremely small and do not pose any risk to people living in the vicinity. It needs to be emphasized that the results of this study may not be applicable to other rendering plants because there can be significant differences in the way the proces is undertaken or in waste management controls.

ACKNOWLEDGEMENTS

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EPIDEMIOLOGICAL RESEARCH OF SALMONELLA, MYCOPLASMA HYOPNEUMONIAE AND LAWSONIA INTRACELLULARIS ON BELGIAN PIG FARMS.

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ABSTRACT

Epidemiological aspects of Salmonella, Mycoplasma hyopneumoniae and Lawsonia intracellularis were investigated in pigs from 144 farrow-to-finish pig herds. Blood was collected at slaughter from 50 pigs per herd. The within-herd prevalence or the proportion of seropositive pigs per herd was assessed for each of these pathogens. Also slaughterline findings like pneumonia, pleuritis, white spots and scabies lesions were collected 4 times within one year. From 71 herds 10 samples were analysed for Porcine Haptoglobine. Herd factors were obtained trough face-to-face interviews of the pig farmers as well as through inspection of the pigs and the pig units. The average within-herd seroprevalence and the herd prevalence of the pathogens were resp.: Salmonella 73.4% and 98.6% for OD 10%, 51.8% and 97.9% for OD 20%, 30.1% and 91% for OD 40%, Mycoplasma hyopneumoniae 69.4 % and 93.2 %, and 68.1 % and 95.8% for Lawsonia intracellularis. Analysis of risk factors is going on.

SAMENVATTING

Op 144 Belgische gesloten varkensbedrijven werd een epidemiologische studie verricht voor volgende aandoeningen: Salmonella, Mycoplasma hyopneumoniae en Lawsonia intracellularis. Er werd bloed verzameld van 50 vleesvarkens van elk bedrijf in het slachthuis. Ook slachtlijnbevindingen zoals pneumonie, pleuritis, white spots en schurftletsels werden verzameld. Deze slachtlijnbevindingen werden 4 keer gedurende één jaar voor elk bedrijf verzameld. Van 71 bedrijven werden er gemiddeld 10 stalen onderzocht op de concentratie van Porcine Haptoglobine (HP). Bedrijfsfactoren werden verzameld door middel van een persoonlijk afgenomen enquête, de verzamelde informatie werd nagegaan tijdens een rondgang in de stallen. De gemiddelde binnen-bedrijfsprevalentie en bedrijfsprevalentie is 73.4% en 98.6% voor Salmonella OD 10%, 51.8% en 97.9% voor Salmonella OD 20%, 30.1% en 91% voor Salmonella OD 40%, 69.4 % en 93.2% voor Mycoplasma hyopneumoniae en, 68.1 % en 95.8% voor Lawsonia intracellularis. Momenteel gaat er gestart worden met de analyses die de verbanden met de bedrijfsfactoren zullen nagaan.

1. INTRODUCTION

A high farm density and a lot of movements of piglets are typically for Belgian pig production. This includes a high sanitary risk, as being illustrated by the outbreaks of classical swine fever in the past. However, present pig production is also characterised by a change in the production from a high quantity to a high quality of the products. Moreover, people get more and more concerned about food safety and quality, integration, and a smaller profit margin for the individual pig holder.

In contrast with our neighbouring countries, assessment of the sanitary risk of pig herds in Belgium is lacking. This assessment is important to develop a good protection strategy in relation to outbreaks of infectious diseases of list A of the OIE, but also for the optimisation of the daily management on the farm. Enzoötic diseases like

Aujeszky Disease Virus, Mycoplasma and Actinobacillus pleuropneumonia, cause often lower technical results, higher veterinary costs, i.e. a lower income for the pig farmers. (6,17). For countries like Belgium which are strongly dependent on export of pig products, export limitations as a result of not being free from diseases mean important economically losses. Therefore the pig farmers strive for a good health status of their herds, but it is important to work as much as possible with preventive measurements.

A tool to support this strategy could be a scientifically based sanitary risk index (SRI). It gives the probability that a certain % of animals has antibodies or lesions against a selected pathogen. The index will be based on the results of risk-factor analyses. Attention was focused on a few important enzootic pathogens, i.e. Lawsonia intracellularis (Law) and Mycoplasma hyopneumoniae (Myco), and on an important zoönotic pathogen, i.e. Salmonella (Sal).

Possible applications of the SRI are:

a) National government:
   - eradication of infectious diseases (11);
   - determination of sanitary contribution and certification (3);
   - contribution determination for insurance against infectious diseases like classical swine fever and Foot and Mouth disease (19);
   - control of zoonotic diseases.

b) Integral chain quality control (7):
   - health status of the herd;
   - quality of the products.

c) Farm level:
   - choice of purchase farms;
   - choice of transport and/ or merchant;
   - improvement of the own farm results.

Preliminary results show that a positive relation exists between certain “acute phase proteins” (like haptoglobine HP), slaughterline findings and the hygienic status of the herd. (13, 14). Relevant health parameters, which may be collected routinely are clinical findings (cough, sneezing, limping) (15, 31), the use of medicines (24) and slaughterline findings (7, 17). Structural parameters like type of the herd the number of animals, purchase and sale police but also density are important risk factors (8, 24, 4, 36).

1.1. Research questions

The SRI will give an answer on the following question:
Has a specific pig herd (or a part of it) more or less risk on the presence of a certain pathogens (such as Salmonella, Mycoplasma hyopneumoniae or Lawsonia intracellularis), and is it possible to estimate the risk by objective, reliable and useful parameters (the risk factors, the X-variables in the statistical models)?

Therefore, the main research questions of the project are:
- What is the prevalence (the prevalence of seropositive herds and the within-herd prevalence) for Salmonella, Mycoplasma hyopneumoniae and Lawsonia intracellularis on farrow-to-finish herds?
- What are the effects of management and other herd factors on the prevalence of these pathogens?
- Is it possible to quantify objectively risk factors for the presence of these pathogens?

Additional research questions of the project are:
- What is the value of slaughterline findings and acute phase proteins for the determination of a health status of a pig herd?
- Is there a seasonal effect in the prevalence of slaughterline findings?
- Is there a correlation between the serological results for Lawsonia intracellularis and the results of the palpation of the small bowels in the slaughterhouse?
- Is there a correlation between the serological results for Salmonella and the bacteriological results for Salmonella on the mesenterial lymph nodes?

2. MATERIAL AND METHODS

2.1 Selection of herds

They are all members of an group based on a quality control system. Out of 195 selected herds 152 were prepared to collaborate (response rate = 78%). During the project eight out of the 152 herds went out because of going out of business, stopping to produce for the integration or having no slaughtering in the period of the investigation.

2.2 Diseases

The investigated diseases were: Salmonella, Mycoplasma hyopneumoniae and Lawsonia intracellularis. Beside this diseases also slaughterline findings and acute phase proteins were investigated.

2.2.1. Salmonella, Mycoplasma, Lawsonia:

- *Salmonella* was serologically analysed with an indirect ELISA (HerdChek) (Idexx Laboratories, Inc.) that uses the LPS of S. Typhimurium and S. Livingstone. The LPS stands for the O antigens 1, 4, 5, 6, 7 and 12 of Salmonella. A positive result means that antibodies are present, i.e. the animal got infected in the past. It is possible that the animal was not infected anymore at the moment of sample taking. Animals that are immune against Salmonella could be carriers or secretors, which are a great risk for contamination of the carcass or the carcass of other pigs with Salmonella.
- *Mycoplasma* was serologically proved with the DAKO Mh ELISA (DAKO, Glostrup, Denmark), but only for pigs not vaccinated.
- *Lawsonia* was serologically analysed with an indirect Fluorescent antibody test. (12).

2.2.2. Slaughterline findings

These were collected in the slaughterline by authorized people of the slaughterhouse. This was done with a hand computer (Psion), specifically designed for this project. Advantages of the use of the Psion in stead of taking written notes on paper are:

- an unequivocal notation;
- hands free for palpation;
- no dirty notes;
- and a fast data handling.

The slaughterline findings, which were investigated, are: pneumonia injuries, fissures, pleuritis, white spots on the liver and scabies.

Pneumonia is an inflammation of the lung tissue. The percentage lung surface that is infected in every lung lobe was multiplied by the relative weight of every lobe (17). The apical lobes represent 20% of the lung surface, de cardiac lobes 14% and the caudal lobes 60%. The accessory lobes were not taking into account and therefore the weight of the cardiac lobes was counted as 20% of the lung surface. Scattered pneumonia injuries can point at a recent *Mycoplasma* infection.

Fissures are the scars of a lung inflammation en were scored as present or not present (1/0).

Pleuritis is an inflammation of the pleura, what can lead to adhesions of the lungs with the thoracic wall. This finding was scored as 0, 1, 2, or 3. Score 1 means an assault of 0 to 25% of the long surface by the inflammation of the pleura or adhesions between various lung lobes. Score 2 stands for an assault of 25 to 50% of the lung surface or adhesions of some parts of the lungs with the thoracic wall and score 3 is an assault of 50 to 100% or adhesions of a large part of the entire lung with the thoracic wall.

White spots on the liver are pathognomic injuries of Ascaris suum. They get a score of 0, 1, or 2. Less than 10 spots is score 1, more than 10 spots is score 2 and none spots is score 0.

The scoring of scabies is based on the spread and seriousness of the skin injuries (papular dermatitis) typically for scabies. Score 1 stands for injuries only on the belly, neck or thigh bone, score 2 for injuries all over the body

and score 3 for injuries all over the body together with crusts. Score 2 and 3 show a great correlation with the presence of scabies var. suis (29).

2.2.3. Acute phase proteins (APP)

Stress, sickness, injuries may cause the increase of cytokines in the blood. These cytokines bind on receptors of liver cells and induce the production of acute phase proteins (APP) that end up in the blood plasma (31). There are as well positive as negative APP, but in our investigation only one positive APP, i.e. haptoglobine (HP), is analysed with an ELISA (10). This protein is called positive because in case of stress, sickness or injuries the concentration of this protein in the blood increases. Negative APP on the contrary causes a lowering of the concentration in the blood. The concentration of these APP respectively rises or lowers with minimum 25% during the first 7 days after tissue damage (33).
From a concentration of 0.5mg/ml HP, the animal may have experienced stress, sickness or injury (=cut-off value).

The reason for the name 'acute' in APP is that they are present in the blood from 4 hours on after an injury or stress situation, and stay in the blood until the injury is present (32). APP can express recent events, which is not necessarily the case for other measurements for example the serological analysis of *Salmonella.* This is rather interesting for inspections and public health.

Because stress can be related to APP (23), the transport and slaughter process just before sampling will probably influence the concentrations of HP in the blood.

2.3 Survey

During the farm visits a survey was taken of the pig holder. In this interview risk factors for *Salmonella*, *Mycoplasma*, *Lawsonia* and some slaughterline findings (lung injuries, scabies, white spots) were checked. These risk factors were selected based on a literature study.

The most important risk factors for Salmonella found in the literature are type of feed, production system, compartimentation, floor type, hygiene, diarrhoea problems, preventive use of antibiotics, number of animal places on the farm, space per pig and the presence of other pathogens (33, 28, 16).

For Mycoplasma the most important factors reported are density, introduction of new animals, production system, compartimentation, floor type, hygiene, volume and space per pig, type of feed, vaccination, antibiotics, sow features, climate and presence of other pathogens (17).

For Lawsonia they were floor type, production system, compartimentation, volume and space per pig, waste, type of feed, hygiene, introduction of new animals, climate and the presence of other pathogens (27, 28, 18, 20).

Risk factors for Ascaris suum based on literature were access to pastures or outdoor space, hygiene, age of the livestock building, floor type and material, climate, % young sows, presence of other pathogens.

Risk factors for scabies found in literature were emptiness after cleansing and disinfecting, treatment, introduction and presence of other pathogens.

The reliability of this survey increased by the personal interview and the check in the livestock building.

2.4 Experimental design

A total of 144 pig farms were followed. Every farm was once sampled, blood was collected of 50 animals in the slaughterhouse at sticking. Salmonella was bacteriologically investigated on 60 farms by collecting mesenterial lymph nodes in the slaughterhouse, and analysed by researchers of the Faculty of Veterinary Medicine (University of Gent). In addition also on average 41 fattening pigs of each of this 60 farmswere investigated for the presence of ileal thickening caused by *Lawsonia* for each of these 60 farms. For 64 of the 144 herds blood was analysed for acute phase proteins (10 samples for each farm).

All these investigations (on animal level) were spread over one year. The year was divided in 4 periods, and in every period 36 farms were followed. The first period was from 21/05/2001 to 15/09/2001 (Summer), the second

from 17/09/2001 to 15/12/2001 (Autumn), the third from 17/12/2001 to 15/03/2002 (Winter) and the fourth from 18/03/2002 to 15/06/2002 (Spring). For this the herds were divided in 8 groups based on the presence or absence of vaccination against Mycoplasma, the number of sow places that were more or less than 150 and the pig density that was lower or higher than 939 pigs per km². These 8 groups were equally spread over the year so that the farms were spread as good as possible for these farm parameters.

During this project every herd was 4 times followed for slaughterline findings (on compartment level) spread over one year, once time per period.

3. PRELIMINAIRY RESULTS

3.1. Y-variables

First the serological results of Mycoplasma hyopneumoniae , Lawsonia intracellularis and Salmonella are presented, followed by the results of the slaughterline findings and the acute phase proteins.

3.1.1 Results of the serological tests

First some terms that will be used in the further presentation.

- Herd seroprevalence: number of positive herds as to the total number of herds in the study. A herd is positive when there is one positive sample.
- Within-herd seroprevalence: number of positive animals as to the total number of animals that was tested for a herd. Doubtful results for Mycoplasma hyopneumoniae and Lawsonia intracellularis were considered as negative.

The following classes were used to present the distribution of all serological investigated pathogens:
Class 0 = 0 % to 19 % positive animals
Class 1 = 20 % to 39 % pos. animals
Class 2 = 40 % to 59 % pos. animals
Class 3 = 60 % to 79 % pos. animals
Class 4 = 80 % to 100 % pos. animals

3.1.1.1. Mycoplasma hyopneumoniae

For Mycoplasma hyopneumoniae 74 herds were tested from the 144, the other 70 herds vaccinated there slaughter pigs against Myco. In total there were 3643 samples analysed, or an average of 49.2 samples for each herd. Of these samples 26.5% is negative, 4.3% doubtful and 69.3% positive. Doubtful results were considered as negative. The herd prevalence is 93.2 % and the average within-herd prevalence is 69.4 % (minimum 0; maximum 100; stdev 31.7), 56.8% of the herds have a within-seroprevalence between 80% and 100% (see figure 1).

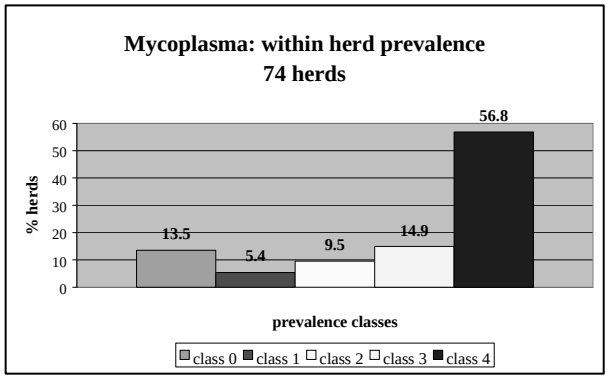

Figure 1. Mycoplasma hyopneumoniae within-herd prevalence for 74 pig herds.

3.1.1.2. Lawsonia intracellularis

For Lawsonia intracellularis blood samples of 144 herds were taken and analysed. In total there were 7141 samples analysed, that is an average of 49.6 samples for each herd. Of these samples 24.4% is negative, 7.3% doubtful and 68.3% positive. Doubtful results were considered negative. The herd prevalence is 95.8% and the average within-herd prevalence is 68.5 % (minimum 0; maximum 100; stdev 29.7), 44.4% of the herds have a within-seroprevalence between 80% and 100% (see figure 2).

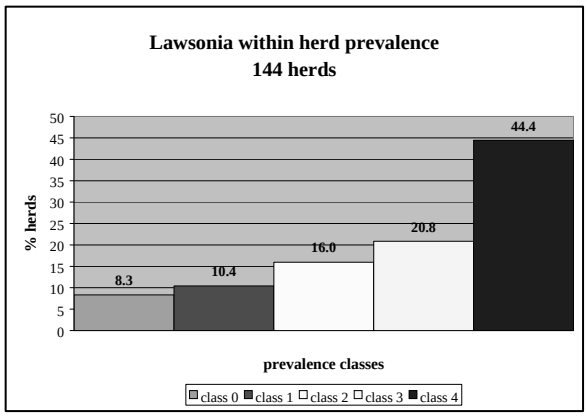

Figure 2. Lawsonia intracellularis within-prevalence in 144 pig herds.

3.1.1.3. Salmonella

For Salmonella blood samples of 144 herds were taken and analysed. In total there were 7141 samples analysed, which is an average of 49.6 samples for each herd. The results are depending of which cut-off value or OD-value is used. Eradication programs use an OD value of 40% as cut-off value at the start, after a time (after a preliminary reduction of the prevalence) they use an OD value of 20%. In scientific research an OD-value of 10% is used. Recommended is to use an OD-value of 10%, 20% and 40% as cut-off value (16,33).

Of the 7141 samples 69.9% are negative and 30.1% positive. The herd prevalence is 91% and the average within-herd prevalence is 30.1% (minimum 0; maximum 98; stdev 29.16), 7.6% of the herds have a within-seroprevalence between 80% and 100% for an OD-value of 40%.

Of the 7141 samples 48.2% are negative and 51.8% positive. The herd prevalence is 97.9% and the average within-herd prevalence is 51.8% (minimum 0; maximum 100; stdev 30.5), 24.3% of the herds have a within-seroprevalence between 80% and 100% for an OD-value of 20%.

Of the 7141 samples 26.7% are negative and 73.3% positive. The herd prevalence is 98.6% and the average within-herd prevalence is 73.4% (minimum 0; maximum 100; stdev 25.9), 54.9% of the herds have a within-seroprevalence between 80% and 100% for an OD-value of 10%.

3.1.2 Results of the slaughterline findings

We have 55 herds followed four times, 65 herds three times, 20 herds two times and 4 herds one time. The reason for missing data was that pigs were not slaughtered in a good slaughterhouse where slaughterline findings were collected.

Figure 3 shows the average percentages of the slaughterline findings for the 55 herds that were followed four times. On average there were 69 pigs inspected for each herd.

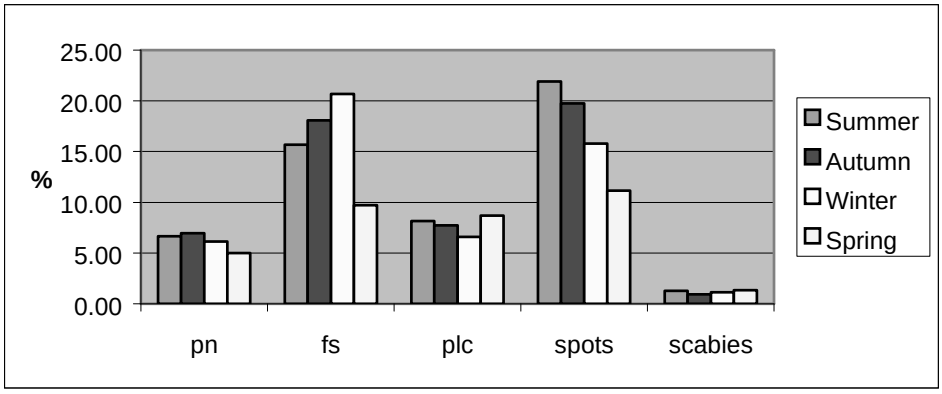

Figure 3: 55 herds during 4 periods followed for slaughterline findings (pneumonia (pn), fissures (fs), pleuritis (plc), white spots (spots) and scabies).

3.1.3. Haptoglobin

On 71 herds an average of 10.6 samples for each herd were analysed for HP. The average value for HP is 1.46 mg/ml on herd level (minimum: 0.54; maximum: 2.97 stdev: 0.49). On herd level high numbers of samples with a value higher then 0.5 mg/ml (normal physiological condition) are found. On an average 85.1 % of the samples on herd level or higher then 0.5mg/ml. On individual level we find an average of 1.46 mg/ml (minimum: 0.01; maximum: 6.37 stdev: 1.03).

No correlation was found between the time of transport, the average transport time is 117.6 minutes (minimum = 30, maximum = 250, stdv = 55.92) and the concentration of HP.

3.2. X-variables

Descriptive statistics of the X-variables or the possible risk factors have been started after comparison with the "proc compare" (SAS) of two independent sets with the same data to check typing errors.

3.3. Development of the sanitary risk index

First of all correlations will be investigated at animal level, between the following results: serology, bowel palpation, bacteriology and haptoglobine. In a next step models will be developed to predict the disease status of a farm based on management and housing conditions. Finally, models will be validated on a new population of farms.

4. DISCUSSION

The median within-herd prevalence for Mycoplasma hyopneumoniae is 84% in this study, which is slightly higher then being found in another study on 150 Belgian farrow-to-finish pig herds, i.e. 76% (17). Some other differences are: resp. 6.7% and 1% herds negative, 4% and 7% herds were all the pigs were positive. Within-herd prevalence was also different, i.e. a greater % of herds with a prevalence was found between 0% - 20% and 80% - 100%, versus a greater % of herds with a prevalence between 20%-80%. The sample size in both studies was resp. 50 and 25 pigs per herd. The seroprevalence in slaughter pigs is resp. 62%, 99%, 91%, 79% and 81.2% in Norway, USA, Sweden, Japan and Germany (9, 25, 37, 38, 34), which is similar to our results.

In literature the following herd seroprevalences for *Lawsonia Intracellularis* are reported:
73% in Belgium in 2000(1), 60% and 52% in Germany in 1998 and 1999 (21), 76% and 96% in The USA (5, 2), 90% in Austria (2) and 81% in Brazil (2). Most of these studies were performed on a lower number of herds and samples, but herd prevalence is as high as in our study. A high number of positive samples is not necessarily correlated with clinical and ileal thickening, because the serological test may also indicate subclinical infections (2).

In literature herd seroprevalences for Salmonella are 93% in Germany, 59% in Denmark, 79% in Greece and 72% in Sweden, evaluated at test cut-off of OD%>10, and herd cut-off of 1 or more seropositive animals (16). The average within- herd seroprevalence was 24% for Germany, 9% for Denmark, 14% for Greece and 10% for Sweden (16). The results in our study are higher, may be the on going risk factor analyses give indications why this is the case.

For the slaughterline findings, fissures are the highest in Winter and white spots on the liver are the highest in Summer, as reported in the literature (29). Pneumonia was found to be higher in Autumn (29), which is not so obvious in our data, it is higher but there is not much difference with Summer values.

A possible explanation for the high average of HP could be that pigs are stressed by transport and slaughter, so that plasma values of HP increase (23).

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A QUALITATIVE ASSESSMENT OF THE RISK OF INTRODUCING FOOT AND MOUTH DISEASE INTO RUSSIA AND EUROPE FROM GEORGIA, ARMENIA AND AZERBAIJAN, MARCH 1999

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ABSTRACT

A qualitative risk assessment was performed to evaluate the risk of introducing foot and mouth disease (FMD) virus into Russia and the rest of Europe from the countries of Transcaucasia, i.e. Armenia, Georgia and Azerbaijan. The assessment was based on data collected during a three-week mission to these countries by a Food and Agriculture Organization (FAO), European Union (EU) and Office International de Epizooties (OIE) mission in March 1999. As the data were not sufficient to allow a quantitative risk assessment to be performed, the investigation served as a useful initial approach.
The risk of FMD virus infection is a function of two elements, namely the probability of the hazard (virus infection) occurring, and the magnitude of the consequences. The probability of the hazard occurring is the product of the probability of entry of the virus and probability of exposure to the virus. The magnitude of the consequences is derived from the probability of transmission and spread.
As a result, the overall risk of introducing FMD virus into Russia and the rest of Europe from Transcaucasia was rated as “low’ at the time of evaluation.
The method and results are presented to serve as a basis for further discussion

SAMENVATTING

Het risico voor besmetting met het mond- en klauwzeervirus (FMD) van Rusland en de rest van Europa vanuit Transkauazië (Armenië, Georgië en Azerbeidzjan) werd ingeschat met een kwalitatieve risicoanalyse. Hiertoe werden in deze landen gedurende drie weken gegevens verzameld door medewerkers van de FAO, EU en OIE, nl. in maart 1999. Deze dataschat was onvoldoende om een kwantitatieve analyse uit te voeren, vandaar deze eerste benadering.
Het risico op een FMD-infectie is afhankelijk van twee elementen, de kans op infectie en de impact van de gevolgen. De kans op infectie wordt bepaald door de kans dat het virus aanwezig is en de kans van blootstelling aan het virus. De impact naar de gevolgen toe is afhankelijk van de kans op transmissie en verspreiding.
Er kon besloten worden, dat het risico om het FMD-virus in Rusland en Europa binnen te brengen eerder laag was in de periode van het onderzoek. De resultaten zijn echter een basis voor verdergaande studies.

1 - Introduction

Assessing the risk of introducing any animal disease from one part of the world to another, is a main preoccupation of veterinary services (5, 8). Performing a quantitative risk assessment seems to represent one the best possible answers. However, it is easy to imagine the huge quantity of data that are needed to pretend to any useful result. So, through an example, here is a proposal of using a qualitative risk assessment approach when a question is really asked and when a first answer now seems to be better than a more complete one later.
This assessment was performed after a three-week mission between Georgia, Armenia, and Azerbaijan in March 1999 (1). Since then, an other mission had been realised in June-July 2000 in the same three countries, which brought more information, but this was not used in this work.
One of the first idea is that any risk assessment must be quite precise in terms of space and time.

The question of the risk of FMD virus spreading from this area to Russia and Europe was asked by the three institutions sending the mission : FAO, EU and OIE. This was linked to a simple observation : the increase in FMD outbreaks in the region, as can be seen from OIE reports (*vide infra*).
Here, we will present the method used, the results, and discuss them.

2 - Method

The method used to conduct this qualitative assessment is based on the work of Zepeda Sein (9). The theoretical bases for any risk assessment, whether qualitative or quantitative, are the same. Once the hazard has been identified, in this case infection with FMD virus, the risk to be assessed is a function of the probability that infection will occur and of the magnitudes of the consequences of such an occurrence. The probability of the occurrence of the infection is, in turn, the product of the probability of exposure to the virus. The appraisal of the magnitude of the consequences must take into account both the probability of the dissemination of the pathogen (transmission plus spread) and the economic impact of the disease.

For a qualitative assessment, Zepeda Sein proposes that each of these events be characterised by a number of parameters and that each parameter be analysed on the basis of all available information, including the experts' opinion, which must be admitted. This includes also impression, beside hard data. In addition, the probability of occurrence of each event is assessed for classification by means of the following descriptive scale :
-negligible, when the probability of occurrence of the event is sufficiently low to be ignored, or the event is possible only in exceptional circumstances
-low, when the occurrence of an event is a possibility in some cases
-moderate, when the probability of the event is a possibility
-high, when the occurrence of the event is clearly a possibility.

Table 1 contains a matrix showing probabilities of occurrence when two parameters are combined (Zepeda Sein 1998).

Parameter 1	**Parameter 2**	**Parameter 2**	**Parameter 2**	**Parameter 2**
	Negligible	**Low**	**Moderate**	**High**
Negligible	Negligible	Low	Low	Moderate
Low	Low	Low	Moderate	Moderate
Moderate	Low	Moderate	Moderate	High
High	Moderate	Moderate	High	High

Table 1 : Combination of occurrence probabilities of two parameters considered in the qualitative risk assessment.

In this study, the probability of occurrence of the hazard (FMD virus infection and the consequences of an epizootic) is equal to the probability of entry (from Transcaucasia to Russia and the rest of Europe), combined with the probability of the exposure of animals susceptible to the pathogen. As FMD virus cannot be transmitted to human, the consequences of an epizootic will be purely economic.
As we will see in the "Results" part, when more than two parameters are combined for any probability calculation, the order of combination of the parameters, two by two, may bring differences in the results. This could be a point to standardize in the method.

3 - Results

3 – 1 - The probability of entry is a combination between three parameters.
-the prevalence of infection in the three countries
The increasing number of outbreaks, as notified to OIE, is a real concern in the area. The origin of the stains is mainly Iran and Turkey, as can be demonstrated through their analysis in the World Reference Centre in Pirbright, UK. The prevalence of the infection in the three countries is shown in table 2. Turkey and Iran have been added as they may represent two of the possible origins of FMD virus in the area. Here, the qualification can be "high".

Countries	1992	1993	1994	1995	1996	1997	1998
Georgia	1	4	0	1	21	36	5
Armenia	5	7	0	0	15	13	1
Azerbaijan	0	0	2	0	4	0	0
Turkey			153	108	133	54	74
Iran			221	270	651	345	342

Table 2 Number of outbreaks of foot and mouth disease reported in Transcaucasia, Turkey and Iran from 1992 to 1998 (OIE)

-the volume of trade in animals and animals products
Officially, no trade of livestock nor meat is allowed between the three countries and Europe. Contact may exist through Summer pastures in the Caucasus with Russian herds. Contacts do exist although in the South, but then the risk is more to introduce the virus from Turkey or Iran to Transcaucasian countries than the opposite. The level of production and the price of meat is anyway more in favour of the introduction of meat in Transcaucasia from Asian countries (India). The qualification is then seen as "low".
-the survival capacity of the virus in the environment
The main danger here is the presence of animal carriers, as even diseased animals may be kept alive. So the qualification is seen as "high".

The calculation here will combine "high" with "low", which gives "moderate", and "moderate" with "high", which gives "high" (table 3). Should we have combined the three parameters in another way ((high x high) x low), we would have found "moderate". However, it is our opinion that the first result i.e. ((high x low) x high)= high is closer from "our" reality.

3 – 2 - The probability of exposure is a combination between four parameters.
-the potential for transmission to susceptible animals in the importing country
The actual movements of live animals in the area are not so important, mainly to Summer pastures in the mountains to the North (Caucasus range), border line with Russian Federation. The economical and political situations were already instable and the local livestock had decreased since 1990 (6, 3). The movement of beef (or any other meat) was mainly importation, not exportation. The given qualification is "low".
-the probability of spread within the country
Animals on the Russian side of the border are said to be vaccinated against FMD virus, with a vaccine adapted to the local virus strains. Here too, the movements of animals and of meat, are supposed to be reduced, even if difficult to monitor. The given qualification is "low".
-factors influencing the survival of the virus.
The survival of the virus is mainly linked to the fate of infected animals. If they are kept alive, then they may become carriers and so the virus will survive. The given qualification is "moderate".
-the role of wild animals as potential vectors.
The mountains goats, sheep and chamois of the Caucasus are under threat, as very few regulations still exist or are implemented over their range (7). To the North, the case of the saiga antelope, which used to be present by thousands in the Kalmykian Autonomous Region, is now of real concern as its population has been in a sharp decline since the beginning of the 1990s (4). The given qualification is "negligible".

Here, the classification matrix is a little larger than with the first three parameters. Here again the order following which the combination is performed could bring slight differences in the results.

The calculation will combine "low" with low" : "low", then "low" with "moderate" : "moderate" and then "moderate" with "negligible" : low" (table 3). Here, not a single parameter is qualified as "high", so different combinations will not change the result so much.

A. Probability of entry

1. Prevalence of infection 'high' (number of outbreaks, surveillance, etc.)
2. Volume of trade 'low' (contacts, border-crossing)
3. Capacity of the virus to survive

'moderate'
'high'

'high'

B.	**Probability of exposure**					
4.	Transmission to		‘low’			
5.	Spread (contacts, border-crossing)	among	‘low’	‘low’	‘moderate’	**‘low’**
6.	Survival in			‘moderate’		
7.	Role of wildlife				‘negligible’	
C.	**Probability of occurrence of hazard** (infection with foot and mouth disease virus)					
A	Probability of entry (A)		‘high’	**‘moderate’**		
B.	Probability of exposure (B)		‘low’			

Table 3 : probability of occurrence of various risk factors

3 – 3 - Magnitude of consequences

Foot and mouth disease is a huge economical problem, as could been seen from the 2001 Western Europe epizootics. The answer, the qualification, could always be here “high”. However, saying this would bring few information and would overweight any assessment. So, it is possible to say than consequences could be different if an outbreak was happening in the Russia Caucasus or in any other part of Europe (2). Here, we think the main area at risk is the Russian side of the Caucasus. Or, by telling it an other way, there is no more probability to imagine an outbreak of FMDV in Europe originating from Transcaucasian countries, than from anywhere else in the world. In fact, there are countries with which we trade meat and which do have foot-and-mouth virus. As a whole, the consequences, not of FMD, but of FMD originating from Georgia, Armenia and Azerbaijan, is qualified as “negligible”. This was written before 2001, but we can discuss it.

4 – Assessment - Discussion

The global assessment combines all previous data, impressions and qualifications. So it combines “moderate” with “negligible”, giving “low”.

The interpretation, as given by Zepeda Sein, is as follows :

-negligible : authorise import without restriction,

-low : authorise import with certain reduction measures, as appropriate,

-moderate : before authorising import, carefully assess risk reduction measures, including efficacy, feasibility of implementation and verification mechanisms,

-high : do not authorise import unless risk reduction measures are proven effective and adequate verification procedures are available to ensure safe implementation.

The assessment looks both at an official import of animals or of meat from these countries to Russia and Europe, which is quite improbable, and at any other movements of animals or animal products from Transcaucasia. However, it is difficult to anticipate every situation.

Risk assessments performed by veterinary services follow rules that ought to be followed by traders....

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CARMA RISK MODEL AND EXPERT STUDY ON TRANSMISSION OF CAMPYLOBACTER DURING CHICKEN PROCESSING

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ABSTRACT

The aim of the CARMA (**Ca**mpylobacter **R**isk **M**anagement and **A**ssessment) project, which started in 2001, is to advise on the effectiveness and efficiency of intervention measures for reducing human campylobacteriosis in the Netherlands. As part of the project, risk models are built for the major routes of infection. To date, the risk model for the consumption of poultry meat is under development. It describes the transmission of Campylobacter through the different stages of the poultry meat production chain, so far focusing on the processing of broiler chickens. An expert study is organised to obtain the (additional) information needed in this chicken processing model, including both qualitative information as well as (quantitative) estimates of the model parameters. This paper presents an outline of the CARMA project in general as well as the chicken processing model and the expert study.

SAMENVATTING

In 2001 is het CARMA (**Ca**mpylobacter **R**isk **M**anagement and **A**ssessment) project van start gegaan. De doelstelling van dit project is het adviseren over de effectiviteit en doelmatigheid van maatregelen gericht op het terugdringen van campylobacteriose in de Nederlandse bevolking. Als onderdeel van dit project worden risico-modellen ontwikkeld voor de belangrijkste infectie-routes. Momenteel wordt het risico-model voor de consumptie van kippenvlees ontwikkeld. Dit model beschrijft de transmissie van Campylobacter door de verschillende fasen van de productie-keten van kuikenvlees, en richt zich tot dusverre op de slachtfase. Ten einde (aanvullende) informatie te verkrijgen voor het slachtmodel wordt een expert studie gehouden. Deze richt zich op het verkrijgen van zowel kwalitatieve informatie als (kwantitatieve) schattingen van de modelparameters. In dit paper wordt een korte beschrijving gegeven van het CARMA project (in het algemeen) alswel van het slachtmodel en de expert studie.

1. THE CARMA PROJECT

1.1 Introduction

Campylobacter infections pose a serious public health problem in the Netherlands. They result in approximately 100,000 cases of gastro-enteritis per year, of which 23,000 cases see a general practitioner and several dozen die. In addition, there are about 60 cases of Guillain-Barré syndrome and several thousand cases of reactive arthritis. Collectively, these disease endpoints result in an annual loss of over a thousand healthy life years (1) and considerable economic losses. An estimation of the economic impact of Campylobacter infections is not available for the Netherlands, but it is expected to amount over fifty million Euro per year (2).

The most important reservoirs of Campylobacter are found among animals, including farm animals, wild animals and pets. These reservoirs continuously contaminate the human environment, including the domestic environment, and food products, hereby creating many pathways by which humans can come in contact with Campylobacter. Different research methods have been used, both nationally and internationally, to evaluate the relative importance of different exposure pathways, including case-control studies, microbiological analyses of patients and putative reservoirs, the typing of isolates of different origins, and statistical methods (3). Many studies have indicated poultry to be an important source of contamination, but this is by no means the only important contamination route. Other identified risk factors are meat from pigs and cattle, raw milk, direct

contact with animals, contaminated surface water, and foreign travel. Drinking water is not important in the epidemiology of Campylobacter in the Netherlands. Little is known about the (relative) quantitative impact of these risk factors. A preliminary estimate, based on limited Dutch data and extrapolation of international data, suggests that poultry is responsible for 40 %, at the most, of all human cases of campylobacteriosis. Other important factors appear to be foreign travel (10-20 %), contact with young dogs (10-20 %) and the consumption of barbecued meat of all kinds (around 10 %). However, these estimates are highly uncertain (3).
Interventions aimed at reducing the contamination of poultry meat are expected to significantly reduce the incidence of human infections with Campylobacter. The contamination of poultry meat originates from the primary production stage. In recent years, intensified hygienic measures have been implemented in the broiler industry, coinciding with a reduction of the prevalence of contaminated flocks from 48 % in 1998 to 35 % in 2000 (4). Additional hygienic measures can be made but will not lead to a guaranteed production of Campylobacter-free broilers. Other intervention measures in primary production, such as reducing the sensitivity of animals to infection (e.g., by vaccination) and suppressing inadvertently introduced infections, are not expected to be very successful in the near future. Hence, additional measures in consequent stages of the food production chain are necessary to further reduce the contamination of poultry meat with Campylobacter. Such measures may include canalisation of contaminated flocks (e.g., logistic slaughtering), improved hygiene during processing and treatment of the end product (e.g., freezing, decontamination, irradiation, mild heat treatment, drying).
Effective prevention of human campylobacteriosis requires a well-balanced set of measures. To this aim, the CARMA (**Ca**mpylobacter **R**isk **M**anagement and **A**ssessment) project has been started in 2001. In this project, the National Institute for Public Health and the Environment (RIVM) collaborates with the Institute for Animal Science and Health (ID-Lelystad), the Agricultural Economics Institute (LEI), the Inspectorate for Health Protection and Veterinary Public Health (KvW) and the State Institute for Quality Control of Agricultural Products (RIKILT). The goal of the project is to advice on the effectiveness and efficiency of measures aimed at reducing campylobacteriosis in the Dutch population. This goal is reached by providing scientific support to a risk management process, as defined by the Codex Alimentarius Commission on Food Hygiene (5). Risk managers are the Ministry of Welfare, Sports and Public Health and the Ministry of Agriculture, Nature and Fisheries.

1.2 CARMA design
Figure 1 shows the general approach of the CARMA project. In the first (completed) phase, all available information was collected and summarised in an extensive risk profile (3). This information is used to assess the relative contribution of different sources of contamination to the incidence of human Campylobacter infections. A risk model will be build for each major route of infection, starting with the consumption of poultry meat. A risk model describes the transmission of Campylobacter for the particular contamination route and combines the resulting exposure estimate with dose-response information in order to assess the incidence of Campylobacter infections. In the disease burden model, different outcomes related to these infections, including gastro-enteritis, Guillain-Barré syndrome, reactive arthritis and mortality, are quantified. The joint disease burden of these end-points is expressed in Disability Adjusted Life Years (DALYs). The economic model evaluates the losses of illnesses due to Campylobacter infections in the starting situation. In consultation with risk managers and stakeholders, a series of potential intervention measures are selected. The effects of these measures on the incidence of infection (risk model), disease burden of related illnesses (disease burden model) and associated losses (economic model) are estimated. In addition, the costs associated with the implementation of intervention measures are evaluated in the economic model. All collected information, including reduced disease burden and its associated losses as well as intervention costs, are combined in the cost-effectiveness analysis in which different interventions are compared based on their (net) costs per DALY gained (or alternatively per life year gained or per averted case of illness). This allows an a priori evaluation of different sets of intervention measures. Absolute effects, costs and cost-effectiveness ratios are important tools to support risk management decisions. However, societal and political factors also have a major effect on decision-making. Therefore, in the project these factors are also described and presented to decision-makers.

1.3 CARMA in progress
Current work focuses on the risk model for the consumption of poultry meat, describing the transmission of thermophilic *Campylobacter* spp. throughout the poultry meat production chain, from the farm level to the consumer. This work will continue in 2003, when it is also planned to combine the resulting consumer exposure estimates with dose-response models in order to estimate the annual number of cases of Campylobacteriosis in the starting situation (the year 2000). In addition, both the associated disease burden and economic losses will be assessed. A series of potential intervention measures has been selected, including interventions at the farm level as well as during processing, and consumer education. In 2004, these interventions will be implemented in the models and their associated costs will be estimated. In the last phase of the project (2nd half of 2004), a cost-

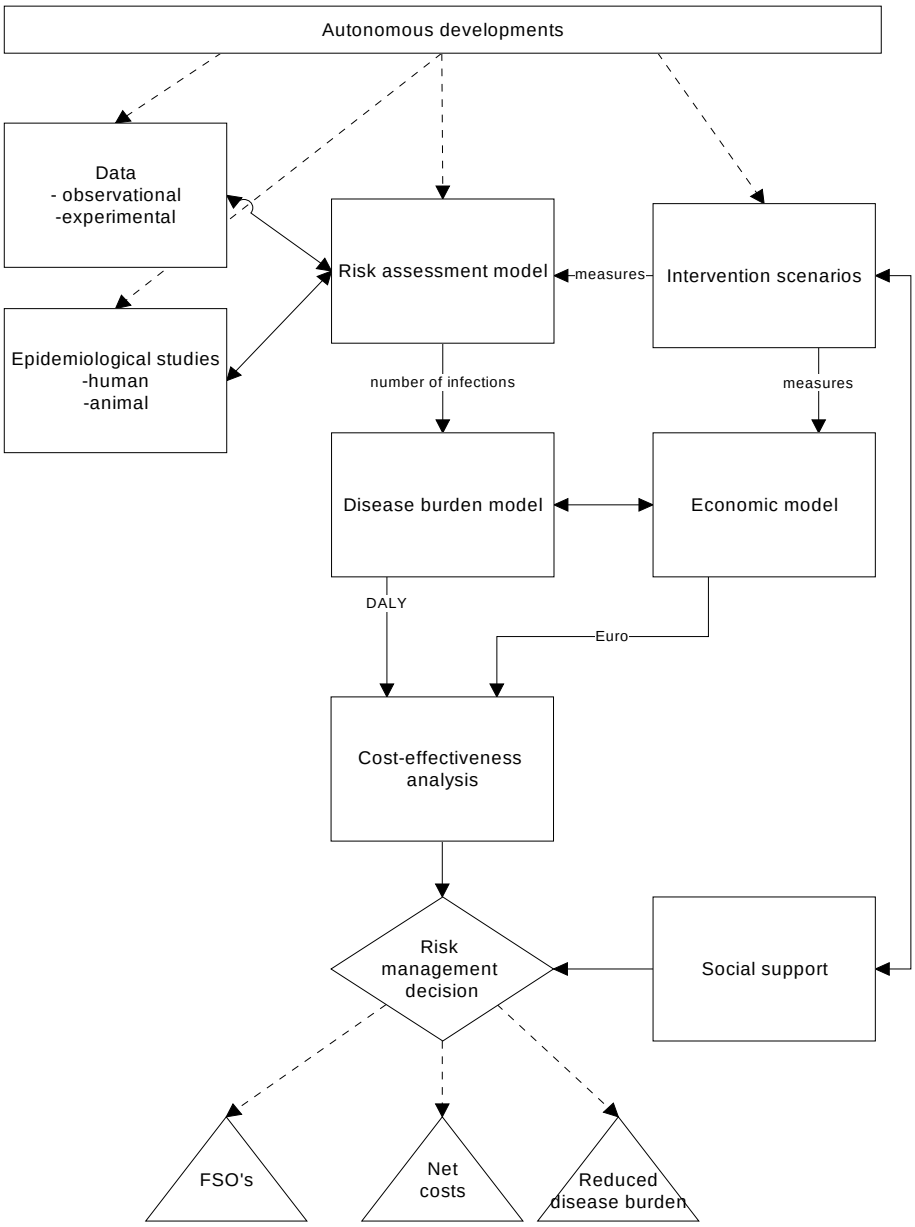

Fig. 1 General approach of the CARMA project

effectiveness analysis will be carried out. A first series of analyses of political and societal factors affecting decison-making has been completed and further work will focus on the support for selected interventions. There appears to be a relationship with costs: intervention measures with a low level of stakeholder acceptance will require larger efforts and thus higher costs for effective implementation.

The rest of this paper focuses on the risk model for the consumption of poultry meat, specifically the transmission model for chicken processing (section 2), and the expert judgement study held to obtain additional data for this model (section 3).

2. THE CHICKEN PROCESSING MODEL

2.1 Model introduction

Several quantitative microbiological risk assessments on Campylobacter in broiler chickens have been performed so far (6-8). In these studies, process risk models were constructed, based on process knowledge and available microbiological data. The methodologies applied were somewhat different, but in each of them stochastic models were built, and Monte Carlo simulations were performed. The 'Farm to Fork' risk assessment methodology applied in these studies has been elaborated in the current risk model for poultry meat to fit into the Modular Process Risk Modelling (MPRM) framework that is under development at RIVM (9-13). Within this framework, a more mechanistic modelling of the basic microbial processes growth, inactivation, mixing, partitioning, removal and cross-contamination is applied. This has the advantage that model construction is less data dependent and more transparent.

The first objective of the poultry meat risk model is to describe the exposure of the Dutch population to thermophilic *Campylobacter spp*. as a consequence of the consumption of poultry meat. The consumers' exposure is derived from modelling the transmission of Campylobacter through the poultry meat production chain, from farm until consumption (Figure 2). The complete poultry meat risk model will include transmission models for each stage of this chain. This paper focuses on the transmission model for (broiler) chicken processing.

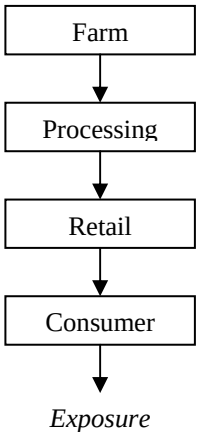

Fig. 2. The poultry meat risk model assesses exposure by modelling the transmission of Campylobacter through the poultry meat production chain. This paper focuses on the transmission model for broiler chicken processing.

The (broiler) chicken processing risk model is currently being developed and focuses on industrial processing (slaughtering and partitioning) of broiler chickens. It describes the change in prevalence (percentage of contaminated birds/carcasses per flock) and (the distribution of) the number of Campylobacter per bird/carcass (both exterior and interior) during processing.

Input of the chicken processing model will be provided by the preceding transmission model for the farm level, which will be developed in the near future. This 'farm model' estimates the percentage of contaminated flocks, the percentage of contaminated broilers in contaminated flocks and the distribution of numbers of Campylobacters on the exterior and in the interior of birds in a flock. Before slaughter, birds may be contaminated with Campylobacter on the exterior and in the interior. After processing only the exterior is relevant. In the chicken processing model, a line of birds/carcasses is assumed to go through consecutive processing stages. So far, only stages of the slaughtering process have been included. With respect to the transmission of Campylobacter, the following stages of this (slaughtering) process are considered relevant: scalding, defeathering, evisceration, washing and chilling (8). In each stage, inactivation and cross-contamination may change both the level and prevalence of Campylobacter. The chicken processing model is constructed such that one model for inactivation and cross-contamination can be applied for each of these five processing stages. As not all elements of this basic processing model are relevant for all stages, a simpler version can be used after evisceration.

2.2 Model description

According to the risk managers and specialists from industry the chicken processing model only needs to consider one type of 'typical' processing plant and, hence, it neglects variability between plants. Seasonal variation only exists in the prevalence and levels of Campylobacter, which is the input of the chicken processing model resulting from the 'farm model' (output).

Consider a line of broilers processed. At any processing stage S, a broiler *i* entering the stage is contaminated with $N_{ext,S}(i)$ cfu Campylobacter on the exterior and a concentration of $C_{int}(i)$ cfu Campylobacter per gram faeces (interior). There is a direct environment of the broiler that gets contaminated. This environment can be anything that gets in contact with the animal and gets in contact with the next animal too, e.g., water, equipment, hands, air. This environment holds $N_{env,S}(i)$ cfu Campylobacter (which, with this conceptual definition, is hard to measure). In every stage, transmission and inactivation (per animal) occurs as presented in Figure 3.

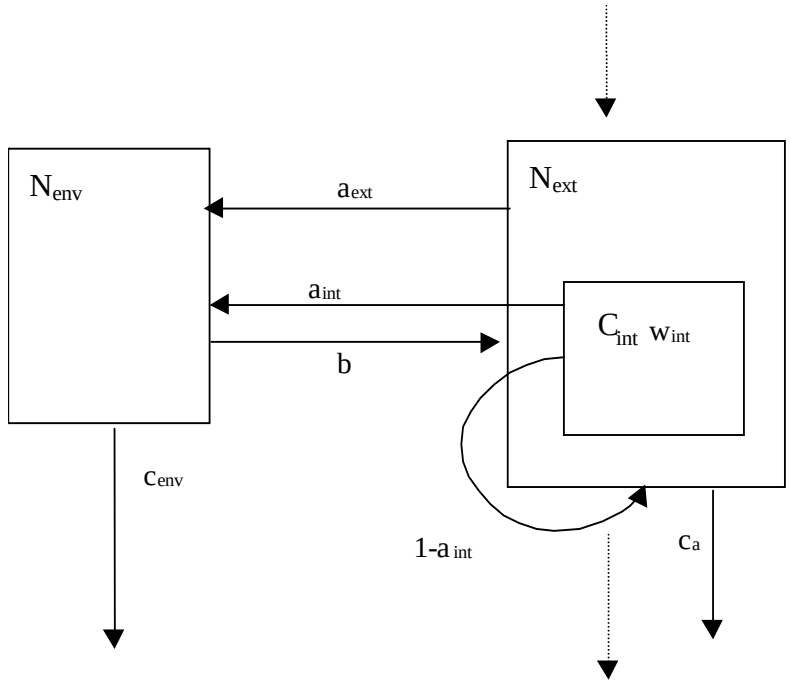

Fig. 3. Diagram of the basic broiler chicken processing model. At any stage during slaughter, consecutive broilers pass an environment (dashed arrows). Cross-contamination may occur when Campylobacters from the exterior and (if appropriate) the interior of the broiler are transferred to this environment, and from the environment to the exterior of the broiler. Next, Campylobacters on the broiler and in the environment may be inactivated. See main text for explanation of the parameters.

The chicken processing model holds the following variables and parameters:

$N_{ext,S}(i)$ number of Campylobacter (cfu) on the exterior of broiler *i* at the start of processing stage S
$N_{env,S}(i)$ number of Campylobacter (cfu) in the 'environment' of broiler *i* at the start of processing stage S
$C_{int}(i)$ concentration of faeces (cfu/gram) in the interior of broiler *i*
$a_{ext,S}$ probability per cfu Campylobacter to move from the broiler's exterior to the environment, per processing stage S
$a_{int,S}$ probability per cfu Campylobacter to move from the broiler's interior to the environment, per processing stage S
b_S probability per cfu Campylobacter to move from the environment to the broiler's exterior, per processing stage S
$w_{int,S}$ amount of faeces (gram) that leakes from the broiler, per processing stage S
$c_{env,S}$ probability of inactivation of Campylobacter (per cfu) in the environment, per processing stage S
$c_{a,S}$ probability of inactivation of Campylobacter (per cfu) on the broiler's exterior, per processing stage S

So, at processing stage S:
- $a_{ext,S}\ N_{ext,S}(i)$ cfu Campylobacter of the exterior of broiler *i* are transferred to the environment
- $a_{int,S}\ w_{int,S}\ C_{int}(i)$ cfu Campylobacter of the faeces of broiler *i* are transferred to the environment
- $(1\text{-}a_{int,S})\ w_{int,S}\ C_{int}(i)$ cfu Campylobacter of the faeces of broiler *i* are transferred to its exterior
- $b_s\ N_{env,S}(i)$ cfu Campylobacter from the environment are transferred to exterior of the broiler *i*
- $c_{env,S}\ N_{env,S}(i)$ cfu Campylobacter in the environment are inactivated when broiler *i* passes
- $c_{a,S}\ N_{ext,S}(i)$ cfu Campylobacter from the exterior of broiler *i* are inactivated

This yields the following model equations:

$$N_{ext,S+1}(i) = (1-a_{ext,S})(1-c_{a,S})N_{ext,S}(i) + b_S N_{env,S}(i) + (1-a_{\text{int},S})w_{\text{int},S}C_{\text{int}}(i)$$
$$N_{env,S}(i+1) = a_{ext,S}N_{ext,S}(i) + (1-b_S)(1-c_{env,S})N_{env,S}(i) + a_{\text{int},S}w_{\text{int},S}C_{\text{int}}(i)$$

With,
$N_{ext,S+1}(i)$ the level of contamination of broiler *i* at the end of stage S (and thus at the start of stage S+1)
$N_{env,S}(i+1)$ the level of contamination in the environment of the next broiler (*i*+1) in line in stage S

Note that for leaking of faeces from the broiler in processing stage S, the mass of faeces leaked ($w_{int,S}$) is needed. This is variable per processed broiler. Leakage occurs with a certain probability, say $p_{int,S}$, and with probability $1-p_{int,S}$ there is no leakage at all ($w_{int,S} = 0$).

The chicken processing model is implemented as a Monte Carlo simulation model in @Risk (an add-on to Microsoft Excel). One run of the model represents the processing of a specified number of consecutive birds of one flock. It provides the distribution of levels of Campylobacter on the exterior of carcasses (N_{ext}) from the processed flock, i.e., the variability between carcasses from a flock. Using second order Monte Carlo simulation, uncertainty analysis may be performed.
Model input includes distributions of the variables N_{ext} and C_{int} per broiler entering the slaughterhouse, which will be provided by the farm model. In applying these distributions, both flock prevalence and animal prevalence are incorporated. The flock prevalence represents the probability that a flock being slaughtered is contaminated with Campylobacter. The animal prevalence is interpreted as the percentage of broilers in a positive flock carrying Campylobacter in their intestines. For each processing stage S, the values of the basic model parameters as well as the initial number of Campylobacter in the environment $N_{env,S}(1)$ are required. The values of these parameters are preferably derived from scientific literature. However, data on the majority of these parameters is lacking or inappropriate. Part of the data needed will be collected by means of additional experimental studies held in the time span of the CARMA project. In addition, expert judgement (section 3) is used to obtain information on parameters for which data collection by experiments is difficult or not possible at all as well as for validation purposes.

3. EXPERT JUDGEMENT STUDY

At the end of 2002, an expert judgement study has been started to obtain additional information on the processing, in particular slaughtering and partitioning, of broiler chickens. The expert study is completely driven by the information needed in the (broiler) chicken processing model described in section 2. It focuses on obtaining both qualitative and quantitative information, and consists of two stages, corresponding with the elicitation of these two types of information. The two stages are outlined in the next section (section 3.1).

3.1 Qualitative information

The first stage of the expert study focuses on obtaining relevant background information on the processing (slaughtering and partitioning) of broiler chickens. This information is used for further development of the conceptual chicken processing model and the definition of the final model parameters. During this first stage, expert information is collected by means of a group meeting followed by two individual questionnaires. To date, the group meeting and first questionnaire, both focusing on the slaughtering of broiler chickens, have been held. The second questionnaire, which will be held in the near future, will focus on the further processing (partitioning) of poultry meat. Expert selection occurs corresponding the particular areas of interest. For the group meeting and the first questionnaire, four experts were selected having experience in the field of the slaughtering process of broiler chickens as well as the behaviour of pathogens, particularly Campylobacter, during this process. They had an occupation either in practice, science or government, and all were willing to participate. During the group meeting, these four experts first were asked to fill-out a questionnaire on the slaughtering process of broiler chickens individually. Their responses were checked for consistency, and at the end of the group meeting inconsistent answers were discussed in a group discussion. The aim of this discussion was to get insight in the background of the differences in the answers given, rather than to obtain consensus. After the group meeting, the four experts were given the first questionnaire, to be filled-out individually and returned by mail. This questionnaire focused on technical information on the slaughtering process of broiler chickens, such as the temperature of scalding. The results of this questionnaire were, together with the information gained during the group meeting, used for finalisation of the chicken processing model, as far as it concerns the stages of the slaughtering process.

3.2 Quantitative information

The second stage of the expert judgement study focuses on the elicitation of quantitative expert estimates on parameters of the chicken processing model, specifically parameters of the slaughtering process. Expert knowledge on continuous variables (such as these parameters) is not certain, but entertained with an implicit level of confidence or degree of belief (14, 15). Hence, the experts will be asked to give their best estimates with their uncertainty on these estimates, cast in the form of subjective probability density functions (PDFs).

This second stage of the expert study is worked out in co-operation with staff members from the Delft University of Technology, experienced with the elicitation of quantitative expert assessments. It follows the formal procedure for a full expert judgement study described, among others, by Cooke and Goossens (15). Application of the 15 steps of this protocol to the current expert study is outlined below.

1) *Definition of the case structure*: The case structure of an expert study includes the model(s) for which expert judgement is needed. In this case, it was defined by the chicken processing model described in section 2, and in particular focuses on the slaughtering of broiler chickens.
2) *Identification of target variables*: Target variables are variables for which experts' uncertainty distributions are needed, in particular including model parameters 1) that are uncertain; 2) for which no relevant measurement data is available at date; 3) for which measurement data is hard or impossible to obtain (within a short time span); and 4) that (are expected to) have a significant impact on the uncertainty of the model outcomes. Target variables of the current expert study include most of the parameters of the chicken processing model, as described in section 2.
3) *Identification of query variables*: In case target variables are not appropriate for direct elicitation, query variables need to be defined. Query variables can be expressed as functions of the target variables, but are (potentially) observable, easier to understand and, hence, expected to be easier to be assessed. They are chosen such that the experts' PDFs on the target parameters can be derived from the estimated PDFs on the query variables. As the majority of the target parameters of the current expert study are difficult to assess directly (most of them are transfer coefficients), query variables were defined.
4) *Identification of seed variables*: The PDFs of the single experts on each parameter are combined to obtain one aggregated PDF per parameter, to be used in the model(s) (in this case the chicken processing model). The individual experts' assessments are weighted according to the (relative) expertise of the particular experts, indicated by their performance on so-called seed variables. Seed variables are variables whose true values or realisations are unknown to the experts but are or will be known to the analyst within the frame of the expert study (16). They may, but need not, to be identified as such in the elicitation session (step 10), and must cover the case structure of the expert study. In the current study, seed variables were derived from different experiments, which were not analysed or published at the time of the elicitation session.
5) *Identification of experts*: Experts were identified as having knowledge of the slaughtering process of broiler chickens as well as the behaviour of pathogens, in particular Campylobacter, during this process. In total 20 experts were identified, the expert panel being diverse in knowledge bases and organisations of employment represented. More specifically, the panel consisted of a mix of experts from the practical field, government and science.
6) *Selection of experts*: Two of the identified experts were selected for use in the dry-run session (step 8) and, hence, can not be used in the expert elicitation session (step 10). The other identified experts were asked to participate in the elicitation session, with the only restriction that one person per organisation attends the expert panel. The final expert panel will consist of those experts, from the 15 being approached, willing to participate and available to this expert study.
7) *Design of the elicitation document*: This step includes the definition of the questionnaire, based on the query variables and seed variables, to be filled-out by the experts during the elicitation (step 10).
8) *Dry-run session*: In a special session, the elicitation document was given to the two experts that were selected for this occasion (step 6). One dry-run expert is working in practice; the other is a scientist. These two experts were asked to give critical feedback to the elicitation document, rather than their best estimates on the variables. After the dry-run session, the elicitation document is finalised.
9) *Expert training session*: Prior to the (individual) expert elicitation (step 10), a group meeting will be held in which the expert panel will be given an introduction to the CARMA project, the chicken processing model and the expert study. Also, training in subjective probability assessments will be given. At the end of this session, the experts will be given the elicitation document for preparation of the elicitation session.
10) *Expert elicitation session*: With each expert, an individual elicitation will be held in which the expert will be asked to fill-out the elicitation document or, when filled-out in advance, to review and discuss his/her assessments given. As typically, the elicitation team will consist of one normative analyst, who is experienced with subjective probabilities and expert judgement studies, and one substantive analyst, who is experienced in the current field of interest. During the elicitation sessions, the (individual) experts will also be asked to give their rationales behind their probability assessments.

11) *Combination of experts' judgements*: The Classical model, embedded in the software package EXCALIBR (17) is used to combine the individual experts PDFs to arrive at one aggregated PDF, the so-called decision-maker's PDF, for each variable of interest (query variables and seed variables). The individual expert estimates can be weighted equally or based on the (relative) expertise of the particular experts, indicated by their performance on the seed variables.
12) *Discrepancy and robustness analyses*: Robustness analysis includes removing one expert or one seed variable at the time and recalculating the decision-maker, to account for the relative information loss to the original decision-maker. Discrepancy analysis identifies query variables and/or seed variables on which the uncertainty assessments of the experts differ most. These variables will be reviewed to ascertain any avoidable cause of discrepancy.
13) *Feedback to the experts*: In case of discrepancy on one or more variables (step 12), which might be caused by misinterpretation of the questions of the elicitation document, the particular experts will be contacted. They will be asked to review their assessments, not to revise them, but whether or not their assessments are according to their views.
14) *Post-processing analyses*: Post-processing is required in case target variables were not suitable as query variables, and other query variables were chosen. It includes probabilistic inversion to translate the elicited PDFs of the query variables into PDFs of the target variables (18).
15) *Documentation*: Noting down all relevant information and data, to be presented to the decision-maker and to the experts, in a formal report. Results of individual experts will be treated anonymously.

At the end of 2002, steps 1 to 5 of the protocol described above had been completed, and steps 6 to 8 were in progress. The expert training session (step 9) and the expert elicitation session (step 10) will be held in January 2003. The post-elicitation steps, i.e., steps 11 to 15, will be worked out shortly thereafter. Preliminary results of the expert judgement study will be shown in the oral presentation.

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BSE: GEOGRAPHICAL BSE RISK ASSESSMENT (GBR)

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ABSTRACT

The Geographical BSE-Risk (GBR) is a qualitative indicator of the likelihood of the presence of one or more cattle (GBR-C) or small ruminants (GBR-S) being infected with BSE, pre-clinically as well as clinically, at a given point in time, in a country. Where presence is confirmed, the GBR gives an indication of the level of infection.

The SSC-methodology for the assessment of the GBR-C is based on the assumption that BSE arose in the United Kingdom (UK) and was propagated through the recycling of bovine tissues into animal feed. Later the export of infected animals and infected feed provided the means for the spread of the BSE-agent to other countries where it was again recycled and propagated via the feed chain.

To determine the GBR-S, the GBR-C methodology was adapted to small ruminants, including other routes of transmission than infected feed, i.e. vertical and horizontal pathways, and a much more widespread tissue infectivity distribution, assuming BSE in small ruminants behaves similarly to sheep and goat scrapie.

SAMENVATTING

Het Geografisch BSE-Risico (GBR) is een kwalitatieve inschatting van de kans op aanwezigheid van één of meer runderen (GBR-C) of kleine herkauwers (GBR-S) besmet met BSE, preklinisch en klinisch, op een bepaald punt in de tijd in een land. In geval van bevestiging, geeft de GBR een indicatie van de besmettingsgraad.
De SSC-methode voor de inschatting van GBR-C is gesteund op de aanname dat BSE in het Verenigd Koninkrijk is ontstaan, en verspreid werd door verwerking van rundvleesafval in het voer. Export van besmette dieren en voer heeft verdere verspreiding in de hand gewerkt, ook via het originele mechanisme.
De GBR-C-methode werd ook toegepast op kleine herkauwers om de GBR-S af te leiden, waarbij zowel horizontale als vertikale besmetting in rekening werden gebracht, inclusief een algemene verspreiding van de infectie. Hierbij werd er aangenomen, dat BSE zich gelijkaardig gedraagt als scrapie bij schapen en geiten.

1. The GEOGRAPHICAL BSE RISK ASSASSMENT for BSE in CATTLE (GBR-C)

1.1 Introduction

The Geographical BSE-Risk (GBR-C) is a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE (Bovine Spongiform Encephalopathy), pre-clinically as well as clinically, at a given point in time, in a country.Where its presence is confirmed, the GBR-C gives an indication of the level of infection.

Table 1 - Definition of GBR-C and its levels

GBR-C level	Presence of one or more cattle clinically or pre-clinically infected with the BSE agent in a geographical region/country
I	Highly unlikely
II	Unlikely but not excluded
III	Likely but not confirmed or confirmed, at a lower level
IV	Confirmed, at a higher level

The Scientific Steering Committee of the European Commission (SSC) has developed a transparant methodology (8), to assess the GBR-C for any country that provides the information required for the assessment. This methodology is limited to bovines and feed based transmission of BSE. It does not take into account any other initial sources of BSE than the import of infected cattle or contaminated feed. It is assumed that the disease first appeared in the UK from a still unknown initial source. An important characteristic of the methodology is that it does not depend on the confirmed incidence of clinical BSE, which is sometimes difficult to assess due to serious intrinsic limitations of surveillance systems. Surveillance should be understood as the process of identifying BSE-cases and animals at risk of being infected.

The qualitative nature of this methodology and its limitations should be understood in the context of present scientific knowledge on BSE and of the availability and quality of data. As they both evolve, and with the advancement of new diagnostic methods, the need may arise for the methodology to be revised and/or its application to particular countries to be repeated.

1.2. Methodology for asssessing the GBR-C

Germany, Italy, Spain, and the Czech Republic and the Slovak Republic all were classified as GBR-C III before they detected their first case. The GBR-C-assessment for Denmark was already in an advanced stage, pointing to GBR-C III, when the first case was confirmed. In addition Japan and Greece have now confirmed first domestic BSE-cases. Also Austria, Finland and Slovenia, all three in GBR-C-II, recently detected a first domestic case of BSE. In all cases active surveillance detected BSE-cases that would have remained undetected by the already existing, passive surveillance, which was targeted at animals with neurological symptoms. The methodology of the GBR-C-assessment, and the model and assumptions it is based on, remains unchanged. Consistency of the past and future assessments is therefore ensured, but the assessment of the external challenge is refined and the process is streamlined since the start in 2000.

Basically the GBR-C–methodology tries to answer two questions:

1. Is there a risk that the BSE-agent was imported into the country under consideration?
2. If the BSE-agent was introduced into a country, would it have been recycled and amplified or was the BSE/cattle system of that country able to eliminate the agent?

The following factors contributing to the incident and propagation risks in a geographical area are to be included in the assessment:

1. Structure and dynamics of the cattle, sheep and goat populations
2. Animal trade
3. Animal feed
4. Meat and bone meal (MBM) bans
5. Specified bovine offals (SBO) and specified risk materials (SRM) bans
6. Surveillance of TSE, with particular reference to BSE and scrapie
7. Rendering and feed processing
8. BSE and scrapie related culling

1.2.1. Basic assumptions

Origin and transmission of BSE: The assessment of the GBR-C continues to be based on the assumption that BSE arose in the United Kingdom (UK) and was propagated through the recycling of bovine tissues into animal feed. Later the export of infected animals and infected feed provided the means for the spread of the BSE-agent to other countries where it was again recycled and propagated via the feed chain.

For all countries other than the UK, import of contaminated feed or infected animals is the only possible initial source of BSE that is taken into account. Other sources such as a spontaneous occurrence of BSE at very low frequency, or the transformation into BSE of other (animal) TSEs (Transmissible Spongiform Encephalopathy) (scrapie, CWD or Chronic Wasting Disease, TME or Transmissible Mink Encephalopathy and FSE or Feline Spongiform Encephalopathy) being present in, or imported into a country are not considered, as they are not scientifically confirmed. In addition surveillance data on other TSEs are generally inadequate for assessing their prevalence.The only transmission vector considered in the model continues to be feed. Blood, semen and embryos/ova are not seen as effective transmission vectors and accordingly, bloodmeal or embryos/ova and semen are not taken into account. The recent results of large scale BSE-testing in combination with reports on feed controls have further underpinned the opinion of the SSC that any cross contamination of cattle feed with mammalian MBM, even well below 0.5%, represents a risk of transmitting the disease. However, the influence of potential cross-contamination on the GBR-C has to be seen in the light of the risk that the animal protein under consideration could carry BSE-infectivity.

Other transmission routes than feed are debated but they are not scientifically confirmed and anyway their potential impact on the GBR-C is regarded negligible in comparison to contaminated feed. This includes vertical transmission as well as any unknown third mode of transmission of BSE. Also transmission via the environment or the possibility that sheep and goats may have become infected with BSE (5,6) and could be a source of BSE are not scientifically confirmed. They will be taken into account once scientific evidence of their existence is available allowing assessing their impact on the GBR-C.

Geographical limitation: So far the present GBR-C risk assessments are only addressing entire countries and national herds. This is because of the limited availability of detailed, regionalised data. However the issue of regional differences, for example in the types of animal husbandry, e.g. dairy or beef, or with regard to feeding or to slaughtering ages is not discounted. If complete data sets could be provided on a regional scale, i.e. clearly relating to a defined geographical area smaller than a country, these could be assessed in the same way as data referring to entire countries.

1.2.2. The external challenge assessment

The term **“external challenge”** is referring to both the likelihood and the amount of the BSE agent entering into a defined geographical area in a given time period through infected cattle or MBM. The following basic guidelines for assessing the external challenge are used (8,14):

1. The external challenge is regarded independent from the size of the challenged BSE/cattle system and in particular the size and structure of the cattle population.
2. The assumed challenge resulting from imports from the UK during the peak of the BSE-epidemic in the UK is the point of reference.
3. The challenge resulting from imports during other periods and from other BSE-affected countries is established in relation to this baseline.

In the light of new scientific knowledge and data it is necessary when assessing the external challenge to take account of imports from all countries with a BSE risk. This includes all countries with one or more confirmed domestic cases or being classified in GBR-C III while not having identified any domestic cases.

Table 2: Definition of BSE-challenge levels

EXTERNAl CHALLENGE	Cattle (n° of heads) imports			MBM1 (tons) imports		
	1988 - 93 from UK	UK-imports before 88 and 94-97: *10; after 97: *100	Imports from other countries with a BSE risk: R1*1000, R2* 100	1986 - 90 from UK	UK-imports before 86 & 91-93: * 10, after 93 *100	Imports from other countries with a BSE-risk: R1*100, R2* 10
Extremely High	> 10.000			> 10.000		
Very High	1.000 - < 10.000			1.000 - < 10.000		
High	100 - < 1.000			100 - < 1.000		
Moderate	20 - < 100			20 - < 100		
Low	10 - < 20			10 - < 20		
Very low	5 - < 10			5 - < 10		
Negligible	0 - < 5			0 - < 5		

1 “MBM” refers to MBM, MMBM, BM, or Greaves but not to composite feed that could contain it.

From the GBR-C assessments so far available it can be seen that the first occurrence of an internal challenge is rather variable. Therefore in all cases where this information is available, only exports after a first internal challenge could possibly have been present in the exporting country shall be regarded as an external challenge to importing countries.

Table 3: GBR-C levels and R1 and R2 challenges

Country Name	GBR-C	R1	R2
Albania	III	No data	1988
Austria	III6	1988	1990
Belgium	III	1983	1987
Cyprus	III	1980	1990
Czech Republic	III	No data	19881
Denmark	III	1985	1990
Estonia	III	19872	19882
Finland	III6	1980	1990
France	III	1979	1980
Germany	III	19803	19883
Hungary	III	1981	1982
Ireland (Eire)	III	1980	1980
Italy	III	1983	1990
Lithuania	III	No data	19942
Luxembourg	III	1983	1987
Netherlands	III	1985	1987
Poland	III	1980	1987
Portugal	IV	1979	1987
Romania	III	No data	1981
Slovak Republic	III	No data	19881
Slovenia	III6	19814	19914
Spain	III	1985	1987
Switzerland	III	1979	1980
Greece5	III	19855	19905
Japan5	III	19855	19905

Table 3: Countries in GBR-C III and IV and the year since when it is regarded possible (R1) or likely (R2) that exports of life bovine or MBM could have represented an external challenge to the importing country.
UK is not listed in this table as it is used as reference case and already addressed in table 2.
1Part of CSSR, 2part of Soviet Union, 3only FRG – incl. GDR only after 1988, 4former Republic of Yugoslavia, 5pending a GBR-C assessment the dates for R1 and R2 are preliminary estimates, 6Austria, Finland and Slovenia were earlier classified as GBR-C II but due to confirmed presence of one or more cattle clinically or preclinically infected with the BSE agent they now fall into GBR-C III. A revision of their GBR-C reports is ongoing.

Table 3 provides for each of the already assessed countries, and Greece and Japan, the year since when it is regarded possible (R1) or likely (R2) that exports represented an external challenge to the importing country. To assess the level of this external challenge the following factors shall be used when working with table 1:

R1 = factor 1000 for live cattle and factor 100 for MBM

R2 = factor 100 for live cattle and factor 10 for MBM.

The dates in the table were derived from the available GBR-C-reports and relate to the time when an internal challenge became possible (R1) or likely (R2) in the respective country.The factors are the same as previously used, only for the periods R1 another order of magnitude was added to reflect the lower but not negligible risk. Greece and Japan are countries with confirmed BSE. Pending the outcome of the ongoing GBR-C-assessment it is assumed that Greece and Japan posed a potential risk (R2) since 1990, i.e. about two incubation periods before the confirmation of the first case. It is also assumed that a lower risk existed already one incubation period before (R1 for the period from 1985-1989).

1.2.3 Regular updating of GBR-C assessments.

From new scientific knowledge and data a need might arise to update the GBR-C-methodology and to re-apply this to countries that are already assessed (8,14). The BSE-cases, recently confirmed in Austria, Finland and Slovenia that were classified as GBR-C II, underlines the appropriateness of this statement. One of the possible explanations for these cases could be that imports into these countries from GBR-C-III countries were not regarded as external challenge when the GBR-C of these countries was assessed.

It is therefore appropriate to verify for all countries, classified so far as GBR-C I or II, if external challenges can now be identified that were not previously been taken into account in the GBR-C assessment. If necessary the GBR-C-report/opinion should be updated.

Table 4. Overview of all countries with a GBR-C classification

N°	Country	Dossier in	GBR-C	Year of adoption
1	**Albania**	**19/10/00**	**III**	**2001**
2	**Argentina**	**1/03/99**	**I**	**2000**
3	**Australia**	**1/03/99**	**I**	**2000**
4	**Austria**	**1/10/98**	**II>III** (case revision pending)	**2000**
5	**Belgium**	**1/10/98**	**III**	**2000**
6	**Botswana**	**31/10/00**	**I**	**2001**
7	**Brazil**	**17/09/00**	**I**	**2001**
8	**Canada**	**1/03/99**	**II**	**2000**
9	**Chile**	**1/03/99**	**I**	**2000**
10	**Colombia**	**13/11/00**	**II**	**2001**
11	**Costa Rica**	**21/03/01**	**I**	**2001**
12	**Cyprus**	**3/11/00**	**III**	**2001**
13	**Czech Republic**	**1/03/00**	**III**	**2001**
14	**Denmark**	**1/12/98**	**III**	**2000**
15	**El Salvador**	**8/11/00**	**I**	**2001**
16	**Estonia**	**7/11/00**	**III** (case assessment pending)	**2001**
17	**Finland**	**1/12/98**	**II>III** (case revision pending)	**2000**
18	**France**	**1/12/1998**	**III**	**2000**
19	**Germany**	**1/11/98**	**III**	**2000**
20	**Greece**	**1/8/01**	**III**	**2002**
21	**Hungary**	**3/11/00**	**III**	**2001**
22	**India**	**1/06/99**	**II**	**2001**
23	**Ireland (Rep.)**	**1/1/99**	**III**	**2000**
24	**Italy**	**1/3/99**	**III**	**2000**
25	**Japan**	**1/11/99**	**III** (cases assessment pending)	**2002**
26	**Kenya**	**29/11/00**	**II**	**2001**
27	**Lithuania**	**31/10/00**	**III**	**2001**
28	**Luxembourg**	**1/1/99**	**III**	**2000**
29	**Mauritius**	**20/11/00**	**II**	**2001**
30	**Namibia**	**3/11/00**	**I**	**2001**
31	**Netherlands**	**1/2/99**	**III**	**2000**
32	**New Zealand**	**1/12/98**	**I**	**2000**
33	**Nicaragua**	**30/10/00**	**I**	**2001**
34	**Nigeria**	**31/10/00**	**II**	**2001**
35	**Norway**	**1/12/98**	**I**	**2000**
36	**Pakistan**	**1/07/00**	**II**	**2001**
37	**Panama**	**17/04/01**	**I**	**2001**
38	**Paraguay**	**1/03/99**	**I**	**2000**
39	**Poland**	**3/11/00**	**III**	**2001**
40	**Portugal**	**3/3/99**	**IV**	**2000**
41	**Romania**	**1/03/01**	**III**	**2001**
42	**Singapore**	**17/11/00**	**I**	**2001**
43	**Slovak Republic**	**3/11/00**	**III**	
44	**Slovenia**	**21/02/01**	**II>III** (case revision pending)	**2001**
45	**Spain**	**1/4/99**	**III**	**2000**
46	**Swaziland**	**24/11/00**	**I**	**2001**
47	**Sweden**	**1/12/98**	**II**	**2000**
48	**Switzerland**	**1/03/99**	**III**	**2000**
49	**United Kingdom**	**1/10/98**	**IV**	**2000**
50	**Uruguay**	**1/07/00**	**I**	**2000**
51	**USA**	**1/12/98**	**II**	**2000**

2. THE GEOGRAPHICAL BSE RISK ASSESSMENT for BSE in SMALL RUMINANTS (GBR-S)

Because it has clearly been demonstrated that BSE can be orally transmitted to certain genotypes of small ruminants, and because it is likely that potentially BSE-contaminated MBM has been fed to some sheep and goats, one has to assume that BSE could have been introduced into the sheep and goat population. (5,6). Therefore it can not be excluded that the risk could persist it, even after an effective implementation of a ruminant feed ban .
The most likely way of introduction has been through infected MBM. It is possible that the BSE-agent has been maintained, propagated and/or recycled by horizontal and vertical transmission in sheep and goats if the agent behaves like scrapie in these species(11).

The same factors contributing to the incident and propagation risks in a geographical area for the GBR-C are to be included in the GBR-S (18).
The GBR-S is based on the exploitation of the GBR-C, with some additional information elements such as:

- Routes of infection: not only through the contamination of the feed chain but also horizontally through direct or contact or by contaminating the pasture.
- Susceptibility of different small ruminants strains: it is known that this varies substantially depending on the breed and on the presence of specific genotypes (7,16). Kao *et al.* (2002)(4) have presented a rationale for considering the speed of spread of BSE infectivity within heterozygous semi-resistant sheep to be slower than in the fully susceptible animals. The incubation period for infectivity is assumed to be approximately 3 years longer than the susceptible group.
- Dose-response: Estimations using the limited data on the proportion of susceptible sheep succumbing to BSE after consuming 0.5g of infected cattle brain, do not allow any treshold dose to be shown to exist.(4)
- Infectivity distribution and total infectivity load: It appears that the main difference between cattle and small ruminants is that lymphoreticular tissues in BSE in sheep and goats, and possibly their blood (2,3,10,12,17,19), should be considered comparable in their level of infectivity with central nervous system tissues.However the amount of infectivity detected in blood is very likely much smaller than that detected in most lymphoreticular and nervous tissues.
- Prevalence of BSE in TSE affected sheep population: there are indications that BSE is likely to be at a prevalence significantly below that of scrapie, and figures based on the failure to detect BSE in samples of TSE affected brains provided an upper bound for BSE-prevalence of about 0.83% till 2%.(1,13,16).
- Prevalence of scrapie in small ruminants: on the basis of the TSE testing results in the frame of the EU programme started in April 2002, the TSE positives are 0.5% of risk sheep and 0.055% of healthy adult sheep
- Prevalence of BSE in small ruminants:on the basis of a maximum TSE infection prevalence of 1.0% in the sheep population, with no more than 1.0% of the scrapie sheep possibly being in reality BSE, the worst case hypothesis is 1 BSE animal in 10 000 small ruminants (0.01%).

The implementation of the GBR-S methodology is recommended only in the case BSE has been confirmed under natural conditions in at least one small ruminant (9,15) and should be done in two steps:

Step one : Countries GBR-C levels III and IV

These countries should be classified into GBR-S level III unless data can be provided showing that, since 1980, significant levele of potentially –infected MBM very unlikely or unlikely reached small ruminant through the feed chain. Important elements are:

- Feeding practices for different types of sheep flocks, prefereably including the relative amounts of MBM fed to sheep as compared to cattle
- Tons of compound feed sold annually for sheep and goats
- Inclusion rate of MBM in these feeds
- Price charts for MBM and alternative protein sources
- Cross contamination
- Regulatory situatioin re-use of MBM for sheep
- Mixed farming practices

Countries in GBR-C level I and II

Should the challenge through the feed chain due to live small ruminants be found negligible throughout, the GBR-S classification would remain identical identical to the GBR-C one. Otherwise the combined

external challenge should assessed and a stability analysis would be necessary for the sheep feeding system since 1980 and a higher GBR-S level would be likely.

Step two: Countries GBR-S level I and II

For countries that remain classified as GBR-S level I and II at the end of step one, it would be necessary to estimate wether BSE might have entered the country through live small ruminants and transmitted through horizontal or vertical routes.

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The Federal Agency for Safety of the Food Chain (FAVV-AFSCA) in Belgium

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Abstract

The new Federal Agency for Safety of the Food Chain is now fully operational. Its mission, competence, management, structure, operational skills, funding and integration within the other Federal Services are explained.

1. INTRODUCTION

The Federal Agency for the Safety of the Food Chain, called Food Agency, came into operation on January 1st 2000. Several departments from the former Ministry of Agriculture and Public Health were merged. It took a while to become fully operational, so it's time for an update.

Shortly after the dioxin crisis of 1999, the Belgian government decided to create a new agency focused on food safety. Experience proved that communication and coordination was lacking between the different and dispersed entities of the responsible administrations, inhibiting a fast and focused solution of potential problems. The request was born for a new agency merging and reshaping all departments being involved in safety control of the food chain and public health. The Ministry of Public Health received the responsibility by Law published on 04.02.2000. In fact, this development was part of a general restructuring of the Federal Services, called the Copernicus treaty. The former Ministry of Public Health is now called the Federal Governmental Service of Public Health, Safety of the Food Chain and Environment (FOD-Public Health). Its departments support decision making in the short and long term.

2. COMPETENCE

The responsibilities of the Agency on food safety (Food Agency) are covering (cover) the whole territory of Belgium. Its core business is to guarantee the safety of the whole food chain, i.e. from fork to farm, which matches the new EC concept. All aspects of food production are envisaged (e.g. animal feed, hormones, antibiotics, fertilizers, seeds, pesticides…), including plant and animal production and food distribution (e.g. retailers, restaurants…). The main tasks of the Agency are:

- Control, investigation and certification of all feed and food and their components through the food chain;
- Control and surveillance of production, treatment, storage, transport, trade, import and export as such, and the sites where it is happening;
- Approval and registration of activities in the food chain;
- Integration, implementation and control of traceability and identification systems for feed and food resources.

Other tasks are:

- Management of information (including scientific opinions) related to food safety;
- Development and application of the policy related to prevention, sensitisation and information in accordance with the other legal entities in Belgium;
- Surveillance of the legal application of all directives related to the food chain.

In fact the Agency is acting at three levels: advice, risk analysis and integrated control. These activities were previously administrated by:

- The Institute of Veterinary Inspection (IVK);
- The General Food Inspection (AEWI);
- The Directorate of Quality Resources and Plant Production (DG4);
- The Directorate of Animal Health and Quality of Animal Production (DG5).

The transfer of staff from the Ministry of Public Health and the Ministry of Agriculture was finished at October 15th 2002. The new Federal Governmental Service for Public Health, Safety of the Food Chain and Environment has mainly a legislative function, i.e. standardisation (veterinary products, pesticides, feed, food), animal health standards and animal welfare (standards as well as control).

3. SCIENTIFIC COMMITTEE

A scientific committee is supporting the activities of the Agency. Members are 18 national experts (9 Flemish, 9 French speaking), and two international experts. The scientific committee expresses it's opinions independently or on request of the Agency. Obviously, the main task is to define problems in advance, so that solutions are available on time. Therefore, it has access to all information available within the Agency. This committee has to be consulted on all legal proposals prior to adoption. Reports of the committee are available (in Dutch and French) on the website of the Agency, i.e. www.favv.be.

4. ADVISORY COMMITTEE

Communication between the Agency and all stakeholders of the food chain, is very important, so that they are represented in an advisory committee. They meet on request of the Minister or the Agency, or on their own initiative. Members are representatives from:

- Consumer organisations (7)
- Agriculture sector (4)
- Organic production sector (1)
- Feed producers (1)
- Food industry (5)
- Retailers (2)
- Federal services (4)
- Regional government (5).

5. OWN CHECK PROGRAMS

The prime responsibility for food safety lies with the operators active in the food chain. The main principle is own check programs by all participants in the food chain, who have full legal responsibility for food safety. Own checks are based on risk assessment, taking into account internationally standardized protocols (HACCP, GMP). Codes of practice are available for implementation of these principles.

Three main criteria are applied:

- Recording of control information over the whole production and distribution;
- Traceability, and
- Notification requirement.

Each problem should be immediately communicated to all possible destinations up- and downstream in the food chain. In case public health is at risk, the Agency has to be informed. An independent organisation (e.g. certified by BELCERT) in collaboration with the Agency is responsible for the control of the whole system. Eventually, the system can be used for the development of a fee protocol to cover the costs of the system.

6. STRUCTURE

Dr. P. VANTHEMSCHE, Chief Executive Officer of the Agency is leading four departments plus some ad hoc units (e.g. communication, crisis management)

- Control policy
- Control
- Laboratories
- Corporate services.

The control policy department is responsible for the design and integration of control procedures and programmes in order to guarantee public health, animal and crop health. In addition also traceability and identification systems are developed for the whole food chain in collaboration with international bodies.

The control department applies the procedures in the field, and is organized in Provincial Control Units (PCU). The keywords are integration and efficiency of operation according to the mission of the Agency. Both departments have support from different certified laboratories, whether or not belonging to the Agency.

The laboratories and corporate services provide the necessary logistic support.

7. COMMUNICATION

Transparent communication is one of the cornerstones of the Agency, which is realized through press releases, a bimonthly newsletter, publications and flyers (e.g. “Knowledge about food”). All this information is available in Dutch and French on www.favv.be.

In order to know consumer’s opinions and perception, a call centre is operational for exchange of information. This centre is operational in French and Dutch from 09.00 to 17.00 h on working days (tel.: 0800 13 550 fax: 08000 13 455; e-mail: meldpunt@favv.be). The aim is to provide available information as soon as possible, so that quick and focused answers are given on specific questions.

8. CRISIS MANAGEMENT

The crisis management is developing a code of practice, where all the SOPs are described in detail. In case of emergency the action plans, responsible people and communication protocols are available in detail. The aim is to realize efficient communication and collaboration between the players in the field. This global crisis and communication system is taking into account emergency plans developed by other Governmental Services, including the routine tasks and available resources.

9. FUNDING

Resources are from different origin: governmental funds, taxes, fines, and fees from stakeholders in the food chain, subsidies from the EC or private initiatives. However, detailed procedures have still to be developed in relation to defining of weighing factors for different interest groups.

10. FOD PUBLIC HEALTH

An important item in the reorganisation of the administration is the clear separation between policy making and it’s implementation.

Policymaking, the preparation of the food safety policy and the standardisation is allocated to the Federal Government Structure Public Health. The FGS Public Health has its own advisory board: the Supreme Health Council. The implementation, guarding that all participants active in the food chain respect all regulations and standards, is executed by the Agency.

This way a clear interaction and intense collaboration between the Agency and the FGS Public Health is guaranteed.

PROBABILISTIC INTAKE ASSESSMENT AND BODY BURDEN ESTIMATION OF DIOXIN-LIKE SUBSTANCES IN BACKGROUND CONDITIONS AND DURING THE BELGIAN 1999 FOOD CONTAMINATION EPISODE.

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ABSTRACT

The objective was to perform a dioxin body burden estimate based on a probabilistic intake assessment of PCDDs, PCDFs and dioxin-like PCBs because of the so-called 1999 'Belgian dioxin incident'. Monte Carlo simulation techniques were used to combine detailed 7-day food intake data on the individual level from a sample of 14-18-year-old adolescents with 'background' and 'incident-related' food contamination data. In background conditions, 3% of the adolescents had an intake <1pg TEQkg^{-1} bw day^{-1}, while 85% had <4 pg TEQkg^{-1} bw day^{-1}. Milk and other dairy products were the basic source of dioxin-like contaminants, while fish constituted the main source at the higher percentiles of intake. During the dioxin incident, the estimated median dioxin intake showed a moderate increase. At the 99th percentile, the highest intake level, and the 95% upper bound uncertainty level, peak body burden — 19.53 ng TEQ kg^{-1} bw for a 16 year old— remained below body burdens that in the experimental animal or in man are accompanied by a population-based observable increase in the incidence of adverse effects. The 1999 Belgian dioxin incident most likely did not affect public health in Belgium in a measurable way, although exceptions remain possible on the individual level.

SAMENVATTING

Het doel van het onderzoek was het effect in te schatten van een probalistische opname van PCDDs, PCDFs en dioxineachtige PCBs in relatie tot de dioxinecrisis van 1999. Monte Carlo simulaties werden toegepast op gedetailleerde individuele voedselopnamegegevens over een periode van 7 dagen bij 14-18 jarigen, geselecteerd uit een een referentiepropulatie en met een achtergrond van voedselbesmetting, resp. een inname van <1pg TEQ t.o.v. <4pg TEQ per kg lichaamsgewicht en per dag. Melk en aanverwante producten waren de bron voor dioxineachtige contaminanten, terwijl vis het grootste aandeel had bij de hogere opnamepercentielen. Tijdens de dioxinecrisis vertoonde de mediaan van de opname een licht stijging. Voor het 99ste percentiel met een betrouwbaarheidsgrens van 95%, was de piekbelasting 19,53 ng TEQ per kg lichaamsgewicht voor een 16-jarige, wat lager is dan in geval van een opname met hoog risico op nadelige gevolgen, zoals experimenteel vastgesteld. Derhalve heeft de dioxinecrisis in 1999 wellicht geen effect gehad op populatieniveau, alhoewel individuele gevallen mogelijk zijn.

1. INTRODUCTION

The Belgian “dioxin” crisis (February 1999), which was actually a PCB accident, involved livestock feed as a route of contamination. Subsequently, enhanced PCB and dioxin concentrations in the human food chain led to a wide-spread public concern about possible adverse health effects.

Starting form a detailed analysis of food consumption data for Belgian adolescents and from background and incident-related food contaminations with PCDDs, PCDFs, and dioxin-like PCBs, we performed a probabilistic exposure assessment. Two dimensional Monte Carlo simulation were used to combined the available data, acknowledging for potential uncertainties.

A full paper of this study has been published in Food Additives and Contaminants, 2002, Vol 19, No 7, 687-700.

2. METHODOLOGY

Fat concentrations in the different food items as well as relative contributions of fat species (milk, egg, pork, beef, chicken, sheep, horse, fish and vegetable) were determined from a 7 day food record of 341 14 to 18 year old adolescents, carried out in 1997. This resulted in a three dimensional database $X_{v,i,t}$ presenting the amount of fat consumed (g), for each combination of fat nature (v), subject (i) and time (t). Background PCDD/PCDF and dioxin-like PCB concentrations in food items were derived from Belgian and Dutch data. Incident-related PCDD/PCDF and non-dioxin-like PCB concentrations were obtained from the data base of the Belgian Ministry of Agriculture.

For each subject i, the average body weight adjusted daily intake via food of dioxin-like contaminants (DI_i) is computed according to equation

$$DI_i = Y_i/bw_i;$$

where Y_i is the subject’s average total daily dose (pg TEQ) and bw_i the corresponding body weight (in kg). The subject-specific average total daily intake is derived by combination of individual food consumption data and concentrations of the dioxin-like contaminants according to:

$$Y_i = \sum_v \sum_t [(X_{v,i,t} C^S_{v,i,t}) \delta_{v,i,t} + (X_{v,i,t} C^B_{v,i,t})(1 - \delta_{v,i,t})] \ / T$$

where $X_{v,i,t}$ represents the amount (g) of fat from origin v, consumed by subject i, at day t ($t = 1,\ldots,T$), $\delta_{v,i,t}$ a binary variable determining whether the particular food item is issued from an incident related production unit ($\delta = 1$) or not ($\delta = 0$) and $C_{v,i,t}$ the concentration of the dioxin-like contaminant expressed in pg TEQ/g fat. The superscript I or B indicates whether the food item stems from a production unit with an incident related contamination or from a unit that remained outside the incident-related contamination (background). Since items from incident related productions were not uniformly distributed across the population, the intersubject variability in the percentage of items consumed from an incident related production unit was modelled according to a unimodal, right skewed, beta distribution $B(b_1,b_2)$ for each contaminated fat species.

The probabilistic exposure estimations, according to this model, were assessed through Monte Carlo simulations (1). The simulation separates variation among the different subjects in each subgroup, from uncertainty due to uncertainties in the incident input parameters. According to the procedure, different models are run consecutively, using each time different values for the vector of input parameters.

The body burden (bb, pg or ng TEQ/kg bw) was calculated according to equation:

$$bb\ (t) = bb\ (t\text{-}1)\ e^{-ke} + f\ DI$$

with $k_e = \ln 2/t½$, DI the daily intake, f the fraction of the dose absorbed and $t½$ the elimination half life. The TCDD values for f (0.5) and $t½$ (7.5 years) were applied to all of the congeners that contribute to the total TEQ intake (2).

3. RESULTS

Non-dioxin-like PCB congener profile analysis of incident related samples and background samples confirmed that the PCB sources were quite similar for both. The 1999 Belgian dioxin-incident has to be seen as a common contamination, accidentally concentrated in time and space.

The combination of adolescent food consumption and food contamination data led to an estimated daily intake of dioxin-like compounds for the background situation and during the 4 month dioxin-incident period (table 1). The simulated, incident-related intake data are reported at the 5%, median, and 95% level of uncertainty. Median uncertainty represents the most likely estimate for the intake during the dioxin-incident, the 95% uncertainty a reasonable worst case. In the background situation, no uncertainty was introduced into the simulation parameters and Figure 1 represents the cumulative distribution functions of intake representing the between-subject variation for total fat intake and for each fat nature separately. The figure shows that, most likely, 3% of the adolescent population remains below a daily intake of 1 pg TEQ/kg bw/day for the sum of PCDDs, PCDFs and dioxin-like PCBs; 85% of the population remains below 4 pg TEQ/kg bw/day. The analysis of each fat nature separately indicates that a significant contribution to the total intake in background conditions, for the entire population, happens through milk and milk derived products. In the subjects with higher intakes, above the 80th percentile, fish and fish oils become the major source of intake of dioxin-like substances. The importance of the other contamination sources (at the 95th percentile) are, in decreasing order: beef, remaining sources, egg, pork and chicken. Remaining sources are horse, sheep and vegetables taken together. During the incident, milk and milk derived products remain important as source for all adolescents. For most of the adolescents the moderate increased intake follows the contamination of chicken, egg, pork and beef. Fish remains an important input for the higher percentiles. Only from the 90th percentile on, chicken becomes more important as source and overtakes fish at the highest percentiles.

Starting at zero body burden at birth, the background body burden was estimated on the basis of the simulated background daily intake. In order to estimate the increase in body burden due to the dioxin-incident, a four month period — the assumed duration of the dioxin-incident — of increased intake were introduced at the age of 16. Table 2 summarises the body burden calculated at age 16 in background conditions and at the end of a 4 month dioxin-incident period. Similar increases in body burden were obtained when the increased intake was introduced at other ages.

4. COMMENTS and CONCLUSION

The main source of background daily intakes of PCDDs, PCDFs and dioxin-like PCBs in Belgian adolescents appeared to be milk, fish becomes important at the higher percentiles of intake. During the dioxin-incident, moderate intake increases were due to moderately increased contaminations of chicken, egg, pork and beef. At the highest percentiles, chicken took the place of fish as the major source. At the end of the dioxin-incident some increase in body burden should have taken place. However, even in a reasonable worst case situation, body burdens remained below values that, in the experimental animal, are accompanied by increased incidence of adverse effects.

It is, therefore, unlikely that the 1999 incident would have a dramatic impact on public health, but it can not be disregarded that some subgroups who were intensively exposed to contaminated food (e.g. farmers eating their own contaminated production) and/or subjects most sensible to dioxins (e.g. women pregnant at or shortly after the incident and with a direct and repetitive access to highly contaminated chickens) would have developed some adverse health effects.

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Table 1: daily intake of the sum of PCDD, PCDF and dioxin-like PCB (pg TEQ/kg bw/d) via food in different percentiles of the adolescent population in background conditions and during the Belgian dioxin-incident. For the incident period the most likely intake (at median uncertainty) as well as the lower (5%) and upper (95%) bound uncertainty are given.

Percentile	Background,	Incident simulation 5% uncertainty	Incident simulation median uncertainty	Incident simulation 95% uncertainty
1	0.68	0.72	0.78	1.24
3	0.93	1.02	1.10	1.84
5	1.15	1.28	1.39	2.11
25	1.85	2.05	2.20	4.46
50	2.53	2.78	2.98	8.49
75	3.30	3.65	4.02	16.91
95	6.52	7.17	8.46	47.23
97	7.47	8.39	10.53	58.04
99	9.65	11.26	19.58	94.62

Table 2: starting body burdens and body burdens at the end of the incident in adolescents for different percentiles and at two incident levels of uncertainty.

Estimated body burden at age 16 (ng TEQ/kg bw)			
Population distribution	Estimated body burden in background situation	Estimated body burden at the end of the dioxin-incident	
		at median uncertainty	at 95% uncertainty
50th percentile	3.890	3.915	4.219
75th percentile	5.074	5.114	5.826
95th percentile	10.026	10.133	12.273
97th percentile	11.486	11.655	14.278
99th percentile	14.839	15.387	19.529

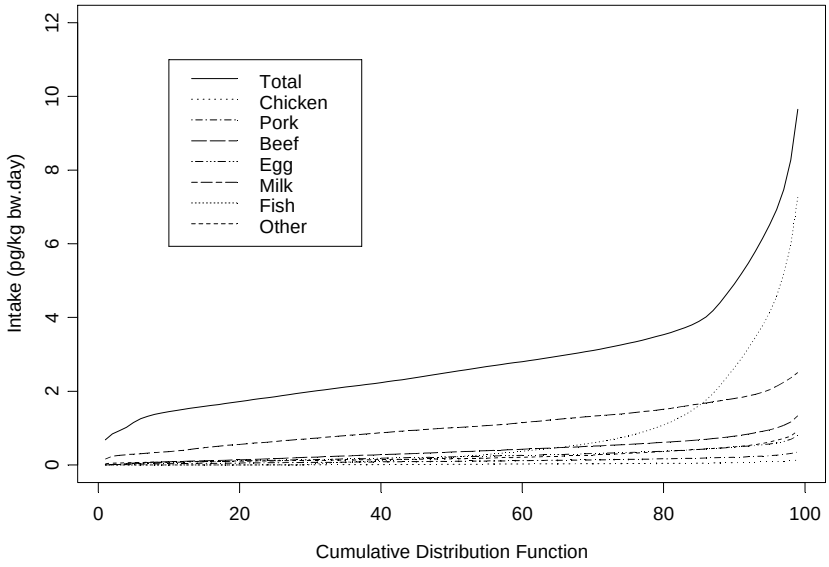

Figure 1: Cumulative distribution functions in background total fat intake and for each fat nature separately in adolescents.
For clarifications see insert.

QUALITATIVE RISK ASSESSMENT – THEORY AND PRACTICE

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ABSTRACT

The paper outlines the basic steps and principles of a qualitative risk assessment. It does not focus on any one particular set of guidelines, as with a sound knowledge of the underlying theory and approaches, the basic method can easily be amended and adjusted to fit any situation and system or set of guidelines. Topics covered include scoping the risk issue, hazard identification, the risk question, the risk pathway (essentially an exposure pathway), data required and data quality, the population exposed to the hazard, estimating the risk to that population, and reporting the results. Many of the basic principles of a qualitative risk assessment apply also to a quantitative risk assessment, and the similarities and differences are indicated, as well as the advantages and disadvantages of qualitative risk assessment. Examples are biased towards food chain risk assessments, but again the principles are applicable to any other sphere.

SAMENVATTING

Dit manuscript beschrijft de basisstappen en principen van kwalitatieve risicoinschatting. De methode kan in wezen op elke situatie toegepast worden, aangezien de onderliggende theorie wetenschappelijk onderbouwd is. Achtereenvolgens worden de volgende onderdelen behandeld: het risico op zich, identificatie van gevolgen, de risicovraag, het risicoproces (in feite het blootstellen aan risico), de vereiste gegevens en hun kwaliteit, de blootgestelde populatie, en verslaggeving van de resultaten. Deze begrippen zijn ook toepasbaar op een kwantitatieve risicoanalyse, maar de verschillen en gelijkenissen zullen uitgelegd worden. Voor- en nadelen van beide methoden zullen vergeleken worden. De basisprincipen zullen geïllustreerd worden met voorbeelden uit de voedingssector om hun algemeenheid aan te tonen.

1. INTRODUCTION

Risk assessment is one of the components of risk analysis. There are a number of systems, or sets of guidelines on how to undertake risk assessment, including those produced by the Office Internationale des Epizooties (OIE) for the International Animal Health Code (AHC) (OIE-AHC, 1999), and those produced by the Codex Alimentarius Commission (CAC) (Codex, 1999). Both these guidelines can be, and are, applied to risk assessments involving food products, and the major difference is that in the OIE system, hazard identification is a categorised as a separate step to risk assessment, whereas in the CAC system, it is classed as a part of risk assessment. However, the underlying principles of these, and other systems, are similar and of more importance than the differences. In addition, for anyone familiar with those principles, they can adapt their knowledge and skills to fit the details of the system in use. Therefore this paper does not focus on any one system, but on the underlying principles of risk assessment and its essential companion, hazard identification.

Risk assessment may be classed as qualitative, quantitative, or semi-quantitative. Although quantitative assessments often ‘grab the headlines’ - numbers can be very seductive - the OIE AHC specifically states that qualitative and quantitative assessments are equally valid when undertaking risk assessments concerning animals or their products. Risk assessments described as semi-quantitative generally involve some kind of categorisation or prioritisation system, but there is some confusion over exactly what is classed as semi-quantitative. Where a system includes numbered categories, some assessors prefer to call it a quantitative assessment because it has numbers! Others prefer to call such a system a qualitative assessment, as it does not have a discrete numerical

risk estimate. There is also controversy about how useful it is, and it is true that there can be dangers involved in interpretation, if qualitative estimates are arbitrarily assigned to categories defined by quantified limits. However, used with care categorisation systems can be very useful under certain circumstances, and where this proves to be the case, it is really not particularly important whether an assessment is called semi-quantitative or something else.

Qualitative risk assessment can thus be considered any risk assessment which is not quantitative, and a quantitative risk assessment is one which presents its results as a numerical estimate of the risk being assessed. In general, qualitative risk assessments attempt to describe conclusions on risk estimates in textual terms, for example the risk is assessed as high, or very low, or negligible. Clearly, unless defined further, these terms are subjective and the interpretation will vary with the person reading them. Not surprisingly, this can cause a problem. Some assessors have attempted to overcome this by assigning numerical boundaries to these terms. However, if this is done, then the only way in which a given textual description can truly be assigned to the result is when that result is a numerical value. This means that a quantitative assessment would have needed to have been done, and defeats the purpose of undertaking a qualitative risk assessment! For this reason, it is frequently the case that no such attempt to assign a description is undertaken. However, although differences in interpretation do occur, it is generally accepted that for example, very low means something smaller than low, and negligible is smaller still, and that the difference between high and low is significant. Therefore, despite the subjective nature, it is still worth attempting to assign a textual description to the assessed risk. In particular, within the same assessment, if a number of possible outcomes are being compared, such a description used to order or prioritise is unlikely to be misinterpreted.

However, subjectivity remains a problem, and in some cases it is simply very difficult to actually assign a meaningful description to the outcome. What, then, is the use of the qualitative assessment, and how is it used? To overcome both these problems it is necessary that the person who wishes to understand the outcome of the assessment must generally read the whole of the risk assessment report, or possibly a well selected executive or technical summary. Given the evidence available, this enables them to reach their own conclusion on the probable level of risk, and their response to that level. For this reason alone, it is crucial that risk assessments are transparent. This means clearly and logically set out, and fully referenced, and this will be considered in more detail later in the paper.

2. A PRELIMINARY CONSIDERATION OF THE RISK ISSUE – OR ‘SCOPING’ EXERCISE

Risk assessments are undertaken on a regular and frequent basis in everyday life. For example, is it safe to cross the road? Or is it safe to eat that food? However, a formal risk assessment can be a complex, time consuming process, requiring teamwork, resources, and often specialist skills and knowledge. Therefore it is generally undertaken by governments, or regulatory authorities, or for legislative purposes. This being the case, a risk assessment will only be undertaken when there is an issue of concern for which the initial perception is that there are significant risks, or that there are potentially very serious consequences. In short, there must be an ‘issue’ about which unease is felt.

This means that the first step involved in any risk assessment is generally concerned with scoping that issue. This may mean somewhat different things, in different systems, but is broadly concerned with gathering enough information to decide whether it is necessary to go further with a formal risk assessment. It may be considered as an initial part of the risk assessment itself, or as a preliminary action; it may be undertaken by the risk assessors themselves, or by the risk manager or a committee; and it may on occasions be very brief. These details depend upon the system in place. However, it must certainly be done or no progress can be made.

A scoping exercise, if it decides that a risk assessment should be done, will consider in some detail which are the actual risks to be assessed, and may in some cases decide which hazards should be included in the assessment and/or the precise risk(s) to be assessed. Usually however, such precision is not reached at this stage – more information is needed to reach these decisions. Ideally the information collected, the conclusions reached, and the risk assessment decisions made in a scoping exercise should be included in written documentation for the use of, or written by, the risk assessor. From this it might be suspected that the scoping exercise is a mini-risk assessment in itself, and this is true.

There are a number of basic steps underlying any risk assessments, whether qualitative or quantitative, and it is therefore often the case that a qualitative assessment precedes a quantitative assessment.

3. HAZARD IDENTIFICATION

Whatever the preliminaries, the time will have come when a risk assessment is called for. Two initial, and related steps, are deciding which hazards are relevant, and specifying precisely which risks need assessing. Hazards are defined as objects or processes with the ability to cause harm. If there is genuinely no hazard, then there is no risk. There are a number of definitions of risk, but a useful one (and that used by the OIE) is that a risk is the probability of an unwanted event occurring, and the magnitude of the consequences if it does occur. A risk assessment is an estimate of that risk. As discussed, some part of this may have been considered in the initial consideration or scoping of the issue. But why are these two steps related? Because the order of action depends, to a certain extent, on the problem to hand. Suppose, for example that the initial risk issue was a worry over the possible adverse public health effects from illegally imported meat. Then the risk question asked (that is the specific risk(s) to be assessed) may already be specified from the scoping exercise as:

> "What are the probable risks to the health of the human population of country X from the illegal importation of meat and meat products?"

If the risk question is framed in this way, then what is the hazard? Perhaps it can be defined as the process of the illegal import of meat and meat products. But this does not move us much further forward. A better definition might be those objects, the microorganisms, toxins, chemicals and parasites which the meat products can carry. This implies a very broad range of hazards –in fact, almost anything which the meat product can transport, internally or externally. In addition, the possible contaminants are likely to vary greatly from one exporting country to another. And humans may not be susceptible to all microorganisms, parasites or toxins which the meat products might be carrying. Clearly, much information must be collected in this case, in order to identify the hazards. In contrast, the risk question asked may be of the form:

> "What are the probable risks of disease in the human population of country X from Campylobacter present in the broiler poultry produced in country X?"

Then the hazard is much more closely defined, being all species of Campylobacter. The source of the hazard is also more closely specified; broilers produced in Country X. This means that hazard identification is a much simpler task. A further variation on the risk question may be:

> "What are the risks to human health from E coli 0157?"

The hazard is defined – but the source is not. The hazard identification now includes an investigation of the possible sources of E Coli 0157. From these examples, it can be seen that hazard identification can vary greatly in its complexity. Acquisition of all this information is a crucial part of the full description of the hazard and is therefore usually incorporated as a part of a hazard identification step. Whatever the terminology system in use, the necessary information certainly needs to be gathered and documented as a part of the risk assessment. To summarise, using pathogens in the food chain as the example, all the information necessary to identify which hazards could be present, what are the possible sources of those hazards, and whether they can have adverse effects on the human population must be identified. This information must be documented clearly and in a logical order, and the information fully referenced.

4. WHICH RISK(S) SHOULD BE ASSESSED?

Where the risk question has not previously been specified in detail, this is the next task. The scoping exercise will have resulted in an identified issue, but this is often of a broad-based nature. In some cases the precise risk question will have been specified, but on many occasions, the detailed specification of the risk to be assessed is reliant upon the completion of the hazard identification process. In any event the risk(s) to be assessed should be subject to review once the hazard identification process is complete. This is an example of the iterative nature of many aspects of risk assessment. As an example, again using the first risk question from above:

> "What are the probable risks to the health of the human population of country X from the illegal importation of meat and meat products?"

As one of the categories of information collected, the hazard identification will have identified the range of pathogens carried by the animal species involved in illegal importation. Many of these pathogens will be

pathogenic for humans, but many more will not be, and this category of information will also have been collected as part of the hazard identification. Therefore it might be decided that for those with no known pathogenicity for humans, they are not considered as hazards, and no further investigation needs to be undertaken. The risk question would then be refined as follows:

> "What are the probable risks to the health of the human population of country X from the illegal importation of meat and meat products, from organisms of known pathogenicity to humans?"

Of course, as well as being part of the hazard identification process, this decision might also be considered as an assessment of the risk (as negligible) from some of the pathogens being carried on or in the illegal meat product imports. Once again, terminology might differ, but principles hold – the decision to include those pathogens in any further investigations, or not, must be made, and the reasons documented. One reason to take the opposite decision and continue to include (some of) them might, of course, be the possibility of mutation to pathogenicity, and an assessment of this probability then becomes a part of the risk estimate.

Even when a preliminary consideration of the risk issue, the scoping exercise, has produced a more tightly specified risk question, the hazard identification process may have introduced the necessity for further consideration of the risk question. An example might be the second risk question illustrated above:

> "What are the probable risks of disease in the human population of country X from Campylobacter present in the broiler poultry produced in country X?"

The hazard identification will have identified a number of different Campylobacter species, some of which have been recorded in both poultry and humans. However, there may be uncertainty about which are pathogenic in humans, and therefore which to include further in the risk assessment. A decision must then be made as to which to include, or whether to include all, perhaps on the assumption that all are equally pathogenic, or simply on the basis that no further information on pathogenicity is available. This is one place where the decision made at this point is, perhaps, simpler for the qualitative risk assessment than the quantitative. For a qualitative risk assessment, it is easy enough to continue to include all Campylobacter species in the total information gathering exercise, documenting appropriate conclusions on differential species risk - which may simply be that no information is available on which to differentiate risks by Campylobacter species. However with a quantitative assessment, this option is not available. A decision as to exactly what numbers to include in the mathematical manipulations is necessary.

Another aspect of the specified risk question which is also somewhat simpler in qualitative risk assessments is that of units. For a quantitative assessment, units must be specified. For example, is it the number of adverse human health effects per year, or per kilogram of meat, or per 100,000 people that we wish to assess? Consistency of units through a mathematical model is crucial. However, with qualitative assessments, although numerical data is collected wherever available, and any data on units should be retained, lack of unit specificity in the risk question is not usually a particular issue. It is often therefore not closely addressed unless and until a quantitative assessment is required.

5. ASSESSING THE RISKS – THE RISK PATHWAY

The risk pathway is essentially an exposure pathway, answering the question:

> "How can this happen?"

For any identified hazard to result in an unwanted event, a series of intermediate events, or steps, are usually necessary. The risk assessment ideally estimates the probability of each of those steps occurring, and thus the overall probability of the whole chain of events occurring. But in order to do this effectively, each of those steps must be identified and ordered logically, in the order in which they must occur. This is crucial to the modelling in a quantitative risk assessment but is also essential, if clarity it to be maintained, in a qualitative risk assessment. This risk pathway must be clearly documented, perhaps as a table, and a diagram is usually a good idea. Information pertaining to each step can then be clearly laid out in the risk assessment report in a logical order. It may be that there is more than one risk pathway whereby an identified hazard can result in a particular unwanted outcome; that is, there may be variability in the system. In this case, each pathway should be described and itemised. There may be uncertainty, that is lack of knowledge, about exactly what steps are in a pathway, or

which is the correct pathway. Again, all possibilities and the information available must be sought and documented.

Food chain risk pathways are generally complex in comparison to other risk pathways commonly found in veterinary and animal health risk assessments. This is because there are usually many steps in the pathway. The typical example is what is sometimes (inaccurately) called a 'farm-to-fork' risk assessment. Here a hazard has been identified as a pathogen carried by a farmed species – and the unwanted outcome is an adverse human health effect. The Campylobacter example above is one such risk assessment. Typical intermediate steps in the pathway therefore include transport from the farm, slaughter, slaughterhouse processes (for example de-feathering, scalding, evisceration, inspection etc.), more transport, processing (perhaps into pies, or minced products), chilling or freezing, retail, storage, cooking, serving and consumption. Another complication on the pathway is the effect of cross-contamination at any point. And since the risk to the human usually depends upon the dose of pathogen ingested which is in turn heavily affected by some of the processes or steps, then it is essential to include those steps in the pathway. Figure 1 is a simplified example of such a pathway, which also includes the unwanted outcome, human illness.

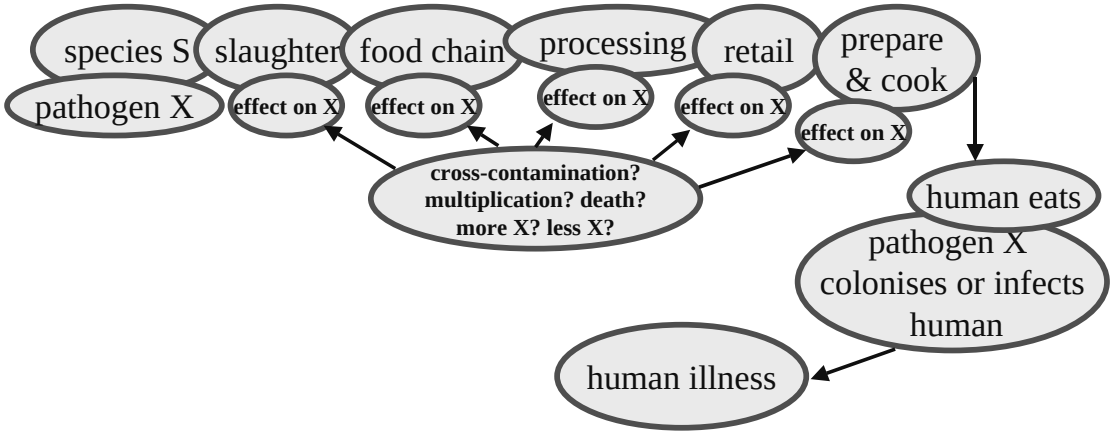

Figure 1. A simplified example of a 'farm-to-fork' risk pathway

Sometimes it is not necessary, or appropriate to go right back to farm level to delineate the risk or exposure pathway. For example, there may not be any information about the farm origin of a specific pathogen, but good information from retail onwards. It may, under such circumstances be appropriate to decide to assess the risks to human health from retailed product only, and the risk pathway would start with product for retail and include perhaps storage, cooking, serving and consumption.

From this description of the risk pathway, it can be seen that it functions as a backbone, or model, for the remainder of the risk assessment. Despite the fact that the risk assessment is not quantitative, it is still appropriate therefore to describe this risk pathway as the model in the risk assessment. Indeed, if a quantitative assessment is subsequently required this pathway, or model, should usually be usable as a basis for the quantitative risk assessment.

6. ASSESSING THE RISK - EXPOSURE DATA

By this stage much data has already been collected, and documented. This includes that on hazard identification, and that to enable the risk pathway to be delineated. Model input data pertaining to the estimation of the probabilities of the hazard passing through each of the steps in the risk pathway, or model, must now be collected. It must then be documented in a logical order following the steps in the risk pathway. For a typical farm-to-fork risk assessment, the starting point is generally the collection of data on the prevalence of the pathogen in the species of interest on the farm.

For two related reasons, food-chain risk assessments dealing with pathogens become yet more complex. The first reason is that microorganisms and parasites can die, and – particularly for microorganisms, they can sometimes

multiply. This means that not only is it necessary to identify the steps in the risk pathway, but also the effect those steps will have on the viability of the pathogen of concern. For example what is the effect of freezing, or pasteurising, or cooking on numbers of viable pathogen. In addition, the probable magnitude of the effect on human health is usually dependent upon the dose – which means, for pathogens, the number of organisms ingested. Therefore it is necessary to be able to estimate the probable amount of pathogen which is present at each step, and whether it can survive the process. In quantitative assessments, the numbers of organisms present at any given step are, ideally, calculated directly from the numbers estimated as being present at the previous step. Except for the on-farm prevalence, direct data on the presence of organisms and their numbers is more generally used to validate the model. However, with qualitative risk assessment, such calculations are by definition not undertaken. The direct data is used instead to provide evidence of the progress of the pathogen through the food chain, and thus the probability of it doing so. Survey prevalence data, for example at retail, therefore provides a very important source of evidence in a qualitative risk assessment of this type. Of course, this information must be considered in conjunction with information on the process concerned, and therefore data on the effect of the processes is essential.

7. ASSESSING THE RISKS – POPULATION EXPOSED

All the food chain examples used all refer to effects upon human health, or disease, as the unwanted outcome. But what effects are possible? And what types of disease might occur? That is, what is the range of possible effects of the hazard, if it does reach the human population? In some systems, this step is called hazard characterisation, in others, consequence assessment.

Given exposure – which for food generally means ingestion, information is necessary for estimating the probable effects. In qualitative assessments, the precise number of organisms ingested is not calculated. Nevertheless information should be collected on the range of effects recorded, and the difference in susceptibility of any sub-groups within the population – that is, any dose-effect information available. In addition, any evidence of differential effects by pathogen strain or sub-type should be collected. This allows an estimation of the type of effect which might be expected to be seen, on an individual basis – important for estimating the overall magnitude of effect. In addition, data on numbers of cases should be collected, as this, in conjunction with the previous information, will assist in the estimate of the probability of identified adverse effects. At this point, consideration should also be given to the possibility that other possible sources of the hazard are causing the effect identified. Further information required includes both data on numbers who consume the food, stratified if possible by age, immunological status etc., and the amount typically consumed. This is used to estimate the overall population effect and risk to the population.

8. DATA RELEVANCY AND QUALITY

It is obvious now that a risk assessment requires the collection of a vast amount of data. It has also been stressed that it must be documented in a logical order, with clarity, and fully referenced. However, there are a number of issues still to consider. Which data do we want, and how do we deal with lack of data, uncertainty, and variability? As with any risk assessment, the data we need is the best currently available data. This of course implies a judgement as to what that data is. A discussion of how to assess data quality is in itself a lengthy subject. However, with a qualitative risk assessment, all relevant data found can, if necessary, be included in the report. Full referencing means that, ideally, the year, source, country, etc. of the data are available, and where relevant should be included in the report. As with any risk assessment, raw data is usually more useful than summarised data, and there is no reason why qualitative risk assessments should not include tables of raw numerical data where appropriate. Therefore, although the assessor may themselves judge some information as less relevant than other information, and may base their (necessarily) subjective risk estimate on that judgement, other readers of the risk assessment report may come to a different conclusion. In this respect, in a qualitative assessment, when subjectivity and judgement have been used in selecting data on which the final risk estimate is based, it is generally more explicit, and therefore more easily identifiable than in a quantitative report. A qualitative assessment and report has similar advantages when the use of expert opinion and assessors' assumptions has been necessary to overcome lack of data. Uncertainty and variability pertaining to the data must both be described, and where the data allows, this should be in numerical terms.

9. ASSESSING THE RISK - ESTIMATING THE PROBABILITY

At this point in the assessment, all data to be used in the risk assessment has been collected, and documented in a clear format and logical order, which is relevant to estimating the risk corresponding to the steps in the risk pathway. For clarity the written evidence is likely to be separated into sections with headings, also corresponding to those steps. It is now only necessary to consider the information available for each step, and make logical deductions from the information available, at any point where that proves possible. These logical deductions will be documented in an appropriate section of the risk assessment report, which is likely either to be at each stage following the information from which the deduction was made, or one section towards the end. Wherever possible, the risk estimate is described in terms which give some indication of its magnitude, for example it maybe assessed as low, high, negligible etc. However, this may not always be possible, where there is great uncertainty and little information – the conclusion may occasionally be that no meaningful evaluation can be made. In particular, it is often difficult to assess the overall probability of an unwanted event from qualitative information on the individual steps in a pathway. The essential feature, in all cases, is that the conclusions documented are logical given the information available. Figure 2 illustrates one possible, simplified format for documenting logical conclusions.

Hazard: Pathogen X **Risk question:** What is the probability of infection with Pathogen X in humans from drinking cows milk produced in Patholand?	
Information available	**Conclusion reached and risk estimate**
Surveys have shown that pathogen X is prevalent in approximately 1% of the cattle in Patholand. No specific data for milking cows is available. If a cow is affected pathogen X can be excreted in the milk. This occurs in approximately 75% of infected cows.	It is possible that Patholand milk is contaminated with Pathogen X. Based on the prevalence and excretion data, the probability of raw milk containing X appears to be low, but certainly not negligible.
Milking cows are tested annually and milk from any positive animal is not allowed into the bulk tank. The bulk tank is tested and any positive samples are excluded from the food chain.	No information is available on the sensitivity of the testing regime, either for the individual animal or the bulk tank. In addition, cross-contamination may occur. These tests will reduce the probability of pathogen X being present, but not eliminate it. Without information on test sensitivity the probability of X being present cannot be assumed as negligible.
Experimental data has shown that pathogen X is very susceptible to high temperatures; sampling has never identified it in pasteurised milk. 98% of Patholand milk is sold pasteurised. The pasteurisation failure rate is recorded as being $1x10^{-6}$%.	Where pasteurisation occurs, the probable post-pasteurisation level of pathogen X in milk is negligible, thus the risk of human exposure is negligible. For milk unpasteurised at retail, there remains a very low, but not negligible risk of exposure.
Humans are very easily infected by pathogen X	The risk of infection from pasteurised milk is negligible. However, although very low, the risk of infection from non-pasteurised milk is not considered negligible.

Figure 2. A simplified example of one possible format for laying out conclusions on risk estimates from qualitative risk assessments

In some cases, although an estimate of the absolute risk might prove difficult, logical conclusions might be that one pathway is likely to be less risky than another, or that a particular process, where incorporated, has always proved lethal. Or, for example, data may show that pasteurisation, if successfully undertaken, is a very effective way of reducing the probable number of many pathogens to undetectable levels. Therefore if, following this step, a survey indicates high levels of contamination in the finished product, cross-contamination might be suspected. If the pathogen can come from a variety of sources, then the pathogen subsequently present may not have come from the food-source under consideration. These kinds of information would be very useful for the risk manager, even if an overall estimate of absolute risk under current conditions is difficult.

10. REPORTING THE RESULTS

In any risk assessment, there is the risk assessment process, and the risk assessment results. In general, the results are presented, along with the data and a description of the method used, in a transparent risk assessment report. In a qualitative risk assessment, the major features which allow an estimate of risks are the gathering and presentation of data in such a way as to allow logical deductions to be made. Thus the risk assessment process is itself largely composed of laying out the data – that is writing a document which is likely to be the major part of the risk assessment report. Precise details of the format will vary, but the diagram above suggests one way in which the conclusions and risk estimates (results) of such a report might be laid out. The essential principle is that it is clear, logical, transparent, and complete, fully referenced and with all assumptions stated.

11. SUMMARY OF STEPS IN A QUALITATIVE RISK ASSESSMENT

Table 1 summarises the steps, and minimum requirements, in a qualitative risk assessment

Table 1. A summary of the steps and minimum requirements of a risk assessment, adapted from a table by Wooldridge (World Trade Organisation, 1998)

Requirement	Explanation
A. A risk assessment must be transparent, that is, it must be clearly presented and fully referenced in the risk assessment report produced.	
B. The hazard or hazards to be addressed must be defined and clearly presented. If a particular hazard has not been specified in the request for a risk assessment, this will require a hazard identification of appropriate breadth.	A decision must be made as to which are the hazards of interest. Hazard may be defined as an object or a process (in which case the process may be similar to the risk pathway).
C. The risk evaluated by the risk assessment must be defined and clearly presented.	This means specifying the 'risk question' to be asked.
D. The potential pathways from the hazards of interest to the outcomes of interest (that is, the sequence of events necessary) must be clarified and clearly presented. Details of any processes incorporated in this pathway (for example, testing for infection, evisceration of carcase, cooking of meat) must be included and details fully referenced where appropriate.	These pathways will be based upon the (mainly biological) requirements which are necessary to arrive at the defined outcomes and are most clearly illustrated as a series of steps in a diagram. Full referencing allows for transparency.
E. For each identified step in the pathway, information (data) must be gathered to evaluate the probability of that step occurring. This data may vary from hazard to hazard, and thus must be hazard-specific where necessary. This information must be clearly presented and the source of this information should be fully referenced.	The information (data) will be either qualitative or quantitative, depending upon the availability of information. Qualitative assessments include quantitative data wherever possible. The assessors should undertake a search which is as thorough as is practicable to find the most appropriate information for the assessment at hand. Full referencing allows for transparency.
F. Making logical deductions from the information collected the probability of the overall pathway of events from hazard to defined outcome actually occurring is evaluated for each defined hazard and outcome, using the information obtained.	Wherever possible this will be given as a probability in qualitative terms (for example, high, low or negligible risk); in addition, there may be other text explaining the logical deductions made.

12. ADVANTAGES AND DISADVANTAGES OF A QUALITATIVE RISK ASSESSMENT

In any risk assessment, it is necessary to identify the hazards, specify the risk question(s), delineate the risk pathway(s), and collect the appropriate data. For a qualitative risk assessment, this is then utilised to deduce logical conclusions, whereas for a quantitative risk assessment it is used as the basis of the construction and manipulation of a mathematical model. It therefore follows that a qualitative risk assessment is likely to be completed more rapidly than a quantitative risk assessment, and require less time, resources and specialist mathematical modelling skills. In addition, the conclusions reached in a qualitative assessment may indicate that a quantitative assessment is not necessary. For example they may be assessed as negligible, or so obviously high that safeguards are essential whatever the precise value. For these reasons, it is therefore frequently considered advantageous to undertake a qualitative risk assessment before deciding whether or not to embark on a quantitative assessment. In addition, numbers can be seductive. The output of a quantitative risk assessment, either as a point value or as a distribution, may be perceived as having spurious scientific precision and accuracy – the uncertainties are frequently discounted, and assumptions ignored. And as has been noted above, even in quantitative assessments, subjective judgements and assessors' assumptions are made, and expert opinion may be utilised. The fact that these subjectivities are generally much more instantly obvious in a qualitative risk assessment is an advantage.

However, qualitative risk assessment estimates presented in a textual form are by definition totally subjective, and the problems associated with this have been outlined in the introduction. In addition, the effect of the individual uncertainties on the risk estimate are harder to ascertain than in a quantitative sensitivity analysis, thus the truly crucial data deficiencies may be less easily identified. In addition, scenario analysis ('what-if' modelling) and the effect of proposed safeguards can both be investigated closely in a quantitative model.

Despite their frequent use to the contrary, neither type of risk assessment stands up particularly well to an adversarial situation, as subjectivity, assumptions, data choices, model and conclusions can always all be challenged. Ideally they should be used as tools providing just one of the types of information necessary to help the risk manager make an informed choice - and the risk manager should always be fully aware of the subjectivity, assumptions and uncertainty involved.

13. REFERENCES

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