

Risk analysis and the importation of animals

In November 1990 sheep descended from animals imported from Denmark and Finland in 1984 were released from quarantine. The first of these Scandinavian-origin sheep were imported as embryos¹ because this method was considered to reduce significantly the risks of introducing unwanted disease along with the new bloodlines.^{2,3} However, the final release of these exotic sheep has provoked, once again, expressions of concern from some farmers' groups who believe that MAF has somehow changed its policies and retreated from a 'no risk' approach to quarantine. Such questioning has also been provoked by recent importations of sheep and goat embryos from Zimbabwe, llamas and alpacas from Chile and sheep embryos from Israel.

MAF does not operate a 'no risk' quarantine policy.² There is only one 'no risk' policy and that is total exclusion of all imports.^{2,4} Such a policy is neither defensible nor desirable.^{2,4} Furthermore, even a total prohibition on importation of animals and animal products would not achieve zero risk because people still travel and, if legal avenues are unavailable, people will find ways to import illegally.

Additionally, in the current global climate of reducing barriers to trade, non-tariff trade barriers are coming under closer scrutiny and a country like ours, which depends so heavily on exporting agricultural products, cannot hope to maintain continued access to important markets while still denying entry to imports from other countries.

Trade in animals and animal products is going to occur. It is the role of quarantine to facilitate this trade whilst, at the same time, assessing systematically the risks associated with imports and reducing those risks to an acceptable level.

When analysing the risks associated with a proposed importation of animal genetic material (be it live animals, embryos or semen) it must be remembered that such imports cannot be made without some element of risk.^{4,5} The benefits of the imports often accrue to a relatively small group of people only, usually the entrepreneurs, initial importers and distributors of the new genetic material.⁵ The risks, on the other hand, are borne by a much broader group which includes all livestock owners whose animals could be infected with an exotic disease agent as well as the general public who could be expected to bear the cost of containing and eradicating an outbreak of exotic disease.^{4,5} For these reasons a risk analysis should, ideally, include a benefits/cost analysis of the proposed importation.

In determining whether or not to allow a proposed import to proceed, MAF must identify the risks involved, attempt

to quantify them and then design a series of safeguards sufficient to reduce the risk to an acceptable level.

Analysis of risk

Risk analysis is a blend of art and science and combines risk identification, risk assessment, risk management and risk communication. Risk identification and risk communication will not be discussed in this article.

Risk, as it relates to the importation of animals or animal products, is a measure of the probability of the introduction of an exotic disease and the seriousness of such an outcome. Risk assessment is the process of estimating, as objectively as possible, the probability that an importation would result in the entry of an exotic disease agent and that local livestock would be exposed to that agent. Risk management is the process by which the risk is reduced.

The first stage in risk analysis is an assessment of the risk entailed by an unrestricted importation of animals or product under consideration. Risk assessment takes into account the prevalence of pathogens in the source population, the probability of pathogens surviving in the animal or product during the process of importation, the probability of the pathogen coming into contact with local livestock after importation and the seriousness of such contact.

Theoretically, each of these factors should be amenable to being quantified in an objective and scientific fashion. In reality, it is seldom possible to quantify them adequately. Much of the assessment ends up being based on guesswork and is thus potentially controversial and open to challenge from either domestic interest groups or overseas trading partners.

Risk management, on the other hand, is usually able to be quantified more objectively. For instance, there should be very little debate over the sensitivity of a particular serological test, or the efficacy of a particular embryo washing regimen for a specific pathogen on embryos of a given species.

Consider for example a serological test having a sensitivity of 0.95 when applied to animals infected with a particular disease agent. The probability, therefore, of missing a single infected individual is thus 0.05.

However, the predictive value of a diagnostic test is also a function of the prevalence of infection in the population under test. The probability that an animal which is negative to a given test is actually infected is calculated as follows⁶:

$$\text{Prob (I | N)} = \frac{p(1-s)}{p(1-s) + (1-p)e} \quad [\text{Equation 1}]$$

where I is infected animals, N is non-reactor animals, p = the true prevalence, e = the specificity of the test and s = the test sensitivity.

In matters of quarantine, the exclusion of "false positive" animals is not usually of major concern, so for the purposes of this discussion let us assume that specificity, e, = 1. With the same test referred to above, where s = 0.95, the probability of a given test-negative animal actually being infected varies with prevalence, p, as illustrated in Table 1.

It can be seen that as the prevalence of infection in the source population increases, the probability of a given test negative animal being infected also increases.

Similarly, at any given prevalence, the probability of including a test-negative infected animal in an importation increases with the number of animals in the group to be imported. Marchevsky and coworkers⁶ have shown that the probability of including even one test-negative infected animal (c) in a group of n animals can be calculated thus;

$$\text{Prob}(c \geq 1 | N) = 1 - \frac{[(1-p)e]^n}{(1-p)e + p(1-s)} \quad [\text{Equation 2}]$$

The effect of increasing the size of the group destined for import is illustrated in Table 2.

With some diseases a policy decision may be made that a positive test result will disqualify only the individual animal which reacted positively to the test. The risks one takes with such a policy are illustrated in the examples just discussed (Tables 1 and 2). However, with some other diseases, it may be decided that a positive test result in any one animal will disqualify the entire group intended for importation. In such cases the probability of disqualifying an infected group increases as prevalence and/or the size of the group increases. Thorburn and her colleagues⁷ proposed that the probability that all animals in an infected flock or herd, size n, will test negative can be calculated thus;

$$\text{Prob}(R=0) = [p(1-s) + (1-p)e]^n \quad [\text{Equation 3}]$$

The difference in risk between the two policies is illustrated in Table 3. It can be seen that where the presence of a single reactor animal disqualifies the entire group destined for export, rather than just the reactor animal itself, the risks of an infected animal being imported are significantly reduced.

However, although logic dictates that the policy of disqualifying the whole group, if even one reactor occurs, is a lower risk policy than when only reactors are disqualified, the equations used above are not actually calculating the same thing and so are not strictly comparable. Equation 2 calculates the probability that one or more infected test-negative animals will be included in the group while equation 3 calculates the probability that no reactors will occur. These are not the same thing. One expects reactors will

occur in an infected group, even if a test has a relatively low sensitivity.

Because the different equations calculate the probabilities of different events, comparisons of the type made in Table 3 will not maintain the same relationship over a wider range of values for group size n. With the same values for prevalence, sensitivity and specificity the relative magnitude of the probabilities does not hold below a group size of around 250.

Whether a positive result to any one test disqualifies only the affected individual or the whole importation, the risks of importing unwanted disease can be further reduced by imposing a series of safeguards. When a series of safeguards is applied to an importation it may be relatively easy to quantify the amount by which the risk is reduced, even if consensus on the magnitude of the initial, unrestricted risk cannot be attained.

At this point it is appropriate to look at some examples of risk management.

Reducing the risk of scrapie

Apart from cases in imported sheep in 1952-54 and 1976-77, New Zealand has remained free of scrapie.⁸ Apart from some importations from Australia, also scrapie free, the release from quarantine of Scandinavian-origin sheep in late 1990 was the first infusion of new genetic material into the New Zealand sheep population in over 40 years.

Table 1: Probability that a test-negative animal is actually infected, given a test sensitivity 0.95 and specificity 1

Prevalence	Probability (I N)
0.01	5.05 X 10 ⁻⁴
0.05	2.62 X 10 ⁻³
0.1	5.52 X 10 ⁻³
0.2	1.23 X 10 ⁻²

Table 2: Probability that a test-negative, infected animal will be included in a group destined for import when only reactor animals are excluded (prevalence = 0.01, sensitivity = 0.95, specificity = 1)

n	Probability (c ≥ 1 N)
10	5.04 x 10 ⁻³
20	1.00 x 10 ⁻²
30	1.50 x 10 ⁻²
50	2.49 x 10 ⁻²
100	4.92 x 10 ⁻²
500	2.23 x 10 ⁻¹

Table 3: Probability that a test-negative infected animal will be included in a group destined for import (prevalence = 0.01, sensitivity = 0.95, specificity = 1)

n	If reactor animal only excluded Prob (c ≥ 1 N)	If a single reactor disqualifies group Prob (R=0)
300	1.41 x 10 ⁻¹	5.71 x 10 ⁻²
400	1.83 x 10 ⁻¹	2.20 x 10 ⁻²
500	2.23 x 10 ⁻¹	8.45 x 10 ⁻³

The Scandinavian imports were from countries free of scrapie (Denmark and Finland). However, interest has been expressed in importing bloodlines from countries where scrapie is present. What follows is an outline of a chain of risk-reducing safeguards which could be imposed to permit the importation of sheep genetic material while still safeguarding New Zealand's scrapie-free status.

Let us assume, at least at this stage, that the initial risk, P(I), is unknown, = X.

The first safeguard (SG₁) is a requirement that all donors be over 5 years of age. We know that at least 70% of scrapied sheep exhibit disease before 5 years of age^{9,10,11}, so SG₁ reduces the risk to 30% of the original level. That is;

$$P(I | \text{importing sheep} > 5 \text{ years of age}) = 0.3X.$$

The second safeguard (SG₂) is embryo transfer. Studies in the United States have indicated that scrapie is unlikely to be transmitted by embryo transfer.¹² By February 1989, 29 sheep, born from ewes implanted with embryos collected from scrapied donors, were still alive and scrapie-free after more than 60 months (W C Foote, pers. comm.). A worst-case interpretation of this result suggests that we can be 95% confident that embryo transfer from scrapied donors will not transmit the disease in more than 12% of transfers.¹³ This means that SG₂ (embryo transfer) = 0.12. So;

$$P(I | \text{importing embryos} \cap \text{donors} > 5 \text{ years of age}) = 0.036X.$$

[A simplification has been made in the calculations at this point. It is usual that each donor produces a number of embryos, several of which may develop into lambs. Should a donor be infected with scrapie, the likelihood of her passing the disease on increases with an increase in number of offspring. However, the more infected offspring that are born in quarantine, the greater the probability of at least one exhibiting signs of scrapie before the termination of quarantine.]

The third safeguard (SG₃) is a bioassay using goats inoculated intracerebrally and intraperitoneally with a homogenate of lymph nodes, spleen and brain tissue collected from the embryo donor animals. Studies with Suffolk sheep have demonstrated that scrapie agent is likely to be present in a pool of these tissues from most, if not all, cases of preclinical scrapie.¹⁴ Other experiments have demonstrated that most, if not all, goats inoculated with such a pool by the intracerebral and intraperitoneal routes will develop clinical scrapie within a 30 month period.^{15,16} On the basis of these published studies and personal communication with workers overseas, we believe that goat bioassay can be expected to detect 80% of preclinical scrapie cases. This means that SG₃ = 0.2, resulting in;

$$P(I | \text{importing embryos} \cap \text{donors} > 5 \text{ years of age} \cap \text{donors are bioassay negative}) = 0.0072X.$$

Holding the group of embryo-derived sheep in quarantine until all are older than 5 years would result in a further 70% reduction in risk. That is, $SG_4 = 0.3$ and;

$P(I | \text{importing embryos} \cap \text{donors} > 5 \text{ years of age} \cap \text{donors are bioassay negative} \cap \text{offspring} > 5 \text{ years of age}) = 0.0022X$.

If the initial risk X is the same as the prevalence, P , in the flock of origin, then this chain of safeguards has reduced the risk to $0.0022P$. That is, if the prevalence in the flock of origin was, say, 20%, the risk of any individual having scrapie after satisfying these quarantine safeguards would be less than 1 in 2,000. However, even this figure overstates the risk because the detection of even a single case of scrapie at any stage of this chain of safeguards would result in the termination of the entire importation.

Reducing the risk of maedi visna

Maedi visna, or ovine progressive pneumonia (OPP), is a retrovirus infection of sheep which is present in many, if not most, of the countries from which sheep might be imported.

The major route by which maedi visna spreads is through the milk of the dam to her lamb. The virus is almost entirely cell associated in lymphocytes and spread between adult sheep is uncommon. Spread by respiratory droplets may occur however, especially under conditions of close confinement. Other, concurrent, respiratory disease may facilitate the spread of maedi by aerosol. *In utero* infection may occur, but is considered rare.¹⁷

In common with other retrovirus infections, maedi visna has a prolonged period between infection and seroconversion. Seroconversion may take many months.¹⁷ However, the serological tests available have relatively good sensitivity and are reasonably reliable in animals over twelve months of age (D J Houwers, R E Oliver, pers. comm.). It is likely that up to 5% of infected sheep fail to seroconvert.

Studies on the transmission of maedi visna virus by embryo transfer have not yet been published. However, a very small study with the closely-related virus of caprine arthritis encephalitis (CAE) failed to demonstrate transmission of infection.¹⁸ A large number of studies have shown that enzootic bovine leucosis (EBL) virus is not transmitted along with embryo transfers¹⁹ and, as the maedi visna

virus and EBL virus are both almost entirely cell-associated, it is valid to assume that the risk of transmitting maedi visna virus is similarly remote.

As in the scrapie example, we shall assume that the initial risk, $P(I)$, is unknown. That is, $= X$.

The first safeguard is a serological test (ELISA) for evidence of maedi visna infection in the donor ewe. The probability that this test will detect infection in animals over 12 months of age is taken as 0.95, so $SG_1 = 0.05$ and;

$P(I | \text{donor ELISA negative}) = 0.05X$.

The second safeguard is embryo transfer. By analogy with enzootic bovine leucosis (see above), for which over 2,000 embryo transfers from infected donors have been made without transmitting infection¹⁹, we can be 95% confident that embryo transfers will not transmit the disease in more than 0.4% of transfers.¹³ That is, $SG_2 = 0.004$ and;

$P(I | \text{importing embryos} \cap \text{donor ELISA negative}) = 0.0002X$.

The third safeguard against introducing maedi visna would be to hold the lambs produced from the embryo transfers in quarantine and test them serologically when they are more than two years old. The probability of infected sheep seroconverting in two years is greater than 0.9. That is, $SG_3 = 0.1$ and;

$P(I | \text{importing embryos} \cap \text{donor ELISA negative} \cap \text{offspring ELISA negative at 2 years of age}) = 0.00002X$.

It can be seen that even if the prevalence of maedi visna is high in the donor flock, the risks of introducing the disease are very slight. With these safeguards, the risk of introducing maedi visna would be around 1 in 100,000 sheep, even if 50% of the donor flock were infected.

'Acceptable' risk

Even in situations where the risk from unrestricted entry can be quantified objectively, and little controversy surrounds the calculation of the extent to which safeguards reduce that risk, it may be difficult to attain agreement on what constitutes an *acceptable* risk. What is an acceptable business risk to the entrepreneur

may be quite unacceptable to the representatives of the established livestock industries. Table 4 lists some commonplace risks of human fatality.²⁰ It can be seen that people routinely take risks with their own lives and these risks are of a similar order of magnitude to those just estimated for the introduction into New Zealand of two exotic diseases.

To conclude, I offer the following parable.²¹

"The young man could open either of two doors. If he opened the one, there would emerge a hungry tiger, the fiercest that could be procured, which would immediately tear him to pieces. But if he opened the other door, a beautiful lady would come forth, a lady ideally suited to the young man's years and station.

"So, which door should the young man open? The first man refused to take the chance. He lived safe and died chaste.

"The second man hired risk assessment consultants. He collected all available data on lady and tiger populations. He brought in sophisticated technology to listen for growling and detect the faintest whiff of perfume. He completed check-lists. He developed a utility function and assessed his risk averseness. Finally, sensing that in a few more years he would be in no condition to enjoy the lady anyway, he opened the optimal door. And was eaten by a low probability tiger.

"The third man took a course in tiger taming. He opened a door at random and was eaten by the lady."

The moral of the story is this: "Those who seek a risk free society have little interest in quantification of the level of risk. Available technology may correctly assess the probability of a hazard but it cannot provide certainty for decision makers. Most important of all is the difficulty of perceiving all possible risks."

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Table 4: Some commonplace risks of human fatality (adapted from Wilson and Crouch, 1987²⁰)

	mean annual risk	
Motor vehicle accident (total)	2.4×10^{-4}	(2.4 in 10,000)
Motor vehicle accident (pedestrian only)	4.2×10^{-5}	(4.2 in 100,000)
Home accidents	1.1×10^{-4}	(1.1 in 10,000)
Electrocution	5.3×10^{-6}	(5.3 in 1,000,000)
Cigarette smoking (one pack per day)	3.6×10^{-3}	(3.6 in 1,000)
Peanut butter (four tablespoons per day)	8×10^{-6}	(8 in 1,000,000)
Alcohol (light drinker)	2×10^{-5}	(2 in 100,000)
Mountaineering	6×10^{-4}	(6 in 10,000)

To report a suspected exotic disease to MAF:

During business hours, ring local MAF office.

If no reply, after hours, weekends or public holidays,

Free Phone (0800) 809-966

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