

Limitations, definitions, principles and methods of risk analysis

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Summary: *Decisions on veterinary biologicals involve large uncertainties, complexities which cut across many scientific and technical disciplines, and large potential adverse impacts on public health and on important sectors of the economy. How should risk assessment help to guide the decision process on veterinary biologicals? How can risk assessment practices be harmonized internationally, given the different regulatory traditions and institutions of different countries? A broad view of risk assessment is needed, that risk assessment is a framework for summarizing applicable scientific judgement in support of regulatory decision-making. Support for this view of risk assessment is found in the major reports which have defined risk assessment as currently practised by many regulatory agencies in the United States of America (USA). However, some interested and affected parties perceive risk assessment in the USA as overly quantitative and narrowly focused on regulatory standards for carcinogens. An example of risk assessment for microbial contamination indicates how quantitative methods can be used when data are sparse and decisions must be made in the face of great uncertainty. Such quantitative methods can be used to improve communication about risk, to promote consensus in support of controversial decisions, and to identify valuable opportunities for research to reduce the important sources of uncertainty.*

KEYWORDS: Assessment of judgemental probabilities – Decision analysis – Planetary quarantine – Risk assessment – Risk management – Uncertainty – Viking Mission to Mars.

INTRODUCTION

The papers presented at this Symposium and those contained in Volume 12 (4), December 1993, of the *Scientific and Technical Review* of the Office International des Epizooties (OIE) devoted to 'Risk analysis, animal health and trade', indicate that the community working to harmonize the regulation of veterinary biologicals has already acquired a sophisticated knowledge of risk assessment. Consequently, this introduction to the subject is brief, and definitions used for the main concepts are those already in the literature, in particular those given by S.C. MacDiarmid (7) in the above-mentioned issue of the OIE *Scientific and Technical Review*. No attempt is made here to reconcile the definitions proposed by MacDiarmid with those of other authors in this issue, but rather they are taken as a point of departure.

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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 analysis** is a blend of art and science, and comprises **risk identification**, **risk assessment**, **risk management** and **risk communication**.

Risk may be defined more broadly as the probability of occurrence of an adverse outcome and the severity of the consequences if the outcome does occur.

MacDiarmid (7) notes that risk analysis must begin with risk identification. The potential adverse outcomes must be listed at the outset of the risk analysis process, and it is a good idea to include the marginal entries on the list. If adverse outcomes (e.g. diseases caused by specific pathogens) do not appear on the list, then the risk analysis could omit aspects of great importance for regulatory decision-making. If some adverse outcomes have such low probabilities or mild consequences that they are clearly not important, then they can be dropped from the analysis. But initially it is better to be inclusive, to err on the side of caution, and to try to anticipate unpleasant surprises. Not all the possible surprises can be anticipated; some adverse outcomes (e.g. disease outbreaks) may be essentially impossible to foresee. But in an uncertain world the best way to avoid adverse outcomes is to make good decisions, i.e. decisions based on what is known – including judgements about uncertainties – and careful consideration of what can be done, what is desirable, and what it is desirable to avoid.

Risk analysis should therefore be comprehensive, but it must remain feasible given the available time and resources. It must be directed towards assisting those responsible for making decisions to do so in a way which is consistent with scientific principles, legal requirements and public values. Clearly, these criteria are not satisfied if potentially significant diseases are omitted from the analysis. But how far does one go in carrying out a risk analysis? The answer is to go far enough to provide the decision-maker with as much assistance as possible, in the time and with the resources available. To accomplish this goal, risk analysis requires skillful judgement as well as scientific rigour.

As MacDiarmid states, it is important to distinguish between risk assessment, risk management and risk communication. Risk analysis comprises all three of these elements:

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 the agent. Risk assessment ought to examine the **effect** of the introduction of an exotic disease. However, very few studies of this nature have been performed anywhere.

Risk management is the process of identifying and implementing measures which can be applied to reduce risk to an acceptable level and documenting the final import decision.

Risk communication is the process by which the results of risk assessment and risk management are communicated to decision-makers and the public. Adequate risk communication is essential in explaining official policies to stakeholders (such as established livestock industry groups), who are often aware of the risks but not the benefits of importations. Risk communication must also be a two-way process, with the concerns of stakeholders being heard by officials and addressed adequately.

Risk assessment and risk management are discussed in greater detail below.

Risk assessment is the process of summarizing a scientific analysis of a particular risk: What are the probability and the severity of the adverse outcome? Full use should be made of the objective data available, in estimating the probability of a disease outbreak. In many situations, however, such data do not exist – usually due to a lack of experience or knowledge (e.g. about key steps in the process by which a pathogen might be released from a host or carrier and transferred to a local livestock population). In such situations, decision-makers must rely on judgement in the absence of data. The most knowledgeable scientific experts should then be called upon to make assessments of the probability of a disease outbreak, as the best basis for a decision.

When faced with complex uncertainties, scientists may be reluctant to express a judgement which may be used as input to a potentially controversial decision. Scientists are often taught that probabilities should reflect frequencies in observed data, and they may be reluctant to give their judgement in the form of a probability. Assessment of judgemental probabilities is often best accomplished by conducting the probability assessment through a series of steps, as illustrated in the example presented below (see 'Example of Risk Analysis').

It is also often useful to distinguish degrees of severity in the consequences of an adverse event. In the case of an exotic animal disease outbreak, it may be very difficult to predict how far an epidemic may spread once the disease is introduced. In the example below, the adverse outcome is considered to be one replication of the life cycle of the pathogen in its new home. If the pathogen can replicate once, its progeny are likely to repeat the cycle many more times.

Risk management is usually the responsibility of administrators, often in government but sometimes in the private sector, in response to regulations established by national or international authorities. Risk managers must consider not only scientific factors, but also the legal requirements that define admissible alternatives, and they must examine not only the potential consequences of their decisions for animal health, but also the economic, political and social consequences of their decisions. In many ways, therefore, risk management is also an art based on judgement, rather than a formula to be applied (as might be the case in engineering situations, for example, where the scientific basis of the risks involved is well understood in quantitative terms).

Decisions are usually delegated from a higher authority and, at least for most of the nations represented at this Symposium, the highest authority is ultimately the electorate, i.e. the general public. Public understanding of and support for the decision-making process are critical, especially in situations where the potential adverse outcome has serious health or economic consequences on a regional or national scale. In the face of conflict and controversy, decision-makers must be able to demonstrate that they are making good decisions. In most situations, such a demonstration requires in-depth, two-way risk communication about the assumptions and findings of the risk assessment and the choice of risk management strategy. Stakeholders may be interested in the details of the risk analysis, as well as the overall results. Often the analysis process leads to important insights motivating the choice of a risk management alternative. When stakeholders understand these insights, they are better able to understand why the decision taken was a good one – even if it may involve some additional cost or risk to their interests.

EXAMPLE OF RISK ANALYSIS: POTENTIAL MICROBIAL CONTAMINATION OF MARS BY AN UNMANNED LANDING

In the early 1970s, both the United States of America (USA) and the Soviet Union were initiating a programme of planetary exploration within their space programmes. A particularly important destination was the planet Mars, which was thought to have the best chance of any of the planets in the solar system of having indigenous life. After photographs from a fly-by mission showed what looked like ancient river beds on the surface of the planet, leading scientists in the USA questioned whether plans of the National Aeronautics and Space Administration (NASA) to land a spacecraft on Mars might pose unacceptable risks of introducing microbes from Earth, which could proliferate in the Martian environment. The USA and the Soviet Union agreed that both nations would carry out their programmes so that the risk of a microbe replicating on Mars was less than $1/1,000$ (10^{-3}) during the period of unmanned exploration. NASA decided that meeting this agreement required maintaining the risk for the first mission, Project Viking, at less than $1/10,000$ (10^{-4}). The planned landing of Viking on the date for the Bicentennial of American Independence, 4 July 1976, together with the large cost of the mission, made this a highly visible goal of the NASA space programme. But NASA had established a Planetary Quarantine Officer, whose job it was to veto the mission if the risk was above the agreed limit. On the recommendation of several of the scientists on the NASA advisory board, the author was asked to carry out a risk assessment to assess the probability of microbial contamination of Mars from the first Viking Mission. This assignment was completed with the assistance of two very able colleagues (4, 15). The Planetary Quarantine Officer certified that the risk was under the agreed limit, and Viking successfully landed on Mars in the summer of 1976.

Given the scant knowledge available about Mars in the early 1970s, such a probability was difficult to assess. Actually, NASA had already performed such an assessment, but there were doubts about whether the assessment was reasonable. The task of the analysts included not only conducting the assessment, but also communicating with the scientists who had raised these doubts, in order to promote consensus that the 10^{-4} risk limit was not being violated.

Preliminary investigations indicated that the Viking Lander contained an estimated 20,000 microbes which were viable, in the sense that they could reproduce in a suitable micro-environment. This knowledge of the microbial load on the spacecraft constituted relatively hard, objective data. Most of the microbes were in the form of spores encased in the plastic which was used to ensure that the solid state electronics on board were resistant to damage from vibration during the launch. The scientists believed that it was relatively likely that Mars might have micro-environments, containing water and nutrients, which might allow some kinds of terrestrial microbes to reproduce. Such microbes would have to be capable of reproducing in the absence of oxygen (i.e. facultatively anaerobic) and under conditions of extreme cold (i.e. facultatively psychrophilic).

The main innovation of the approach adopted was a technique now widely used in risk assessment: to assess probabilities of initiating events, and then assess probabilities conditional on the initiating event for subsequent events leading to the adverse outcome of concern. Probabilities on alternative scenarios for the mission were defined and assessed, followed by the assessment of probabilities for the survival and reproduction of the microbes (conditional on the outcome for the mission, the location

of the microbe on the spacecraft, and the way in which the microbe was released from the spacecraft into the Martian environment). The possibility that the life-detection experiment on board Viking might become contaminated was also considered, as this could have led to reproduction of microbes on the spacecraft and the release of a much larger population on Mars.

A diagram illustrating the risk assessment approach is shown in Figure 1. The first box (on the far left) describes the processes for sterilization of the spacecraft and recontamination, including contamination of the bio-experiment for life detection. The five arrows leading from this box describe the estimated numbers of microbes in four categories of location on the spacecraft, plus the probability of bio-experiment contamination and the population of microbes which would be released if the experiment were contaminated. The second box describes the possible outcomes for the mission: failures leading to a hard crash-landing, or the planned soft landing of the spacecraft on three pads which would be in contact with the Martian soil. For each scenario, estimates were made of the expected number of viable terrestrial organisms (VTOs) released in one of three ways:

- a) direct implantation in the soil (from the bottom of a pad or a piece of broken-up spacecraft ploughing into the Martian soil in a crash-landing)
- b) release from a surface due to vibration
- c) release of microbes encapsulated in plastic, or from interior surfaces, as a result of erosion of the spacecraft by Martian dust storms.

The third box describes the transport processes through which a microbe released by vibration or erosion might be carried a considerable distance through the Martian atmosphere to a point where a potentially hospitable micro-environment might exist. The final box describes the assessment of whether a microbe that reached such a micro-environment would find the necessary nutrients and would be of a type that could reproduce at low temperature and without oxygen.

The overall assessment of the probability of a microbe reproducing on Mars was therefore built up from approximately twenty inputs describing microbial burden by location, and probabilities assigned to mission outcomes and Martian environmental conditions. The scientists who co-operated in the risk analysis found it relatively easy to understand both the structure of the analysis and how their judgements would be used. When a complete set of inputs was assembled, the assessment was reviewed together with these scientists. The nominal results are shown on the arrows in Figure 2. Extensive sensitivity analysis was made to determine how changes in the inputs, singly and in combination, would lead to changes in the computed probability of contamination.

The pattern of the numerical results suggested a reason why the calculated risk was more than one order of magnitude below the limit of 10^{-4} . Most of the viably-released organisms resulted from erosion. In the thin Martian atmosphere, only very small particles can remain suspended for long enough to be transported a significant distance away from the spacecraft. Such small particles would not provide sufficient shielding to protect the microbes from the high flux of ultraviolet (UV) radiation from the sun, which easily penetrates the thin Martian atmosphere. It was therefore highly likely that UV radiation would sterilize any microbe-bearing particles in the atmosphere, except those particles so heavy that they fell to the surface near the spacecraft. Scientists did not need to go through the details of the calculations to understand this reasoning.

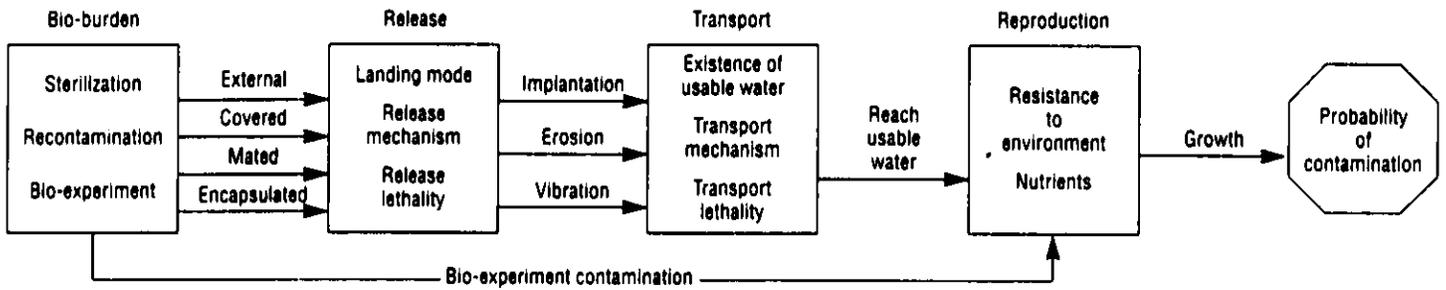


FIG. 1

Risk assessment for microbial contamination of Mars by the Viking Mission: assessment framework (15)
 Arrows represent transfer of viable terrestrial organisms

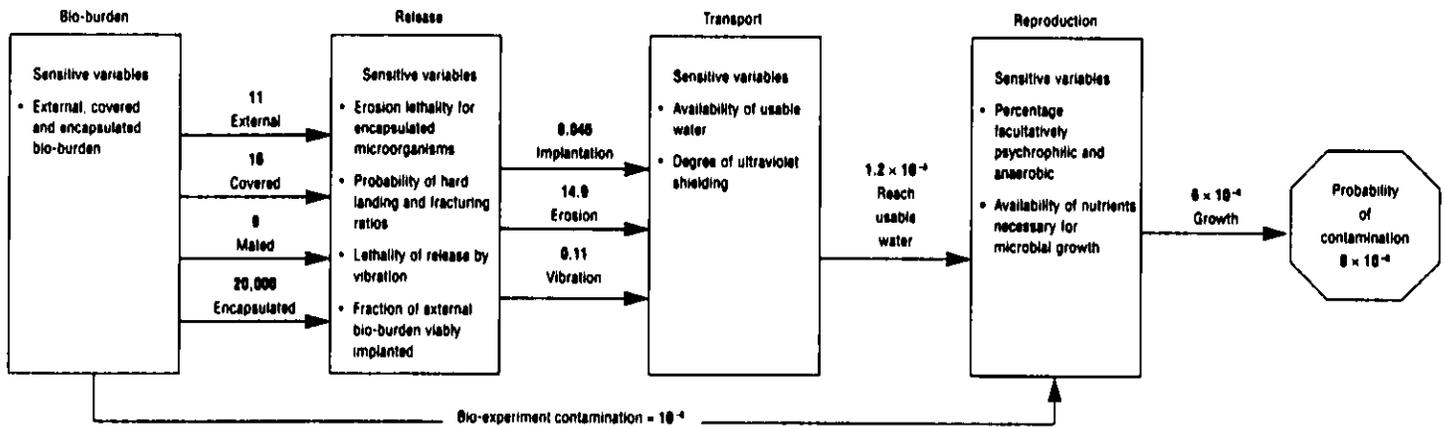


FIG. 2

Framework for risk assessment for microbial contamination of Mars, with nominal results (15)
 Numbers indicate the expected numbers of viable terrestrial organisms

Within a short time, the scientists who had expressed concern about the risk of contamination agreed that the objective of holding the risk for the first Viking Mission below 10^{-4} had been met, and that the Mission should proceed without the need for further steps to reduce the microbial burden on the Viking Lander.

This example contains a number of lessons for future applications of risk analysis in the field of veterinary biologicals. First, use should be made of the objective scientific information available. Subjective expert judgement should complete the analysis, if necessary, and a clear description should be given of what has been done and how. Extensive sensitivity analysis should be performed. With luck, the result may show either that the proposed programme for importing animals or animal products has an acceptably low risk, or that the risk is unacceptably high. If the risk is near the borderline of acceptability, the analysis might help to identify the most important input factors. Insights on which factors are most important may lead to modified proposals with reduced risk, or research opportunities to reduce important uncertainties before the risk management decision is taken to approve or deny the proposed import programme.

Risk analysis is best used to develop insights, and not to develop numerical results which might mistakenly be considered to be highly precise. The discipline of numerical calculation can help to sharpen thinking about risks involving high levels of complexity and uncertainty, and thereby enable conclusions to be drawn which could not have been reached solely on the basis of qualitative reasoning. Risk assessment provides powerful tools for reasoning, but the numerical results can easily be misinterpreted both by decision-makers and by stakeholders among the public. The discussion and recommendations from this Symposium recognize these limits on the proper ways to conduct and interpret risk assessments.

SOME CONCLUDING COMMENTS REGARDING EXPERIENCE WITH RISK ANALYSIS ON ENVIRONMENTAL ISSUES IN THE UNITED STATES OF AMERICA

Much of the author's thinking on risk analysis derives from training in the analysis of decisions in the face of uncertainty. While this field owes much to scientists, philosophers, and statisticians from Europe (2, 6, 17), techniques and practical experience in dealing quantitatively with uncertainty have evolved considerably within the USA over the past thirty years (1, 3, 5, 8, 16, 19, 22).

Since being founded nearly twenty years ago, the Society for Risk Analysis has provided a professional forum for engineers, health scientists, and social scientists interested in risk (13). The society now has approximately two thousand members. While the majority of these members are in the USA, flourishing sections hold annual meetings in Europe and Japan, and a scattering of active members work in many other countries. It is hoped that there will be increasing interaction between the Society for Risk Analysis, and its membership, and the animal health/veterinary biologicals community. There is much to learn from such co-operation.

For the past twenty years, the author has been involved in decisions and risk analysis relating to the regulation of toxic chemicals and similar threats to public health and the environment, participating in a number of studies and initiatives in this area by the

National Academy of Sciences and the Science Advisory Board of the United States Environmental Protection Agency, and observing others at close range (9, 10, 11, 12, 20, 21). There are strengths and weaknesses in these experiences, and in the USA there is an ongoing debate on how best to use risk assessment in support of risk management decision-making. Some parties in this debate view risk assessment in the USA as overly quantitative and narrowly focused on regulatory standards for carcinogens, and there is much merit in some of these criticisms (14, 18). Others seem to look to risk assessment for numerical estimates of benefits from regulation, on problems where assessment of health and environmental impacts is plagued with complex uncertainties and value judgements. My own view is that we must be humble and realistic. Risk analysis provides a useful tool kit for dealing with uncertainty and complexity, but it does not make difficult problems simple, especially where societal values are involved. For the foreseeable future, risk analysis is going to be as much an art as a science. Skilled practitioners will not be plentiful, especially in accomplishing effective two-way risk communication.

It is my hope that, in a world which increasingly resembles an interdependent and electronically-linked 'global village,' we will continue to share our experiences through publications, professional meetings and symposia, and through ongoing dialogue with professional colleagues. In this fashion, we will learn much from each other as we try to improve our processes for making difficult and controversial decisions about environmental and health risks, including risk management for veterinary biologicals.

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LIMITES, DÉFINITIONS, PRINCIPES ET MÉTHODES DE L'ANALYSE DES RISQUES. - D.W. North.

Résumé : Les décisions relatives aux produits biologiques à usage vétérinaire se heurtent à d'importantes incertitudes et à la complexité des disciplines scientifiques et techniques auxquelles elles font appel. Elles peuvent, en outre, avoir de sérieux effets secondaires sur la santé publique et sur des secteurs clés de l'économie. En quoi l'analyse des risques peut-elle faciliter le processus de décision dans le domaine des produits biologiques à usage vétérinaire ? Comment harmoniser au plan international les pratiques dans ce domaine, étant donné la diversité des traditions et des institutions de réglementation dans les différents pays ? Il faut une vision d'ensemble de l'analyse des risques qui permette à celle-ci de constituer un cadre résumant les opinions scientifiques sur lesquelles se fondent les décisions des autorités chargées de la réglementation. Telle est la conclusion des principaux rapports définissant l'analyse des risques que pratiquent actuellement de nombreux organismes de réglementation aux États-Unis d'Amérique. Certaines parties intéressées considèrent, néanmoins, que les États-Unis mettent trop l'accent sur l'évaluation quantitative et limitent l'analyse au cadre étroit des normes applicables aux substances cancérigènes. Un exemple d'analyse des risques appliquée à la contamination microbienne montre comment recourir aux méthodes quantitatives lorsque les données sont rares et que les décisions doivent être prises alors que les incertitudes demeurent importantes. Ces méthodes peuvent permettre d'améliorer la communication des résultats, de promouvoir un consensus sur des décisions controversées et d'ouvrir d'intéressantes voies de recherche pour réduire les sources d'incertitude les plus importantes.

MOTS-CLÉS : Analyse des décisions - Evaluation des probabilités - Evaluation des risques - Expédition « Viking » sur Mars - Gestion des risques - Incertitude - Quarantaine planétaire.

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LIMITACIONES, DEFINICIONES, PRINCIPIOS Y MÉTODOS DEL ANÁLISIS DE RIESGOS. - D.W. North.

Resumen: Las decisiones relativas a los productos biológicos de uso veterinario entrañan grandes incertidumbres, complejas cuestiones en las que están implicadas numerosas disciplinas científicas y técnicas, e impactos negativos potenciales sobre la salud pública y sobre importantes sectores de la economía. ¿Cómo debería la evaluación de riesgos contribuir al proceso de toma de decisiones sobre los productos biológicos de uso veterinario? ¿De qué manera, dadas las distintas tradiciones e instituciones reguladoras existentes en los diversos países, pueden armonizarse las prácticas de evaluación de riesgos a nivel internacional? Es necesario adoptar una visión amplia de la evaluación de riesgos, contemplarla como un marco para la elaboración de criterios científicos aplicables que faciliten la toma de decisiones por parte del regulador. Esta idea viene avalada por los importantes informes a partir de los cuales se ha definido la evaluación de riesgos tal y como ésta se practica actualmente en numerosas instituciones reguladoras de los Estados Unidos de América. No obstante, algunas de las partes interesadas y afectadas perciben la evaluación de riesgos en Estados Unidos como excesivamente cuantitativa y centrada de modo demasiado exclusivo en las normas reguladoras sobre carcinógenos. Un ejemplo de evaluación de riesgos aplicada a la contaminación microbiana explica cómo emplear los métodos cuantitativos cuando los datos disponibles son escasos y deben tomarse decisiones en circunstancias de gran incertidumbre. Los métodos cuantitativos de este tipo pueden emplearse para mejorar la comunicación sobre los riesgos, para promover el consenso en apoyo de decisiones controvertidas y para identificar aquellas coyunturas favorables para la reducción, a través de la investigación, de las importantes fuentes de incertidumbre.

PALABRAS CLAVE: Análisis de decisiones - Cuarentena planetaria - Evaluación de probabilidades - Evaluación de riesgos - Expedición «Viking» a Marte - Incertidumbre - Manejo de los riesgos.

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