ANALYSIS OF THE CREDIBILITY OF SOUTH AFRICAN RISK GOVERNANCE OF GENETICALLY MODIFIED ORGANISMS AND PESTICIDES

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DECLARATION

I declare that this thesis entitled,

ANALYSIS OF THE CREDIBILITY OF SOUTH AFRICAN RISK GOVERNANCE OF GENETICALLY MODIFIED ORGANISMS AND PESTICIDES

is my own original work, and has never been submitted for any academic award to any other institution of higher learning.

June 2013

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FW Jansen van Rijssen **Date**

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PAPERS PREPARED FROM THIS THESIS

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LIST OF ABREVIATIONS AND ACRONYMS

AC	GMO ADVISORY COMMITTEE
ABS	AFRICAN BIOFORTIFIED SORGHUM
ARC	AGRICULTURAL RESEARCH COUNCIL
AVPMA	AUSTRALIAN PESTICIDE AND VETERINARY MEDICINES AUTHORITY
AVCASA	AGRICULTURAL AND VETERINARY CHEMICALS ASSOCIATION OF SOUTH AFRICA
BCH	BIOSAFETY CLEARING HOUSE
BSE	BOVINE SPONGIFORM ENCEPHALITIS
CAC	CODEX ALIMENTARIUS COMMISSION
CAIA	CHEMICAL AND ALLIED INDUSTRIES ASSOCIATION
CBUI	CONFIDENTIAL BUSINESS INFORMATION
CEC	COMMITTEE OF THE EUROPEAN COMMUNITIES
CEMAC	CENTRAL AFRICAN ECONOMIC AND MONETARY COMMUNITY
CG	CYANOGENIC GLYCOSIDE
COMESA	COMMON MARKET FOR EASTERN AND SOUTHERN AFRICA
COMEST	WORLD COMMISSION ON THE ETHICS OF SCIENTIFIC KNOWLEDGE AND TECHNOLOGY
CONABIA	NATIONAL ADVISORY COMMISSION ON AGRICULTURAL BIOTECHNOLOGY
CPAC	INTER-STATE PESTICIDES COMMITTEE OF CENTRAL AFRICA
CPB	CONVENTION ON BIOLOGICAL DIVERSITY
CSIR	SOUTH AFRICAN COUNCIL FOR SCIENTIFIC AND INDUSTRIAL RESEARCH
DAFF	DEPARTMENT OF AGRICULTURE, FISHERIES AND FORESTRY

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DEA	DEPARTMENT OF ENVIRONMENTAL AFFAIRS
DOH	DEPARTMENT OF HEALTH
DST	DEPARTMENT OF SCIENCE AND TECHNOLOGY
DTI	DEPARTMENT OF TRADE AND INDUSTRY
EC	GMO EXECUTIVE COUNCIL
EU	EUROPEAN UNION
EFSA	THE EUROPEAN FOOD SAFETY AUTHORITY
EP	EUROPEAN PARLIAMENT
ERA	ENVIRONMENTAL RISK ASSESSMENT
EU	EUROPE UNION
FAO	FOOD AND AGRICULTURE ORGANISATION
FOSIE	FOOD SAFETY IN EUROPE
FSA	FOOD STANDARDS AGENCY (UK)
FSANZ	FOOD STANDARDS AUSTRALIA /NEW ZEALAND
GE	GENETICALLY MODIFIED ORGANISM
GMO	GENETICALLY MODIFIED ORGANISM
HEAG	HUMAN EXPOSURE ASSESSMENT GROUP
HCN	HYDROCYANIC ACID
INDAC	INTERDEPARTMENTAL ADVISORY COMMITTEE FOR SAFE GUARDING MAN AGAINST POISONS
IPS	IDENTITY PRESERVATION SYSTEM
IRGC	INTERNATIONAL RISK GOVERNANCE COUNCIL

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JECFA	JOINT EXPERT COMMITTEE ON FOOD ADDITIVES
JMPR	JOINT EXPERT MEETING ON PESTICIDE RESIDUES
LMO	LIVING MODIFIED ORGANISM
mRNA	MESSENGER RIBONUCLEIC ACID
MRL	MAXIMUM RESIDUE LIMIT
NRC	NATIONAL RESEARCH COUNCIL (USA)
OGTR	AUSTRALIAN OFFICE OF THE GENE TECHNOLOGY REGULATOR
OECD	ORGANISATION FOR ECONOMIC COORDINATION AND DEVELOPMENT
PA	PRECAUTIONARY APPROACH
PP	PRECAUTIONARY PRINCIPLE
RAFB	RISK ASSESSMENT FRAMING BODY
RAFRB	RISK ASSESSMENT FRAMING AND REPORTING BODY
RAGEE	RISK ASSESSMENT GROUP FOR ECOTOXICITY AND ENVIRONMENTAL FATE
rDNA	RECOMBINANT DEOXYRIBONUCLEIC ACID
SADC	SOUTHERN AFRICA DEVELOPMENT COMMUNITY
SAGENE	SOUTH AFRICAN COMMITTEE FOR GENETIC EXPERIMENTATION
SAHPRA	SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY
SENASA	THE NATIONAL AGRIFOOD HEALTH AND QUALITY SERVICE (ARGENTINA)
SPS	SANITARY AND PHYTO-SANITARY
TAG	TOXICOLOGY ASSESSMENT GROUP
TBT	TECHNICAL BARRIERS TO TRADE
TOXSA	TOXICOLOGY SOCIETY OF SOUTH AFRICA

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UK	UNITED KINGDOM
USA	UNITED STATES OF AMERICA
UNEP	UNITED NATIONS ENVIRONMENTAL PROGRAMME
UNESCO	UNITED NATIONS EDUCATIONAL SCIENTIFIC AND CULTURAL ORGANISATION
UNCED	UNITED NATIONS CONFERENCE ON ENVIRONMENT AND DEVELOPMENT
USA	UNITED STATES OF AMERICA
USEPA	UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
VCC	VETERINARY CLINICAL COMMITTEE
WHO	WORLD HEATH ORGANISATION
WTO	WORLD TRADE ORGANISATION

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GLOSSARY

ACCOUNTABILITY: Obligation to demonstrate that work has been conducted in compliance with agreed rules and standards or to report fairly and accurately on performance results vis-à-vis dated roles and/or plans. This may require a careful, even legally defensible, demonstration that the work is consistent with the contract terms. Note: Accountability in development may refer to the obligations of partners to act according to clearly defined responsibilities, roles and performance expectations, often with respect to the prudent use of resources. For evaluators, it connotes the responsibility to provide accurate, fair and credible monitoring reports and performance assessments. For public sector managers and policy makers, accountability is to taxpayers/citizens (OECD Evaluation of Development Programmes, Glossary).

CENTER OF ORIGIN OF DIVERSITY: The place or region where the source of diversity is located (UNEP 1995).

CONTAINED USE: Any operation, undertaken within a facility, installation or other physical structure, which involves living modified organisms that are controlled by specific measures that effectively limit their contact with, and their impact on, the external environment (Cartagena Protocol on Biosafety, Article 3).

ECOLOGICAL RISK ASSESSMENT: this includes three primary phases: problem formulation, analysis, and risk characterisation (US-EPA 1998 p. vii)

EFFECTIVENESS: The extent to which the development intervention's objectives were achieved, or are expected to be achieved, taking into account their relative importance (OECD Evaluation of Development Programmes, Glossary).

EXPOSURE ASSESSMENT: The qualitative and/or quantitative evaluation of the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant (CAC 2011, pp.112-113).

GENETIC MODIFICATION: Modern biotechnology used to alter genetic material of living organisms in order to make them capable of producing new substances or performing new functions (UNEP 1995).

HAZARD CHARACTERISATION: The qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical and physical agents that may be present in food. For chemical agents, a dose-response assessment should be performed. For biological or physical agents, a dose-response assessment should be performed if the data are obtainable (CAC 2011, pp.112-113).

HAZARD IDENTIFICATION: The identification of biological, chemical, and physical agents capable of causing adverse health effects and which may be present in a particular food or group of foods (CAC 2011, pp.112-113).

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HAZARD: A biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect (CAC 2011, pp.112-113).

INDEPENDENT EVALUATION: An evaluation carried out by entities and persons free of the control of those responsible for the design and implementation of the development intervention. Note: The credibility of an evaluation depends in part on how independently it has been carried out. Independence implies freedom from political influence and organisational pressure. It is characterised by full access to information and by full autonomy in carrying out investigations and reporting findings (OECD Evaluation of Development Programmes, Glossary).

LIVING MODIFIED ORGANISM: Any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology (Cartagena Protocol on Biosafety, Article 3).

MODERN BIOTECHNOLOGY: The application of a) in vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (rDNA) and direct injection of nucleic acid into cells or organelles, or b) fusion of cells beyond the taxonomic family (Cartagena Protocol on Biosafety, Article 3).

RISK ANALYSIS: A process in food safety assessment consisting of three components: risk assessment, risk management and risk communication (CAC 2011, pp.112-113).

RISK ASSESSMENT: A scientifically based process consisting of the following steps: i) hazard identification; ii) hazard characterisation; iii) exposure assessment; and iv) risk characterisation (CAC 2011, pp.112-113).

RISK ASSESSMENT POLICY: Documented guidelines on the choice of options and associated judgments for their application at appropriate decision points in the risk assessment such that the scientific integrity of the process is maintained (CAC 2011, pp.112-113).

RISK CHARACTERISATION: The qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterisation and exposure assessment (CAC 2011, pp.112-113).

RISK COMMUNICATION: The interactive exchange of information and opinions throughout the risk analysis process concerning risk, risk-related factors and risk perceptions, among risk assessors, risk managers, consumers, industry, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions (CAC 2011, pp.112-113).

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RISK EVALUATION STEP (STAGE): A stage between risk assessment and management. Evaluation serves to better understand possible differences in views held by interested parties, experts, and official on the assessment outcome to compare the risks, costs, and benefits and their distribution (König et al. 2010).

RISK MANAGEMENT: The process, distinct from risk assessment, of weighing policy alternatives, in consultation with all interested parties, considering risk assessment and other factors relevant for the health protection of consumers and for the promotion of fair trade practices, and, if needed, selecting appropriate prevention and control options (CAC 2011, pp.112-113).

RISK: A function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard(s) in food (CAC 2011, pp.112-113).

STAKEHOLDERS: Agencies, organisations, groups , or individuals who have a direct or indirect interest in the development intervention or its evaluation (OECD Evaluation of Development Programmes, Glossary) or actors (Dreyer et al. 2006, footnote 3, p.9).

STRESSOR: Any factor that may harm plants or animals: includes chemical , physical and biological.

SUSTAINABILITY: The continuation of benefits from a development intervention after major development assistance has been completed. The probability of continued long-term benefits. The resilience to risk of the net benefit flows over time (OECD Evaluation of Development Programmes, Glossary).

TERMS OF REFERENCE: Written document presenting the purpose and scope of the evaluation, the methods to be used, the standard against which performance is to be assessed or analyses are to be conducted, the resources and time allocated, and reporting requirements. Two other expressions sometimes used with the same meaning are ‘scope of work’ and ‘evaluation mandate’ (OECD Evaluation of Development Programmes, Glossary).

TRIANGULATION: The use of three or more theories, sources or types of information, or types of analysis to verify and substantiate an assessment. Note: by combining multiple data sources, methods, analyses or theories, evaluators seek to overcome the bias that comes from single informants, single methods, single observer or single theory studies (OECD Evaluation of Development Programmes, Glossary).

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ABSTRACT

ANALYSIS OF THE CREDIBILITY OF SOUTH AFRICAN RISK GOVERNANCE OF GENETICALLY MODIFIED ORGANISMS AND PESTICIDES

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In this study, two diverse scientific areas of research, namely, biological-chemical and public administration, were drawn upon to find an answer for improved risk governance of genetically modified organisms (GMO/GM) and pesticides. The need for such a study appeared from the constraints experienced with regulatory approval of GMO crops in South Africa. The knowledge gained from research on risk governance of GMOs could also be applied to pesticides. Protracted procedures causing delays in approval and increasingly stringent regulatory requirements of GMOs resulted in negative implications for research, development and commercialisation. Approval of several South African co-developed GMOs has been delayed or rejected that resulted in withdrawal or reducing of research activities, apart from appeals against decisions. The objective of the study was to identify some of the reasons for delays as experienced in risk assessments and to propose remedial actions, including the critical interface between role players in risk governance. The approach taken in this research was to obtain, by means of a questionnaire, a broad view of risk governances of GMOs as measured with criteria of good governance experienced by scientists of biotechnology and related disciplines. This was followed by another questionnaire with focus on one specific area that caused delays for GMO permit applicants. The investigation included analysis of South African legislation, guidelines and interviews. The research on risk assessment narrowed down to the two areas, illustrated by South African applicable case studies, namely, food risk/safety

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assessment of GMO cassava and environmental risk assessment of GMO sorghum. Approaches to improve assessments are being recommended. Uncertainty in risk assessment is an important reality because of humankind's limited knowledge of nature. Uncertainty is further addressed by precautious management, described as the precautionary principle is a norm legislated by the South African government in line with international agreements (the Cartagena Protocol on Biosafety). The terminology, precautionary approach and principle are used interchangeably in literature. The application of the precautionary principle in South African legislation and the difficulty that could be experienced in decision making are illustrated in the case study on 'possible unintended changes in endogenous allergens' in GMO maize. The research showed the importance of timely risk communication between risk assessors, risk managers (decision makers) and stakeholders in advance of the commencement of risk assessment. The importance of timely consideration of socio-economic impact of GMOs and pesticides is touched on. Risk governance structures, for both GMOs and pesticides are proposed, based on the most democratic and transparent governance models taking into consideration the European initiatives for improved risk governance. This included an interface for interaction among role players, namely, risk assessors, risk managers, scientists and stakeholders. The up-front role of an array of scientists, as the most trustworthy communicators in contentious scientific issues, is of specific importance because of the fast developing and very broad field of genetic modification of many crops. South Africa's national research institutes should play a much bigger role as scientific advisors in scientific risk policy making and framing for risk assessments. It is of great importance that risk assessments are focused on risks and not on the gathering of bucketsful of data; therefore, training in approaches to assessment of risk should be a priority. To achieve improvement on risk governance, the importance of policy development and the roles of all participants should be clear. Proposals for future research cover the many aspects that comprise trust in governance and the increased awareness of consumers and stakeholders of environmental risks and food safety. This study also paves a way for research on governance of phytopesticides and phytomedicines because of growing interest in these rich sources of new information that could be of great benefit to mankind.

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CHAPTER 1: INTRODUCTION

GENERAL

Food safety and food security are important national South African strategies. So is the protection of biodiversity. However, these may lead to conflicting objectives between government departments. Regulatory decision making is further complicated because of economic and social trade-offs. Regulating activities related to modern biotechnology (genetically modified organisms or GMOs), in addition to the mandates of government departments, experience elements of scientific uncertainty in which precaution features. Strategies or policies on such matters could have opposing results if they are not coordinated by national policy. Aerni (2002) remarked that South Africa was neglecting the role of science and technology in sustainable development, because biotechnology was seen only as a threat and not as a 'potential contribution to the conservation of biodiversity' (Areni 2002, p.13).

The Genetically Modified Organisms Act (South Africa 1997, as amended) was developed in the absence of a policy framework (Andanda 2009). Only in 2001 was the South African National Strategy for Biotechnology approved by parliament with the aim to promote a single biotechnology vision (South Africa 2001). However, there was no mention of a 'public good policy' that could help address problems of national priorities. One of its objectives was to establish a biosafety and regulatory platform. After about 10 years, the national biotechnology strategy needs to be revisited. An important issue, not realised over the years, is coordination of considerations regarding the importance of the application of genetic modification.

The GMO Act is administered by the Department of Agriculture, Forestry and Fisheries (DAFF), whereas environmental protection is the responsibility of the Department of Environmental Affairs (DEA). A number of other government departments have a role in regulating GMOs, as will be described in this study. Regulatory instruments for biotechnology in South Arica are summarised in Table 1-1.

The South African GMO Act (South Africa 1997) legislates all GMOs, including GM seed and grain, GM micro-organisms and GM animals. All activities are included from importation, contained use, trials, general release, monitoring and exportation. The South African area planted according to 2011 statistics (James 2011) are a combined 2.3 million hectares of GM maize, GM soybean and GM cotton (maize 72% or 1.873 million hectares of total maize planted; soybean 85 % or 1 873 million hectares of total; cotton 100 % or 15 000 hectares). No microorganisms or GM animals have been approved for general release. GM vaccines are only in clinical trials.

The role of the Codex Alimentarius Commission (CAC) is important in laying down international food safety standards and developing food safety guidelines. The Cartagena Protocol on Biosafety (Secretary of the

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Convention on Biological Diversity, online), to which South Africa is signatory, needs special mention because of a clause on a precautionary approach to environmental risk, which resulted in controversial interpretations.

1.2 PROBLEM IDENTIFICATION

1.2.1 Regulatory requirements: GMOs and new pesticides

In an address to the USA government, Beachy (2011, p. 4 of 7) made the statement that 'there have been no new (genetically modified) products released to the market from universities for more than 10 years, in part because of the time and cost necessary to bring the new product forward'. In South Africa, regulating the process appears to be moving in the direction of greater scrutiny and seems to be 'delaying rather than preventing approval', according to Wolson (online p. 2 of 13). Scientific research and compliance with regulatory requirements are essential in the process leading up to regulatory approval. In South Africa, national research on and release of genetically modified organisms (GMOs) have been negatively affected by increased requirements and appeals against government decisions (DAFF 2006 to 2012). Protracted decision making by government has resulted in increasing costs to applicants, as well as the withdrawal of research from South Africa, for example biofortified sorghum (Council for Scientific and Industrial Research (CSIR) 2009). A cause could be the shortcoming in the guidelines risk assessments, which fail to give details on quality of data, methodologies and assessment criteria (McGeoch & Rhodes 2006). In addition, GMO legislation that was not well considered or understood has resulted in serious importation and exportation consequences in the grain trade (executive director, AFMA: interview 31 May 2012; AFMA Chairman's Report 2011 to 2012).

The registration of new pesticides is another case in point. For several reasons, pesticide registration has been delayed for a number of years, resulting in a court order against government in favour of the industry (chief executive officer, AVCASA, email 1 August 2012).

1.2.2 Compliance costs and consequences of delays

The cost of compliance and protracted procedures will affect national research and development, and the careers of young biotechnology scientists.

It is becoming increasingly expensive to bring a new product to the market, whether it is a GM crop plant or a new pesticide molecule. The following information is proof of the cost of bringing a product to the market and the consequences of delays to the developer.

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1.2.2.1 Genetically modified organisms

Keetch, Green and Webster (Keetch et al. n.d.) estimated that a South African applicant would have to pay R641 000 (one US$ equivalent to about eight South African Rand) for a conditional release permit (general planting) for a GM crop. There may be additional expenses for example for trait introgression into local varieties. The core biosafety assessment constitutes merely a fraction of the total regulatory cost. Duplication and administrative burdens will form a large part of the expenditure if more and more regulatory authority requirements have to be complied with (Qaim 2010; De Greef 2011).

Kalaitzandonakes, Alston and Bradford (2007) analysed the direct costs of regulatory compliance (excluding research and development) for insect-resistant maize and herbicide-tolerant maize as US$ 7 060 000 to US$15 440 000 and US$6 180 000 to US$14 510 000, respectively. The calculations were based on approved submissions of four multinational companies and their subsidiaries that own or co-own about 80% of all biotech traits. The costs varied from one regulatory submission to another, with differences in the numbers and types of field trials, analytical tests, bioinformatic analyses, animal studies and other comparative safety assessments for 10 major producing and importing countries.

A study in the Philippines (Bayer, Norton & Falck-Zepeda 2010) showed that the costs regulatory compliance which include research and development, contained use, confined trials and open field trials could amount to $90 765 793 for the purpose of resistance to papaya ringspot virus; US$220 373 603 for *Bacillus thuringiensis* (*Bt*) rice; US$16 748 347 for resistance to a mosaic virus on tomato; and US$20 466 196 for *Bt* eggplant. The authors also calculated the expenditure under various assumptions of changing regulatory expense and time lag. The conclusion was that a small firm or public-sector institution may be deterred from, delay or abandon commercialisation of potential valuable products. The estimated cost for maize developed in the Philippines amounted to $2.6 million, including the entire product development (Manalo & Ramon 2007).

1.2.2.2 Pesticides

The total cost of discovery and development of a crop product (pesticide) increased by 21.1% from $152 million in 1995 to $184 million in 2000. From 2000 to the 2005 - 2008 year period, expenditure increased by 39.1% to $265 million (McDougall, 2010, survey conducted for CropLife International). Only 1 in 20 000 chemicals makes it from laboratory trial to commercial use.

1.2.3 Communication and capacity building

In a study prepared by Pole (2007) for the National Environmental Advisory Forum, concern was raised for improved communication, particularly public participation in the context of the GMO regulation in South Africa.

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This was confirmed by Ananda (2006) and Aerni (2002). In another study, Jaffe (2008) evaluated the South African regulatory system and identified matters for improvement. These included improved transparency in decision making and procedures, guidance to the applicant on the inclusion of socio-economic considerations, and improvement in the overall efficiency of the application decision-making process. He also identified the need to build capacity at the executive council (EC) because 'many EC members know little about agriculture, the biology of different crops, or the potential risk issues for GMOs'. Capacity building is a requirement in the Convention on Biological Diversity (Secretary of the Convention on Biological Diversity, online).

1.2.4 Trust in risk governance

According to a number of international organisations, consumers have the right to sufficient, safe food (FAO 2002; Consumer International online 15 October 2012). Sustainable food security and food safety are major matters in providing for consumers' needs (Pretty et al. 2010). Effective proactive safety governance before food products such as GM food and agricultural inputs such as pesticides are placed on the market is only one of the matters that influence sustainability and food safety. In recent years consumers have become more aware of food safety, especially in Europe, after a number of scares, including mad cow disease, and are now questioning the regulatory system (Dreyer & Renn 2009). Consumers are critical of the procedures and the decisions that are made by regulators on food safety-related matters, including pesticides (glyphosate and 2, 4-D herbicides) and genetically modified organisms (ACB online, 15 October 2012). Extensive South African labelling of all goods that contain GM ingredients or components is under revision and will be implemented, despite current stringent safety assessment requirements to provide information and a choice to consumers (South Africa 2008), In a survey of stakeholder attitude towards trust in institutions regarding GMO information in South Africa, it was found that national academia were perceived to be the most trusted stakeholders and the military and government were trusted least. (Aerni 2002, Aerni & Bernauer 2006).

1.2.5 Conclusion

The long delays in, and rejections of applications for GMO permits, resulting in increasing cost of compliance, could be pointing to deficiencies in a number of critical issues. Those identified are no national policies for harmonious approaches to risk assessments including benefit assessment; no progress in establishing a biosafety and regulatory platform; limited communication at all levels of governance, including participation and transparency in risk analysis matters; insufficient scientific capacity to make decisions on very complex biotechnological matters; and, possible little in trust in governance. These are indicators of possible concern at the level of credibility of risk governance of GMOs in South Africa. For this reason, it was considered important to conduct a critical investigation into governance of GMOs.

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The long delays of pesticides registration resulting in legal action against DAFF is indication of a serious concern. The methodology and results from the study with GMOs could therefore contribute to proposals for improvement of pesticide governance.

1.3 AIM

- To investigate the trust (described as credibility) in South African risk governance of GMOs, and to propose improved institutional arrangements.
- To investigate and propose improved governance for toxicological assessment of new pesticide molecules.

1.4 OBJECTIVES

- To describe governance models for risk analysis (Chapter 2)
- To analyse South Africa's existing risk governance of GMOs according to the criteria for good governance (Chapter 3)
- To focus on those good governance criteria of priority importance that needs improvement (Chapters 4, 5 and 6).
- To propose improved institutional arrangements for GMO governance (Chapter 7)
- To consider applying good governance principles to the toxicological assessment of new pesticides and propose improved governance (Chapter 8).

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Table 1-1: South African legislation, biotechnology strategy and environmental framework

Act /strategy/framework	Scope
Fertilisers, Farm Feed, Agricultural Remedies and Stock remedies Act, 1947 (Act No, 36 of 1947) (South Africa1947)	To provide for the appointment of a Registrar of Fertilisers, Farm Feeds, Agricultural Remedies and Stock Remedies; for the registration of fertilisers, farm feeds, agricultural remedies and stock remedies, sterilising plants and pest control operators; to regulate or prohibit the importation, sale , acquisition, disposal or use of fertilisers, farm feeds, agricultural remedies and stock remedies; to provide for the designation of technical advisers and analysts; and to provide for matters incidental thereto
Foodstuffs, Cosmetics and Disinfectants Act, 1972 (Act No. 54 of 1972 (South Africa 1972)	To control the sale, manufacture and importation of foodstuffs, cosmetics and disinfectants; and to provide for incidental matters. Section (1)(b)(ii) which contains or has been treated with...substance… deemed to be, harmful or injurious to human health'
Genetically Modified Organisms Act, 1997 (Act No,15 of 1997)as amended (Act No. 23 of 2006) (South Africa 1997)	To provide for measure to promote the responsible development, production, use and application of genetically modified organisms; to provide for adequate level of protection during all activities involving genetically modified organisms that may have an adverse impact on the conservation and sustainable use of biological diversity, human and animal health; to giver attention to the prevention of accidents and the effective management of waste; to establish common measures for the evaluation and reduction of the potential risk arising out of activities involving the use of genetically modified organisms; to lay down the necessary requirements and criteria for scientifically based risk assessments, environmental impact assessments, socio-economic consideration and risk management measures; to establish a Council for genetically modified organisms; to ensure that genetically modified organisms are appropriate and do not present a hazard to the environment; and to establish appropriate procedures for the notification of specific activities involving the use of genetically modified organisms; and, to provide for matters connected therewith

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The National Biotechnology Strategy, 2001 (South Africa 2001)	The strategy developed by Department Science and Technology that outlines the intentions of government to focus and co-ordinate interventions aims at stimulating the development of biotechnology (particularly modern biotechnology) in South Africa
Environmental risk assessment framework for genetically modified organisms (DEA n.d.)	Document by Department of Environmental Affairs to provide a framework for assessment of genetically modified organisms

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CHAPTER 2: MODELS FOR GOVERNANCE OF RISKS

2.1 INTRODUCTION

'Political system' or governance is a concept that emphasises the interaction of a political 'sphere' and its environment (Almond & Powell 1978, p.3). The environments include international, socio-economic and cultural ones and, for the purpose of this study, specifically the technical/scientific environments. The interactions with environments are expressed in various ways over many years of development of political systems. Governance of risks presents a specific case. Research on South Africa's governance of risk is described in the following chapters according to the plan summarised in Table 2-1.

This chapter includes:

- A brief reference to the criteria for good governance applied in the research (section 2.2)
- Characteristics of models as identified in the continuum of development, to guide the reader (section 2.3)
- Thoughts on the most advanced model for risk governance that includes more information on the 'framing' step (section 2.4)
- Some detail on the historical development of the paradigm, risk analysis (section 2.5)
- Examples to illustrate the application of the models by different countries and the African region (section 2.6, 2.7)
- Notes on international bodies (section 2.8).

2.2 GOOD GOVERNANCE CRITERIA

Criteria for good governance introduce a dimension to an assessment of governance models. These criteria are applied to the level of implementation of principles. The criteria identified were ethical conduct, independency, accountability, excellence, transparency, openness, participation, and effectiveness. Although these are interlinked and overlapping and may not be well comprehended by scientists that are not in the field of governance, these are, nevertheless, a broad indication of perceptions that people may have of good governance. The criteria are described in more detail in Chapter 3 as well as Chapter 8.

2.3 CHARACTERISTICS OF DIFFERENT GOVERNANCE MODELS FOR RISK ANALYSIS

The democratisation of the decision-making process of a political system concerning 'risks' is characterised by the evolution of a continuum of various models. Three characteristic models can be identified (Millstone 2007, p. 484). A brief explanation of the evolution of governance models should suffice to comprehend the importance of

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considering improvement of South African governance of GMOs and serves as reference to compare the progress in development of the South African governance of genetically modified organisms (GMOs) and also governance of toxicological assessment of new pesticides (crop protection products).

The earliest model, the technocratic model, assumes that policy decisions are based on 'sound science' only. The model does not permit separation between science and decision making (risk assessment and risk management) and operates independently of social, cultural and economic conditions. Functional separation between the policy makers and risk assessors is not clearly defined in many countries, lending itself to political influences. This has changed to some extent since the mad cow disease debacle in Europe (Dreyer et al. 2006, p.10). In the 'decisionist' model, functional separation between risk assessment and risk management is a prominent feature, though socio-economic considerations are of some interest.

The 'co-evolutionary model', described by Renn (2008) as the 'transparent' model (democratic model described by Millstone 2007), improves on the decisionist model by including 'other legitimate factors' such as socio-economic considerations in a holistic concept of risk governance. This model, according to Millstone (2007), is motivated by institutional and legal arrangements of governance within environments that keep on changing. Millstone et al. (2008, p.11) commented that in many countries this model is still not invoked in legislation.

Structures for risk governance in general are currently emerging under the auspices of the newly established International Risk Governance Council (IRGC, online). The emphasis of these models on the importance of socio-economic matters, whether risk or benefit, is of particular importance as a recent requirement in risk governance. This is the focus of research globally.

The expression 'risk governance' is now widely used and often relates to bridging 'sound science' with democratic 'participation' (De Marchi 2003, p.171). 'Ideal' risk governance in a democratic system, illustrating the broad scope of democratic governance, is defined as:

> *The totality of actors, rules, conventions, processes and mechanisms concerned with how relevant [food] risk information is collected, analysed and communicated, and decisions on [food] safety management are made. [Food] risk governance includes, but extends beyond, the three components of risk analysis (risk assessment, risk management, risk communication). It also involves co-ordination between public bodies, commercial and civil society actors, and wider contextual factors such as institutional arrangements, legislative procedures and political culture (Dreyer et al. 2006, footnote 3, p.9).*

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2.4 THOUGHTS ON THE MOST ADVANCED MODEL

2.4.1 SAFE FOODS Project

The SAFE FOODS Project, funded by the European Commission, was designed to assist in improving food safety governance for Europe. One of the important achievements was a model for food safety/risk governance (Figure 1) (König et al, 2010). The model proposed by this project falls within the most advanced category of models, the 'transparent' model.

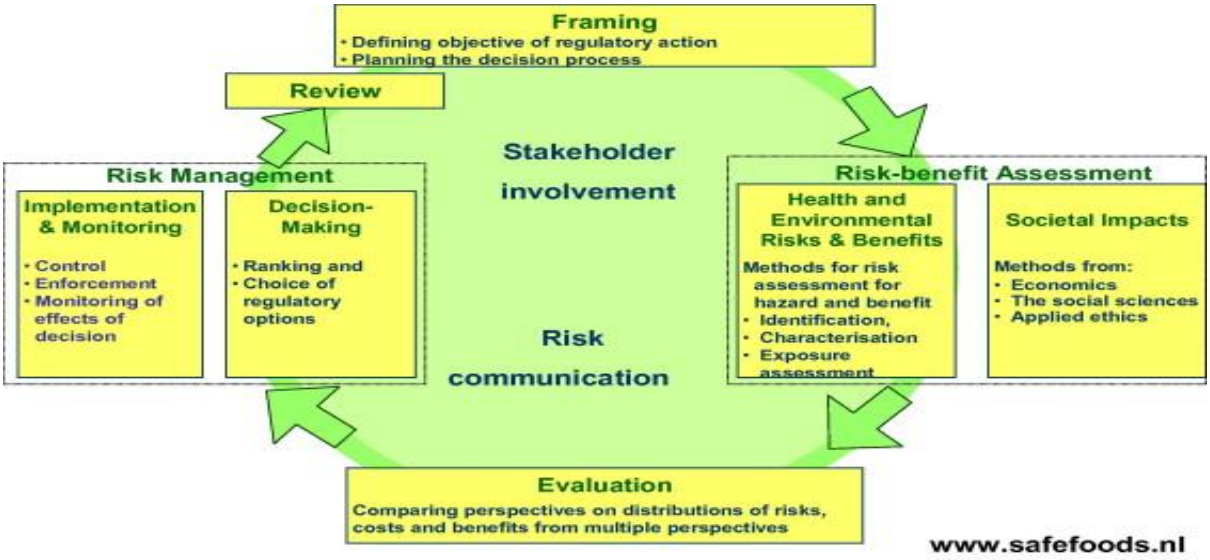

Figure 2- 1: The SAFE FOODS framework (König et al 2010) (ELSEVIER, license number 3118270887989)

The 'risk governance' model proposed by SAFE FOODS for the European Commission details the requirements of the transparent model. It comprises five components, which include the three constituents of risk analysis that is, risk–benefit assessment, risk management (decision making, implementation and monitoring) and risk communication, as well as two additional steps (or phases). These are a 'framing' step before the risk assessment, which relates to the 'risk assessment policy' step by the Codex (CAC 2011); and an 'evaluation' step before risk management. The purpose of these additional two steps is to promote efficient and transparent mechanisms of interaction between risk assessment and risk management (Koenig 2010, Ely et al, 2009). Communication and engagement with stakeholders and the public are integrated into every stage of the process (Ely et al, 2009).

In a special issue of the journal Food Control, various authors gave thought to the implementation of the proposals from the SAFE FOODS project. Of note, are the application to GMO assessment (Kuiper & Davis 2010), the role of an interface committee to improve transparency, open and participatory management

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(Knudsen 2010), methods and approaches to assess social impact (Cope et al. 2010), and economic assessment (Trail & König 2010).

2.4.2 Framing

A 'framing' step in risk analysis in the most advanced governance model mentioned in section 2.3 is of importance in this study and described in more detail here. See also the definition for risk governance in section 2.3

Framing for assessments of possible risk (food safety and environmental risks) is considered the 'meta-level' of risk governance as it refers to all process within the dynamic iterative nature of risk analysis (Ely et al 2009, Kuiper & Davis 2012). It is a continuous, exploratory process with goals of food and environmental safety. More specific to the new assignment for assessment, the problem is formulated and the assessment planned according to the objectives of risk analysis as well as formal evaluation step to weight risk, cost and benefits (Kuiper & Davis 2010).

The role players are risk managers, risk assessors and stakeholders (CAC 2011, Ely et al 2009). It serves as formal opportunity for role-players to communicate prior to risk assessment and is the guideline to follow in case of value judgements (Jackson & Jansen 2010). Codex views the framing step (risk assessment policy step) as primarily a managerial initiative, whereas the European Food Safety Authority (EFSA) has risk assessment policy development as a self-tasking activity. It is suggested by Ely et al. (2009) that policy development should be undertaken jointly by risk managers and risk assessors and as a matter of transparency in a democratic milieu, with inputs from a wide range of stakeholders.

Three stages in framing have been identified (Ely et al 2009):

1. *Review*: This is an on-going process of adapting and improving as a response within the global context of scientific and technical developments, socio-economic and political changes and new legislative requirements but also from own experience and insight. During the review process those activities that govern the selection and characterisation of the threat (harm), as well as criteria that are employed in screening, are included. Decision (policy decisions) are made regarding uniform risk assessment methodologies (approaches, principles), sufficiency of scientific and technical data and priorities for allocating resources to different aspects of screening, assessment and evaluation and management.

2. *Referral*: This is the stage where the safety/risk problems are identified, and assessments formulated. The responsibility of risk assessors at this stage is to 'screen' the product for the most appropriate approach for assessment.

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3. *Terms of reference*: During this stage, uncertainties and data gaps are identified, as well as external experts and specific participatory procedures, if required. The questions are formulated to be addressed and guidance on management of the possible risks.

In a study on risk assessment of chemicals of food and dietary importance, the Food Safety in Europe (FOSIE) Project, the framing step is described by emphasis on problem formulation. This is a process described by 'planning dialogue' to clarify management goals, the purpose and scope of the assessment and the available resources to conduct the assessment. It is an iterative process that should undergo rigorous review by risk managers, scientific peers, and other stakeholders (Renwick et al. 2003, pp.1216 - 1217). The objectives include 'harmonising principles applied to risk assessment, interpretation of data, consensus scientific transparency and justifiable issues in risk assessment issues and a description of the problem formulation with the outcome of a plan as the initial step in risk assessment. The process includes consideration of whether assessment is needed; who should be involved in the assessment and management; how it will provide information to the decision makers; whether data is available for an evaluation of risks; the level of available resources and a timeline for completion of the assessment. Specific information is described as a detailed inventory of prior knowledge and information on exposure such as the population and geographical area. Consideration should be given to relevance for the society and the range of health endpoints to identify quantifiable indicators or processes in risk characterisation. The assessment that follows should be such that scientifically sound and credible characterisation of the risk could be described, to make appropriate managerial decisions' (Renwick et al. 2003, pp. 1217-1218).

2.5 HISTORICAL DEVELOPMENT OF THE PARADIGM: RISK ANALYSIS

2.5.1 General

As early as 1983, recommendations were published from a study on USA governance of risk assessment (NRC 1983). The report came at a period of increased public concern for the effects on human health and the environment of chemicals such as asbestos. The study had been commissioned because many of the 'decisions of federal agencies in regulating chronic health issues have been bitterly controversial' (NRC 1983, p.1). The report included proposals for improving 'institutional mechanisms to ensure that government regulation rests on the best available scientific knowledge and to preserve the integrity of scientific data and judgements' (NRC 1983, p.1). It included proposals for regulatory agencies to take steps to establish and maintain a clear conceptual distinction between assessment of risks and to considerate risk management alternatives, so that scientific findings and policy judgments embodied in risk assessments should be 'explicitly distinguished from the political, economic and technical considerations that influence the design and choice of regulatory strategies' (NRC 1983, p. 151). The rest of the recommendations concerned issues such as independent science advisory

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panels, peer reviewing, guidelines that make explicit the distinction between science and policy, and risk assessment methods (NRC 1983, p.177). This view had an impact on the future development of the risk analysis model published by the Codex Alimentarius Commission (CAC or Codex) (CAC 2011), a body responsible for international food safety standards, under the joint auspice of the two United Nations bodies, the Food and Agriculture Organization (FAO) and the World Health Organization (WHO). The entire scope of risk analysis includes interactions between risk assessment, risk management and risk communication (CAC 2011). Although the consultations concerned interactions between the United Nations bodies involved in food safety (above), the framework and principles are of equal importance to national food safety governance.

The FAO/WHO Expert Consultation (1995, p.29) recognised:

- 'Increased consumer interest in food safety
- WTO's Sanitary and Phytosanitary (SPS) and Technical Barriers to Trade (TBT) Agreements
- Harmonisation initiatives
- Calls for increased scientific rigour
- The need for transparency
- Shrinking national regulatory resources'

The same consultation for the FAO/WHO, at the request of the Executive Committee of CAC at the 41st Session in June 1994 in Rome (CAC, 1994), was to provide recommendations to FAO, WHO, CAC and member countries for the most appropriate approach to the application of risk analysis to food standards and safety issues in the work of Codex (FAO/WHO 1995). The recommendations of the expert group were to include definitions of risk analysis terms; principles for risk assessment methodology; and recommendations to promote the implementation of harmonised and transparent risk assessment methodologies. They recognised that an important principle in risk analysis was functional separation of risk assessment and risk management with a number of interfaces, such as establishing priorities and policies for risk assessment by inputs from risk management. The need for better information to enhance the risk assessment process was identified and it was realised that only in rare instances could all the necessary information be available (uncertainties). The transparency and credibility of the risk assessment process of the advisory bodies of Codex Alimentarius that is, the Joint Expert Committee on Food Additives (JECFA) and the Joint Expert Meeting on Pesticide Residues (JMPR) were important because of promoting quality and consistency of toxicological and other data; standardised test protocol; and minimum data requirements that had to be recommended by recognised independent international experts (FAO/WHO 1995).

In 1997, another joint FAO/WHO Expert Consultation (1997) made recommendations on risk management and food safety. Food safety risk analysis was recognised as an emerging discipline, a methodological basis for risk assessment and management. In their assessment and recommendations to the international bodies, the

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consultation applied these elements as a risk management framework: risk evaluation, option assessment, implementation, and monitoring and review. Compliance with certain principles was important. Risk management should follow a structured approach (FAO/WHO 1997, pp. 6-7):

- Protection of human health should be the primary consideration in risk management decisions
- Risk management decisions and practices should be transparent.
- Determination of risk assessment policy should be included as a specific component of risk management.
- Risk management should ensure the scientific integrity of the risk assessment process by maintaining the functional separation of risk management and risk assessment.
- Risk management decisions should take into account the uncertainty in the output of the risk assessment.
- Risk management should include clear, interactive communication with consumers and other interested parties in all aspects of the process.
- Risk assessment should be a continuing process that takes into account all newly generated data in the evaluation and review of risk management decisions.

One of the outcomes of the deliberations that is applicable to national governments was the FAO/WHO guide for national authorities (FAO/WHO, 2006), confirming that the support and participation of key stakeholders and the functional separation of risk assessment and risk management were of critical importance. Food safety risk analysis has subsequently become a new discipline, according to the FAO/WHO (2006).

2.5.2 Perspective on European risk governance of food

A turning point in European risk governance of food came with the outbreak of Creutzfeldt-Jakob disease and on recognition of the dangers of consuming meat infected with bovine spongiform encephalopathy (BSE) (EP 2000). Food safety concerns for genetically modified (GM or GMO) foods were points of great dispute in Europe when they were officially approved in the United Kingdom. An example is the dispute at international level of the World Trade Organisation between the USA and Canada versus Europe, when Europe imposed a moratorium on the GM hormone recombinant bovine somatotropin (rBST) for use as a veterinary product for stimulating lactation in cows (EP 2000). In South Africa much concern was raised over mycotoxin contaminated groundnut butter, which was provided in the school feeding scheme in the late 1990s (personal experience of one of the authors FWJvR).

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Investigations into regulatory decision making and interaction with scientific evidence were made as a result of these scares. Prior to these episodes, member states in Europe, without exception, functioned without differentiating between risk assessment and risk management (EP 2000), resulting in the extreme situation of BSE policy making by the United Kingdom in which decisions on risks were not based on independent scientific advice (EP 2000).

The findings in Europe resulted in the establishment of the European Food Safety Authority (EFSA) in 2002 (EC 2002) as a centralised independent risk assessment body that prepares opinions on matters of food safety, including food derived from GMO, presence of pesticides in food, food contaminants (mycotoxins) and food additives (EFSA online). The conclusion was that separating the science of risk assessment from the political influence of risk management deliberations was one of the most important criteria for improving trust in food safety governance in Europe.

2.6 EXAMPLES OF DIFFERENT STRUCTURES

2.6.1 Reform in European countries

The reform efforts in Europe were studied for five European countries (United Kingdom, France, Germany, Hungary, and Sweden) as well as for the Europe Union (EU) (Dreyer et al. 2006). These countries and the EU started from mainly a technocratic model and moved to a more decisionist model of the risk policy-making process. The intensity of the need to restore trust after the BSE crises was high, especially in the UK, France and Germany. The reforms consisted of either institutional segregation or functional segregation. Stakeholder participation received more emphasis. Risk information increased in most cases, but the extent of communication on scientific uncertainty varied (Dreyer et al, 2006). Concern was expressed that the decisionist model applied by the various jurisdictions in Europe did not seem to be a ‘workable’ solution and was still not the ideal (Dreyer et al, 2006).

2.6.2 European Food Safety Authority

The Committee of the European Communities (CEC) (Commission in short) presented the White Paper on Food Safety (CEC 2000) and the White Paper on European Governance (CEC 2001), in which the need was expressed for an establishment of an authority that could guarantee a high level of food safety. The key tasks were to embrace scientific advice on all aspects of food safety: the operating rapid alert system; ensuring effective communication and dialogue with consumers on food safety and health issues; and networking with national agencies and scientific bodies. The idea was also to bring coherence to the corpus of legislation covering all aspects of food products from ‘farm to table’ (CEC 2000, p.8). A new legal framework was to be proposed. Apart from the integrated food safety controls, consumers’ need for information was highlighted. The

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Commission was convinced that transparency at all levels of a food safety policy would 'contribute fundamentally' to enhancing consumer confidence in EU food safety policy' (CEC 2000, p.5). The White Paper on Food Safety emphasised 'risk analyses as the foundation' on which food safety policy should be based' (CEC 2000, p.9).

The system for providing scientific advice to the Commission was re-organised in 1997. Because of increasing demands for risk assessments until 1997, it was soon realised that the existing system was handicapped by a lack of capacity and of accurate, up-to-date scientific data. One solution was to exploit the existing scientific networks. It was proposed that an independent European food authority that was responsible for risk assessments and communication on food safety issues should be established on principles of good governance: accountability, openness, participation, effectiveness and coherence, as criteria of democratic governance (CEC 2001, p.10). A few of the matters that were discussed in much detail, were: the relation between science and policymaking (independency also separation between risk assessment and risk management), independency of scientific experts, lines of accountability, framing by a prior set of assumption for scientific risk assessments and (excellence), risk communication, and transparency (EP 2000, p11, pp.76-86). The criteria for risk assessment in particular, were formulated as: independence, scientific excellence, and transparency (EC 2000, p.17) Centralising risk assessment raised concerns that, inter alia democratic accountability would be diluted. It was then decided that risk management responsibilities would remain with the CEC. The advantages of such an authority were that scientific risk assessments would be accepted by all member countries, which would be conducive to the effectiveness of execution of actions. The White Paper was published in 2000, consultation and proposals the same year and enabling legislation in December 2001 and the authority began operation in 2002 (EC 2002). The EFSA is currently recognised as a leading role player in preparing 'opinions' on for example GM food safety. Its important role in debates is respected for example in the debate on endogenous allergens (EFSA, online). However, its positions are often disputed in the European Parliament. Political influence at that level of decision making is not excluded.

2.6.2.1 European Food Safety Authority: GMOs

The consultation process for preparing opinions on GMOs illustrates the development of opinions by EFSA. The process is described in two sets of legislation: the Dir. 2001/18/EC (EC 2001) deliberate release into the environment, and Regulation (EC) No 1829/2003). The processes for these two legal routes differ. They are not described in further detail here (EFSA online).

Each GMO risk assessment is carried out by EFSA's GMO Panel, which is made up of 21 independent scientific experts. The safety of each GM product is assessed on a case-by-case basis. The GMO panels share their experience and knowledge and member states have an opportunity to give scientific input. The scientific panels

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and scientific committee members are selected from the best scientific experts in their field. Independence is ensured by a mandatory declaration of commitment of independence and declarations of interests. This is done annually and through public comment on the EFSA website. Any interest must also be declared at each meeting. EFSA realises that to maintain and gain expertise, the members must be active in their field and must have experience and knowledge of the GM products to be investigated. In addition, the opinion of EFSA is collective and not from individuals.

EFSA takes on 'self-tasking' projects such as development or risk assessment guidelines 'in order to stay in the forefront of new scientific developments' and to develop GM risk assessment approaches for example statistics, allergenicity, animal feeding trials, post-market environmental monitoring and medicinal products. It is open to scientific contributions from third parties. Stakeholders contribute directly by public debate on GMO issues through a stakeholder consultative platform and at specific meetings. The EC organises additional public consultation on its website whereby all third parties may comment (EFSA online)

EFSA could be considered as representing the technocratic model with strong tendency to progress towards a transparent model. What was apparently lacking, at the stage before the SAFE-FOOD project investigations, was sufficient participation at the level of 'framing'. It is, however, a commendable example of risk governance to follow, in planning for improved South African risk governance of GMOs.

2.6.3 United Kingdom

The UK addressed its critical situation by creating a UK Food Standards Agency (FSA) that carries out both risk assessment and risk management by maintaining functional separation between the two entities. Risk assessments are carried out by in-house scientists, but they seek the opinions of independent scientific advisory bodies of which there are ten, when an independent view is essential. Risk management is carried out by the FSA's board. The FSA has an extensive system for engagement with stakeholders. Opportunities for communication occur at the points of scientific information gathering, risk assessment, risk management options, and FSA policy and advice. (Atkins & Norman 2009). By this open and transparent approach the FSA views this model as having the ability to 'winning the trust of stakeholders' (Atkins & Norman 2009, p.207).

2.6.4 Argentina

Information about the way in which Argentina approached the assessment of GMOs was obtained from a publication by one of its senior officials (Burachik &Traynor, 2002). The situation may have changed since then. The Argentinean approach to risk analysis of GMOs is an important illustration of the involvement of multidisciplinary teams.

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The National Advisory Commission on Agricultural Biotechnology (CONABIA) is a multidisciplinary inter-institutional advisory body consisting of scientists representing the public sector (government directorates, services and institutes, a research council, the ecology society and a university), as well as the private sector (seed growers, veterinary product manufacturers, fertiliser manufacturers and a biotechnology forum). The applicant has to approve of the two scientists of CONABIA that would have access to his or her confidential business information (CBI). It has been customary for the most part that only CONABIA's scientific advisory staff members and an official from the National Agrifood Health and Quality Service (SENASA) should review CBI information. During this review, the applicant has the 'right' to require the presence of a representative and give opinions and outside experts may be called on when needed. The rest of the CONABIA members make recommendations on non-CBI information. Two technical advisory committees with membership representing consumers, farmers and industry interest provide for transparency and improvement in the quality of the review process. The processes for considering new applications and executing decisions are conducted according to stringent rules and guidelines.

Broader policy issues on agricultural biotechnology are developed by a national advisory commission, which includes representatives from the public bodies involved in biotechnology as well as external advisors. The Argentina authorities are involved in 'market reviewing' and in 'research and development 'in one way or another.

At the time of this review in 2002, Argentina was considering adoption and implementation of a biosafety law.

2.6.5 Australia – New Zealand

Food safety assessment became a joint activity between Australia and New Zealand (FANZ). Functional separation of risk assessment from risk management is achieved by separate science groups for veterinary and pesticide risk assessments (FSANZ online).

The Office of the Gene Technology Regulator (OGTR, online) for regulating GMOs is an example of a model that includes the three phases of risk analysis and a well-developed communication system.

GMOs are regulated under the Gene Technology Act 2000 and Regulations. The regulatory, supported by staff from the Regulator's Office, is a statutory office holder that reports directly to the Australian Parliament. The Gene Technology Ministerial Council consists of representatives from all Australian jurisdictions and oversees implementation of the regulatory system. Two committees serve the regulator and the council, the Advisory Committee for Ethics and Community Consultation, and the Gene Technology and Technical Committee, which serves in an advisory and consultative capacity. The latter committee consists of eighteen expert members from a range of disciplines. It is central to peer reviewing of risk assessments and management plans developed by the Regulator's Office. Decisions are made by voting. Communication between the regulatory, applicants,

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stakeholders and the public occurs at four stages: hazard identification; risk assessment; risk management planning; and a step to discuss risk management licence conditions (Australian Government 2009, Linacre et al. 2006).

Linacre et al (2006) investigated reasons for the slow process taken to approve planting commercial crops. They concluded that division of powers between the national and state governments led to regulatory paralysis; that cost-benefit analysis had a role in societal decision making; that qualitative risk assessment had some deficiencies when used to guide public policy; that probabilistic risk assessment might be more useful; and that voting as a way of decision making could be problematic.

2.7 CENTRALISED RISK ASSESSMENT INITIATIVES IN AFRICA

The Common Market for Eastern and Southern Africa (COMESA) proposal for centralised risk assessment follows the approach taken by the European Union in the establishment of EFSA. It includes some ideas taken from the functioning of the expert committees (meetings) of FAO/WHO (member of the Panel of Experts of COMESA, personal communication, 28 August 2012). The development of policy guidelines started in 2009 but these are still be approved by the relevant ministers of COMESA countries. The progress is slow as it is focusing on all trade harmonies (COMESA, online).

The Central African Economic and Monetary Community (CEMAC) established an Inter-State Pesticides Committee of Central Africa (CPAC) officially in November 2007. It comprises three experts or representatives from each member state of CEMAC, as well as representatives of the CEMAC Commission, African Union and FAO and WHO. Its mission includes examining pesticide registration application (CPAC, online).

2.8 INTERNATIONAL ORGANISATIONS

International organisations play significant roles in policy development for risk analysis. Codex Alimentarius contribution has been described in previous sections and in different following chapters. Two more organisations need mentioning.

2.8.1 World Trade Organization

The World Trade Organisation's Final Act, which included the Sanitary and Phytosanitary (SPS) and the Technical Barriers to Trade TBT Agreements, was an important stimulus in the development of analysis of food safety and risks. These agreements have implications for Codex standards, guidelines and recommendations, in that they reflect international consensus on the requirements to protect human health (WTO, online).

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2.8.2 Organization for Economic Cooperation and Development

The Organization for Economic Cooperation and Development (OECD) fulfils an important need in facilitating trade. It has developed a number of guidelines for testing chemicals and biopesticides, and has published consensus documents on the composition and nutritional assessment of crops plants, and the biology of crop plants, as well as scientific documents on matters for guidance in risk assessments and risk management (OECD, online). These documents are prepared by government and independent scientists, are approved by about 30 member countries and are used as references in risk assessments. The OECD is noted for the development of 'substantial equivalence', a concept agreed by Codex member countries and now the basis of the risk/safety assessment of GMOs (OECD 1993).

2.9 CONCLUSION

The concept of risk analysis has been developed over many years to the point that models for good governance can be identified on a continuum. The short review on governance structures showed a development towards more democratic decision making. The institutional arrangements of a number of governments and international bodies are described in this chapter. The role of international bodies in contributing to improved structures for risk analysis and in particular risk assessment is significant. The descriptions serve as a baseline to analyse the South African institutional arrangements for risk analysis of genetically modified organisms and for the toxicological assessment of pesticides.

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Table 2-1: Study plan

ANALYSIS SEQUENCE	METHODOLOGY	CHAPTERS
PROBLEM IDENTIFICATION / AIM / O BJECTIVES	Statements	1
IDENTIFYING PROBLEM AREAS BY MEANS OF CRITERIA OF GOOD GOVERNANCE	• Questionnaire: • Criteria for good governance	3
IDENTIFYING SPECIFIC CONCERNS	• Questionnaire: • Reasons for delays/ Remedial actions	3
ANALISING IDENTIFIED CONCERNS WITH CASE STUDIES	• Approaches to risk assessment food/ environment. • Exceptions to suggested risk assessment approach – food • Precautionary principle	4, 5 and 6
PROPOSE SOLUTION(S) TO IDENTIFIED CONCERNS	• Models for risk governance	7
APPLICATION OF PROPOSAL TO SIMILAR REGULATORY PROBLEM AREAS	• Model for toxicological assessment of pesticides	8

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CHAPTER 3: A CRITICAL SCIENTIFIC REVIEW ON SOUTH AFRICAN GOVERNANCE OF GMOs

ABSTRACT

Credible governance of genetically modified organisms (GMOs) is essential because of public concerns internationally and also in South Africa. In a preliminary study, the opinions of a number of scientists with experience and/or interest in GMO governance were probed by means of two questionnaires to determine their perceptions of the credibility of risk governance of GMOs in South Africa. The results indicated that, according to criteria of good governance, 'some improvement' was required. However, criteria such as excellence (quality of risk assessment) and effectiveness, for example protracted regulatory processes needed 'some to much improvement'. The scientists' responses were evaluated against an analysis of the South Africa GMO Act, regulations, policy guidelines and available information. The act provides a proactive basis for good governance comparable with internationally described risk governance models, but implementation seemed to follow the less advanced technocratic model. A number of reasons were identified, for example unclear roles of decision makers. Some of the causes for protracted decision making identified by respondents were a) excessive precaution in decision making, and b) different mandates resulting in no unanimity among government departments. Proposals for improvement in credibility included communication as a critical component of risk governance and continued training reviewers and decision makers.

Key words: Genetically modified organisms, risk assessment, risk governance, South Africa

3.1 INTRODUCTION

A recent study, confirming the need for further investigation of the South Africa risk governance of genetically modified organisms (GMOs) (Jaffe 2008) points to various deficiencies in governance that could impact on credibility and could be a cause for delays in processing of permits, resulting in increasing costs of registering new GMO products. Incidences that raised concern to address risks in a scientific way (Paarlberg et al. 2000) were (DAFF, online):

- Protracted decision making, for example the embargo on commodity clearances (import of GM grains) since 2005 until 2011 (DAFF, online)
- Delays in stacked trait cotton approvals and several appeals against decisions (DAFF, online)
- Socio-economic reasons for refusal of permits (DAFF, online)
- The DTI's mandatory labelling of genetically modified ingredients and components (not defined) in the Consumer Protection Act (South Africa 2008) to enable food choices, despite existing labelling regulations

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by the DoH (South Africa 1972, 2004). This illustrates conflicting approaches between departments that could affect credibility.

The current study addressed the question: How credible is governance of GMOs in South Africa as perceived by scientists with knowledge of the system?

Much has been said on improvement of trust in governance in general, such as more transparency in decision making (FAO/WHO 2006). Health hazards such as the bovine spongiform encephalitis (BSE), a transmissible, neurodegenerative fatal brain disease of cattle, and debates on foods GMOs in Europe resulted in changes in government food safety systems (Dreyer et al. 2006; Atkins & Norman 2009). The establishment of the European Food Safety Authority (EFSA) in 2002 as an independent and transparent organisation to advise the European Commission on food safety was one of the major reforms in Europe to restore public trust (CEC 2002).

The concept of risk governance has received considerable attention lately (Dreyer et al. 2006, Dreyer & Renn 2009; König et al. 2010, CAC 2011). The Codex Alimentarius Commission (CAC 2011) has proactively described the process of risk analysis (risk assessment, risk management and risk communication) and the principles that could be applied by governments to improve open and transparent decision making. A comprehensive scope of food safety/risk governance that could equally be applied to environmental safety /risks has been defined as:

> *The totality of actors, rules, conventions, processes and mechanisms concerned with how relevant food risk information is collected, analysed and communicated, and decisions on food safety management are made. Food risk governance includes, but extends beyond the three components of risk analysis (risk assessment, risk management, risk communication). It also involves co-ordination between public bodies, commercial and civil society actors, and wider contextual factors such as institutional arrangements, legislative procedures and political culture (Dreyer et al. 2006, footnote 3 p. 9).*

Millstone (2007) identified three successive models of governance as technocratic, decisionist and co-evolutionary, demonstrating increasing interaction with stakeholders and including matters of socio-economic importance. The roles of risk assessors and risk managers (decision makers) are not well separated in older governance structures that are categorised by technocratic governance models, resulting in poor decisions, for example the BSE scandal in the United Kingdom (Dreyer et al. 2006). The decisionist model strongly favours functional separation. This is a recommendation made by Codex 'to ensure the scientific integrity of the risk assessment, to avoid confusion over the functions to be performed by risk assessor and risk managers and to reduce conflict of interest' (CAC 2011, p.106). The co-evolutionary or democratic model (transparent model according to Renn 2008) additionally includes structured reciprocal links between science (risk assessment) and policy (risk assessment framing, management and decision making), as well as an evaluation step for risks versus benefits which calls for stakeholder participation (Millstone 2007; Dreyer et al. 2009, König 2010, Morris

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2011). Currently, more in-depth research is being conducted on the concept of participation. The role of democratic decision making depends on people being able to take part in public debate. To do this, they must have access to reliable information to be able to scrutinise policy process in its various stages (Ely et al. 2009; Millstone et al. 2008). Consultation occurs through advisory committees, business test panels, ad hoc consultations, public hearings, and instruments such as Green and White Papers.

Criteria of good governance referred to in this study were described as independency in risk assessment, ethical conduct, transparency, openness, participation, accountability, scientific excellence and effectiveness (CEC 2000, 2001). Legislative matters as criterion included the risk assessment component in governance models as one indicator of the current state of development of GMO governance in South Africa. Models of good governance (Millstone 2007) were used to compare development of South African governance of GMOs with international examples of GMO governance.

A European project, the SAFE FOODs project, funded by the European Commission's Sixth Framework Program for Research and Technology Development, needs special mentioning as it describes the details of the most advanced model for food risk governance to be implemented in Europe. This framework is referred to in more detail in Chapter 2 (2.4.1).

The South African GMO Act (South Africa, 1997) regulates all GMOs including GM seed and grain, GM micro-organisms and GM animals. All activities are included from importation, contained use, trials, general release, monitoring and exportation. The SA area planted according to 2011 statistics (James 2011) are a combined 2.3 million hectares of GM maize, GM soybean and GM cotton (Maize 72% or 1.873 million hectares of total maize planted; soybean 85 % or 1,873million hectares of total; cotton 100 % or 15000hectares). No microorganisms or GM animals have been approved for general release. GM vaccines are only in clinical trials.

In South Africa the GMO Act (Act 15 of 1997) is often held as an example for future food safety governance models (Chanda, Fincham & Venter 2010).This model partly resembles the framework for risk governance in Europe. With the exception of the labelling of GM foods, governance in South Africa of GMOs is legislated in terms of the GMO Act as amended (South Africa 1997) and administered by DAFF. The act establishes a decision-making body, the EC, constituted in practice of one representative from each of six government departments plus the chairperson of the AC. The government departments have mandates in terms of their own legislation except for DST, whose mandate also derives from the National Biotechnology Strategy for South Africa (South Africa 2001). DOH reactively regulates the safety of food (South Africa 1972). DEA has additional responsibility for environmental safety of GMOs in terms of the National Environmental Management: Biodiversity Act (South Africa 2004). The AC consists of independent scientists from academia, research institutes and the private sector, and submits recommendations on permit applications to the EC.

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The risk assessment step in risk governance is of necessity partly non-transparent because of the confidentiality of certain company information. Government policy may reduce transparency. This was exemplified by the fact that the EC discouraged government GMO regulatory scientists responding to the survey by stipulating that they first obtained written ministerial approval. Therefore, determination of credibility could not be based on first-hand information, but only on perceptions by those who viewed the system from outside. However, perceptions should not be underestimated as they provide an indicator of problem areas. This study should be regarded as preliminary because of the exclusion of policy makers and scientists directly involved in the regulatory process.

3.2 METHODOLOGY

The study, considered as preliminary, included an analysis of applicable legislation and available official guidelines, interviews with government officials, as well as two questionnaires distributed to scientists with knowledge of GMO legislation and/or risk assessments. The Ethics Committee of the Faculty: Natural and Agricultural Sciences dealing with research pertaining to humans approved the study in 2008 for the first questionnaire and again in 2009 for the second questionnaire.

The construction of the first questionnaire included pretesting by a small number of food scientists and a few consumers as well as individual scientists. The questionnaire contained the approved University of Pretoria 'Research Participant Consent' form. In the introduction to the questionnaire the purpose of the study, some information on risk analysis as well as complete instructions for completing the questionnaire is given. The respondents were assured of anonymity. The questionnaire was forwarded by electronic mail, during April 2008 and reminders forwarded after 2 weeks and at regular intervals afterwards. The last responses were received in September 2008. Those that did not respond were telephoned or electronically mailed. The questionnaire commenced in the first section, with outlining criteria in 'closed-ended' statements, followed by control statements (closed-ended) in subsequent sections as depicted in Table 3-1 and 3-2. Opportunities for comments (open-ended) were provided for. The target group of the first questionnaire was scientists from industry, public research and academic institutes involved in biotechnological related matters

The first questionnaire was designed to:

a) Qualitatively describe a credibility profile of South African governance of GMOs from responses to criteria and sub-criteria described in Table 3-1a (criteria 1 to 9).

b) Probe perspectives in general on criteria of good governance based on the statements in Table 3-1b. These statements and results were grouped under three pillars of good governance, namely policies / procedures (statements 10.1 to 10.15), scientific excellence (statements 11.1 to 11.8) and transparency (statements 12.1 to 12.9

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For the first questionnaire, 24 responses (10.2%including possible responses from regulatory authorities and members of the AC) were obtained and considered as a fair number of in this field, considering the constraints encountered. The low response rate could be ascribed to:

- Some potential respondents were unfamiliar with the subject.
- Government officials as well as advisors to government (a possible 54 responses) did not participate and neither did anti-GM lobby groups.
- In a number of cases, a single response was received per biotechnology seed company or research institute, instead of responses from individual persons. This was confirmed in discussions with some of the respondents.
- The Internet approach for questionnaires presented several technical problems.

The participants could be considered a homogenous group, representing applicants or potential applicants for permits and having marketing (or general release) of GMO products or an academic interest in common.

Reponses to statements in the categorised sections of the questionnaire indicated a reasonable general understanding of 'good governance' among respondents. Although the response numbers were relatively low, valuable information was obtained that should lead to a more in-depth future study of risk governance. The current study focused on assessment of priority needs for improvement in legislation, policy and implementation.

In the second questionnaire, a follow-up on the first questionnaire in 2009, with focus on the scientific reasons for poor effectiveness, a few key scientists from the agricultural biotech seed industry in South Africa and scientists responsible for preparation of permit applications were questioned regarding their views on reasons for delays in issuing of permits and proposed remedial actions. The questionnaire and responses are depicted in Tables 3-2a and b. Six responses were obtained. The participants were all holders or potential permit-holders who had submitted new applications in the last five years.

Importers of GM grain were also invited. They were dependent upon technical owners obtaining commodity clearance permits. They were not inclined to respond to the questionnaire as they were contemplating a legal dispute against government at the time of the study.

3.3 RESULTS AND DISCUSSION

3.3.1 Criteria

The majority view of the scientists was that some improvements were required to ensure credible governance. In particular, results to responses 'transparency', 'openness', legislation' and 'participation' needed 'some

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improvement'. 'Effectiveness, 'scientific excellence' and 'accountability' needed 'some to much improvement', whereas 'ethical' conduct and 'independency' in risk assessments needed 'none to some improvement' (Figure 3-1).

The results are discussed in more detail in terms of three categories that underpin credible risk governance:

- Functional separation between risk assessment and risk management (policies and procedures);
- Scientific excellence (risk assessors and reviewers, review procedures) ; and,
- Transparency in governance (communication, participation).

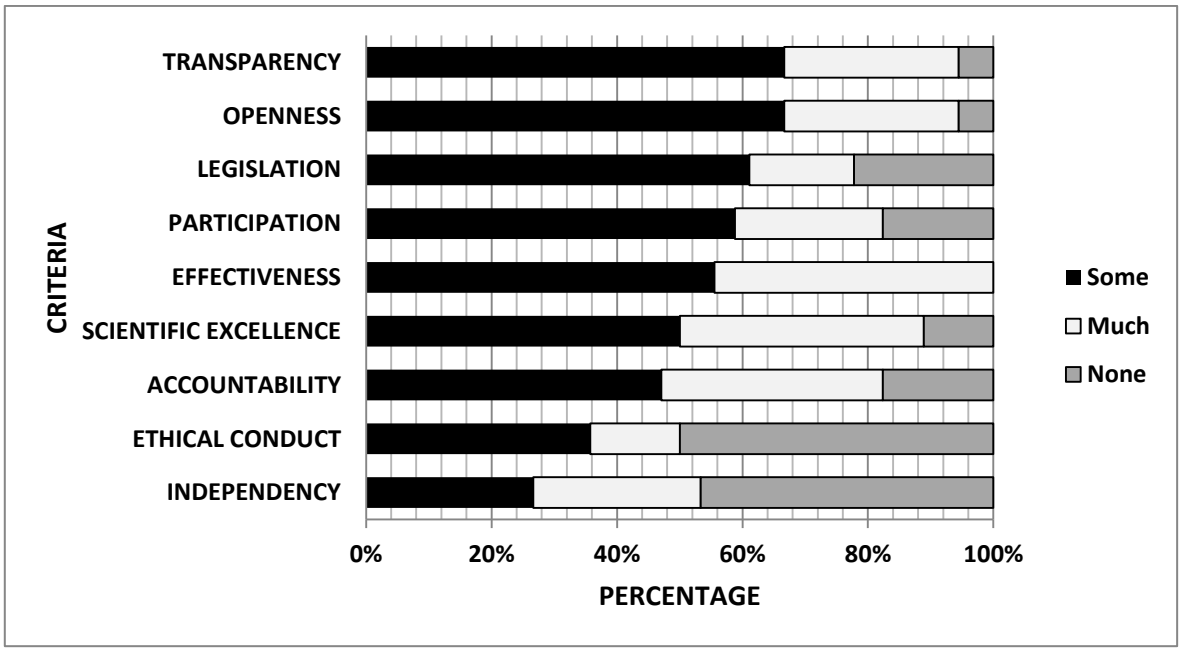

Figure 3- 1: Responses to status of GMO risk governance sorted on 'some improvement needed'

3.3.2 Functional separation between risk assessment and risk management

The legal framework for governance of GMOs in South Africa provides for functional separation between risk management and risk assessment (South Africa 1997).This brings South Africa in line with Codex guidelines (CAC 2011), and also with the most developed examples of independency in risk governance, for example the European Food Safety Authority (EFSA website information online).

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Almost all responding South African scientists agreed on the importance of separate roles for the EC (Table 3-1b, 10.5) and AC (Table 3-1b, 10.3), but felt that some improvement was needed in clarifying those roles (Figure 3-1, Table 3-1a, 3). The statement 'EC members do not have a role as reviewers of risk assessment data/information' (Table 3-1b, 10.4) created some disagreement (21% disagree, 67% agree, 12% unsure). Some felt that government by virtue of its own legislation has a responsibility to conduct independent reviews. This is indeed the case with proactive South African environmental legislation (South Africa 2004) and is now included in the amendment to the GMO Act (South Africa 1997). One respondent felt that 'the legislation needs some work' – the DEA calls for 'coordinated regulations of GMOs, but undertakes its own risk assessments'. The respondent suggested that 'the AC …will undertake a complete risk assessment of all safety issues. The EC members must address non-safety issues, such as cultural impact, loss of traditional knowledge, impact on trade and labour, etc.'

Independency as a criterion for credibility was regarded as important. The majority of respondents (92%) agreed that risk assessment should be conducted independently from risk management (Table 3-1b, 10.2). Respondents also agreed that risk assessors were independent and not subject to pressure from policy makers or stakeholders, and that the members of the AC were acceptable to most respondents (Table 3-1a, 4). One area of future concern, though not identified by respondents to the questionnaire, is that representation on the AC in terms of the amended GMO Act may include two officials representing the 'undefined' public sector (South Africa 1997). Presumably, they could be from semi-state institutes or government departments. The concern is that government officials are bound by political policy and may not be regarded as independent.

A specific characteristic of 'independency' is that the risk assessment should be 'a purely scientific activity' (CAC 2011) and the majority of respondents agreed that this was the case (Table 3-1b, 10.1). This is the requirement in Section 3.3a of the GMO Regulations, which states that applicants must submit a 'scientifically-based risk assessment', repeated in the heading of Section 4 (South Africa 1997). Some sociologists are contesting this view as not completely possible; as risk assessors (or reviewers) would to some extent approach the assessment subjectively (Meghani 2009).This argument is held in favour of more transparency in assessment of risks that need to be considered in new governance models.

Ethical conduct relates to the criterion 'independency from pressure of applicants' and includes 'confidential clearance' and lack of 'conflict of interest'. Some respondents were uncertain of the degree of lack of conflict, probably because names of the sub-committee and most of the AC members were not publicly available (Figure 3-1, Table 3-1a). One respondent remarked that it was impossible for scientists not to have vested interests.

The AC has a general advisory function, but also specific functions prescribed by the GMO Act (South Africa 1997). Respondents gave strong support for specific functions in addition to reviewing of dossiers. These

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included advising on uncertainties and disagreements at EC level (Table 3-1b, 10.6, 100%), being proactive by proposing specific activities and projects (Table 3-1b, 10.7, 91%), and initiating new policies pertaining to assessments, for example guidelines (Table 3-1b, 10.9, 92%). Such pro-activity exists in the self-tasking functions of the EFSA. Availability of competent scientists could be a limiting factor for members of the AC as they are mostly employed full time by universities or research institutes and though appointment to the AC is a prestigious position, their available time is limited. The respondents felt that there seemed to be a need for more risk assessors (reviewers) (Figure 3-2a).

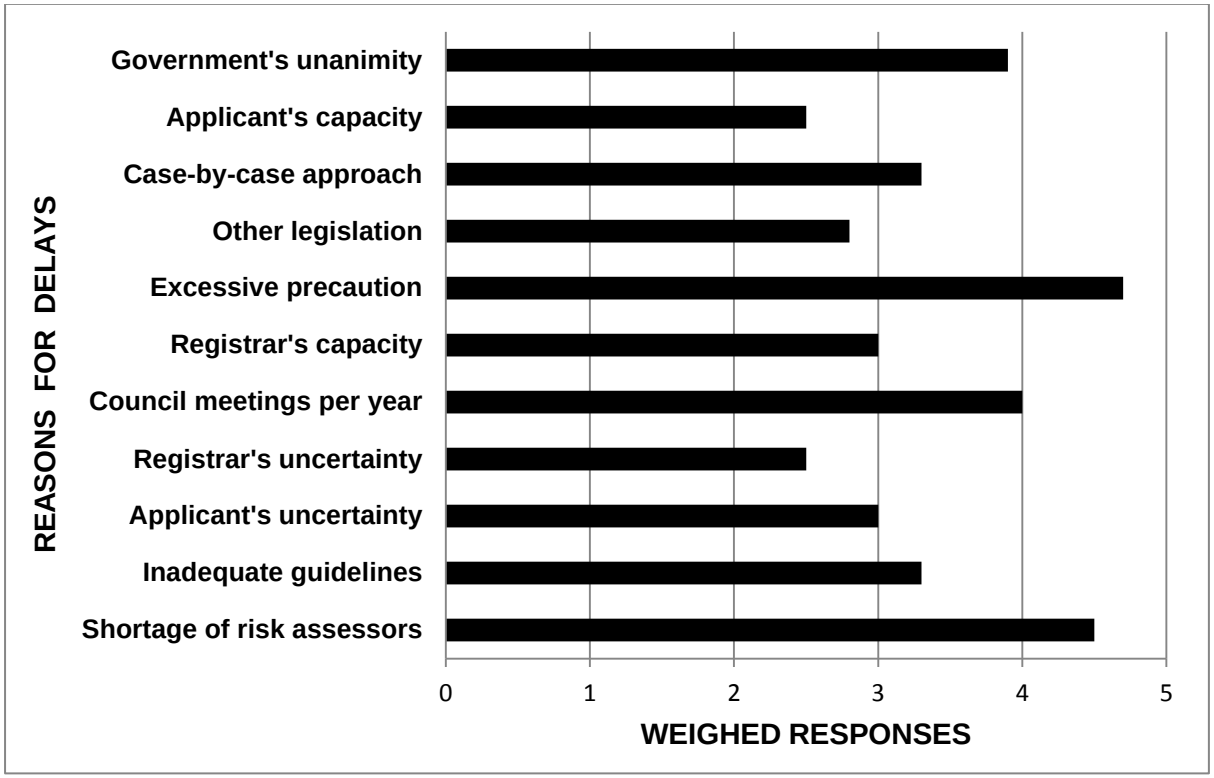

Figure 3-2 a: Responses from the agricultural biotechnology industry / applicants on the reasons for delays in approval of GMO permits.

Respondents highlighted the need for improved effectiveness in the regulatory system. Only a few procedures were touched on in this study, for example managerial responsibility such as planning (Table 3-1a, 2) and decision making (Table 3-1b, 10). Effectiveness was reflected by the time taken to reach a decision on the issuing of a permit, for example approvals for commodity clearances were delayed from 2005 until 2011. A number of reasons for delays were given (Table 3-2a). There seemed to be inconsistency in requests for more information from different panels or similar information repeatedly requested, and requests for additional information not requested before. Excessive precaution in decision making, shortage of risk assessors, infrequent EC meetings, no unanimity in government departments on national policy; and inadequate guidelines were cited as main causes. However, on the contrary, this study did not consider, for example, the need for

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improvement of quality of dossiers and more training of applicants as often experienced in regulatory situations (FWJvR, former regulator). An example of poor quality and incompleteness of a dossier was the case of a banana application (African Centre for Biosafety (ACB) 2011). Effectiveness of the regulatory system needs addressing in detail.

3.3.3 Scientific Excellence

The quality of risk assessments appeared to require substantial improvement (Table 3-1a, 5). Codex guidelines were generally followed and the opinion was that international guidelines were being adhered to (Table 3-1a, 5.7, 5.9). It is possible to conclude that a reviewer with less experience tends to request much more additional information than an experienced reviewer. Reviewers undertake their tasks independently and therefore may form a variety of opinions. There is little opportunity for reviewers to discuss among themselves or for inexperienced reviewers to learn from their more experienced colleagues. In these circumstances it may also be that Codex guidelines are interpreted differently by different reviewers. It is also unclear what approaches to risk assessments are followed: the comparative risk analysis approach (CAC 2009, Kuiper et al. 2001) or a toxicological risk assessment (Millstone, Brunner & Mayer 1999). Excessive precaution in decision making was identified as main reason for delays in approvals (Figure 3-2a). Training of risk assessors (reviewers) and decision makers was considered an important remedial action (Figure 3-2b).

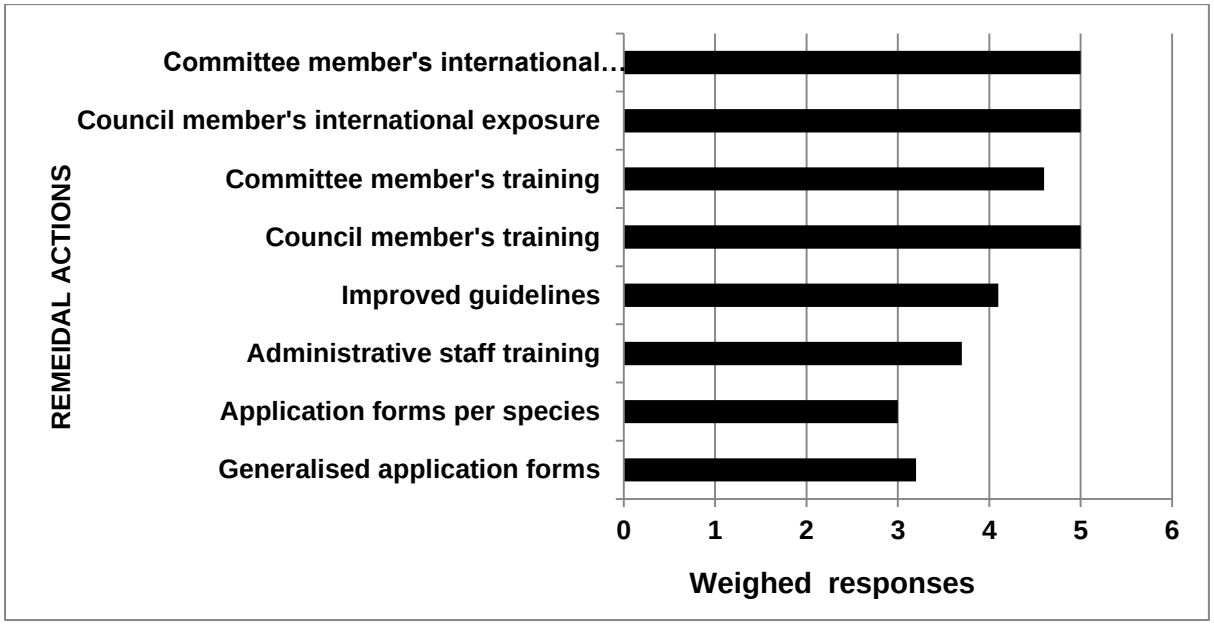

Figure 3-2 b: Respondents from agricultural biotechnology industries/applicants on proposed remedial actions for delays in GMO permit approvals.

All respondents agreed on the importance of peer review of risk assessment reports (Table 3-1b, 11.1) and that a single multi-disciplinarian could not replace a team of specialists (Table 3-1b, 11.2). The current procedure

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(South Africa 2008) is to appoint, on a case-by-case basis, a panel of three reviewers from the AC subcommittee with a member of the AC as chairperson. Each reviewer's report and recommendations are included in a final report to the EC. Additional information may be requested from the applicant by the reviewers. It is not clear from the guidelines (South Africa 2008) DAFF, online) whether the full AC meeting would discuss or review the final report. The procedure seems to emphasise 'reporting' rather than 'reviewing'. The EC would consider the AC reports, public inputs, as well as reviews from the government departments. This moved final reviewing to the EC rather than to AC level. The current procedure reduces time taken for finalising initial reviews, but could lead to inconsistent recommendations and requests for more information, causing delays, as identified in the second questionnaire (Table 3-2a). Adequacy of expertise within small panels to cover a number of disciplines such as both food and environment issues in general release permits may be a constraint. These may be too broad for the small panel to cover, although additional expertise could be co-opted. An option would be to conduct peer reviewing at the level of the full AC meeting where a greater diversity in expertise is present. Another option would be to conduct reviewing by focused sub-panels. Against this approach, one respondent remarked that 'there is also a need for overall multi-disciplinary understanding as opposed to over-specialised'. Peer reviewing needs to be critically investigated for optimisation of this process.

Respondents agreed that a PhD degree with at least three years of experience or an MSc degree with at least five years of experience in relevant disciplines seemed adequate for eligibility for the AC. There was no consensus on the particular number of reviews that should have been handled before being nominated (Table 3-1b, 11.6 to 11.8). Countries such as Brazil require a PhD degree as minimum qualification. That may not be a practical suggestion because of lack of capacity at this stage in South Africa.

The respondents identified the lack of sufficient adequately trained risk assessors as a problem (Table 3-1b, 5.1; Figure 3-2a). Reasons could be the poor remuneration, which is considerably lower than that stipulated in the guidelines of the South African Council for Natural Scientific Professions (South Africa 2003). It could also be exposure to criticism or lack of interest or inadequate time allocated. Respondents recommended that a detailed roster of potential risk assessors should be kept (Table 3-1b, 11.5). Such a roster of expertise is a requirement of the Biosafety Clearing House (BCH) established under the CPB (Secretariat of the Convention on Biological Diversity 2000) At present no experts from South Africa are listed on the BCH website, despite many names having been submitted, making it difficult to source expertise. In addition, the latest protocol records show that the Ministry of Environment is the national focal point, with only one communication record having been received. This department and the Ministry of Agriculture are listed as competent authorities, and four records and 13 decisions (permit approvals) have been received from DAFF, though more than 350 permits are granted annually (DAFF, online). DAFF's clearing house link seems to be inoperative.

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As a remedial option to address delays, respondents agreed on the need for AC members to have continued exposure to new information, to attend international meetings and conferences, and to be involved in research and new developments in relevant disciplines, including risk assessment approaches (Table 3-1b, 11.3 and 11.4). Training of EC and AC members was regarded as essential to help reduce delays in the regulatory process (Figure 3-2b).

One respondent felt that assessors (reviewers) needed 'contact and input from industry experts and practices'. Industry, especially the multinational industry, has the means to employ world-class specialists to conduct research in specialised areas'. Knowledge and experience of scientists from the industry may be considered in specific cases, according to the FAO/WHO expert group (2006).

International outreach programmes often focus only on regulatory authorities unless the need of risk assessors (reviewers) is brought to their attention. Where skills and experience are scarce, capturing of institutional memory collectively is important. This has not been well exploited in the South African risk analysis framework. Coordination is important. The majority of respondents felt that scientists who were members of the AC should be included in government delegations to international meetings/conferences. There seemed to be general awareness of the importance of access to international scientific exposure and the need for improvement (Table 3-2a, 5.3 to 5.5). In a strategic review of Food Standards Australia New Zealand (FSANZ 2003-2004), it was stated that credibility 'was founded on the quality of its science and its scientific risk assessments'. One of the recommendations was that the FSANZ continued to forge strong linkages with international experts and other regulatory agencies. FAO (FAO/WHO 2006) confirmed continuous exposure to international developments was important.

3.3.4 Transparency

The majority of respondents rated transparency as needing some improvement. The questionnaire tested a few pertinent issues, namely clear procedures; communication of uncertainty; and identification of the risk assessors (Table 3-1a, 9.1-3). The need was identified for some improvement in all three areas. Procedures, guidelines, application forms, and permits are adequately published on the website of the DAFF, but there appears to be a lack of transparency in EC decision making. The minutes of the EC meetings are too cryptic, suffer delayed listing, and risk assessment recommendations are not available. The Promotion of Access to Information Act (South Africa 2000a, p.2), which aims to 'foster a culture of transparency and accountability', provides at a nominal fee a legal opportunity to demand for information. Compared to the extent of accessibility of reports in Food Standards Australia New Zealand (FSANZ online), the Australian Office of the Gene Technology Regulator (OGTR, online) and EFSA (EFSA 2006, 2009), South African website information (DAFF, online) is limited.

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3.3.5 Participation

The majority of respondents agreed that stakeholder participation regarding the evaluation of the potential risk in the context of socio-economic impact was invaluable (Table 3-1b, 12.4). Participatory procedures are not new to South African decision making, but a new concept to the risk analysis process. In general, respondents indicated that significant improvement was needed for participation in the South African system, including participation in policy development and risk assessment (Table 3-1a, 8). All respondents agreed that risk analysis policies should be developed in collaboration with stakeholders (Table 3-1b, 12.1) and that communication was important (Table 3-1b, 12.2). Opportunity for public input is included in the GMO Act (South Africa 1997) which should be exploited in a structured way.

In line with Article 26 of the Cartagena Protocol on Biosafety (CPB) (Secretariat of the Convention on Biological Diversity 2000), the GMO Act includes provision for socio-economic assessment as part of the risk analysis. This may include cost-benefit and risk-benefit comparisons, but Section 5.1 in the regulations is extremely vague on required, but undefined, consideration of the socio-economic impact on biodiversity, access to natural resources, cultural traditions, knowledge, and practices. The majority (75%) of respondents agreed that socio-economic analysis should take place prior to decision making (Table 3-1b, 10.14). At this point 'opening up the governance process through public participation' (Ely et al. 2009, p. 25; CEC 2000) would be important. Stakeholders may contribute to 'democratic' decisions of the risk managers at some stage in the process. One respondent stated that 'non-safety issues should be considered by the EC (mandate to review) and not the AC (focus on safety and science). Non-safety issues are relevant only to general release, not to contained or confined activities, which are experimental and short term'. Another respondent commented that 'socio-economic effects should have a minor influence on risk decisions'. Although socio-economic issues may be addressed as a requirement of the GMO Act (South Africa 1997) little information regarding the procedures and requirements for socio-economic analysis is available.

3.3.6 Limitations of the model

- Statistical analysis of the survey although the ideal way of analysis, is not possible with small target groups. This is unfortunately the case with a much specialised field such as risk governance of GMOs in a country with limited resources. In an almost similar study by Wentholt et al. (2009) on the risk analysis of GMOs, only 33 out of 106 invited European respondents participated and 19 out of 60 international non-EU participants. They were from a range of professions and occupations.
- The experience of regulatory authorities in the process of risk assessment is of great importance to identify needs of applicants and would have contributed to an assessment of the system

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- One deficiency identified in the study is the opinion of regulators on the degree of professionalism in completion of applications and provision of required information.
- The responses should largely be regarded as 'perceptions'. Experiences of the respondents are real, perceived, or from hearsay. Perceptions are valid observations that can be changed by improving the system and need be taken into consideration in participative policy development, particularly on sociological matters.
- This study illustrates the part of some stakeholders at the time of the study. This may change with time for the same group. A group (different segment of the population) with priorities other than marketing of their products may have a different perception of credibility.
- The contents of the questionnaire are not within the experience of most consumers.
- The study should be regarded as preliminary as a more balanced opinion would include the experience of those intimately involved in South African risk governance of GMOs according to the criteria. They should include regulatory authorities, and advisors to government as well as members of the AC.

3.4 CONCLUSION AND RECOMMENDATIONS

This paper sets out to answer the question: How credible is governance of GMOs in South Africa as perceived by scientists with knowledge of the system?'

In general, respondents felt that 'some to much' improvement is necessary to ensure credibility. An analysis of the GMO Act, policy guidelines and delays in issuing of permits, as well as available information on the implementation of the act, confirmed the perceptions. Based on these results an indication is given where improvements are most needed to increase credibility of the system.

Although functional separation of risk assessment (AC) and decision making (EC) has been achieved in the South African legislation, the scope of decision makers' responsibilities needs be clearly defined as it seems that the EC still functions according to intentions of the 'technocratic' model that may override recommendations by the advisory body. This could cause increase in the workload and may be outside the expertise and mandate of some EC members, resulting in further delays in decision making.

A clearly identified deficiency was excellence in performance. This implied the need for improved review processes, and elimination of delays. The degree to which potential poor preparation of application forms contributed to delays could not be assessed due to lack of participation by regulators. Continued constructive exposure to new information, research and/or development as well as training of both decision makers and risk assessors were identified as priorities. Improved guidelines that address new challenges such as assessment of stacked traits need urgent attention.

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Many aspects of transparency really need some improvement. 'Participation', in particular, as a democratic principle, has not yet been clearly developed in South African governance of GMOs. This includes stakeholders and scientists' contributions to framing of the assessments. Framing includes scientific inputs, policy development on various matters, for example scientific approaches to risk assessments and socio-economic impacts and cultural considerations. New research on how to address participation by stakeholders at different stages of risk analysis needs attention.

Government has to consider development of integrated strategies and policies for good governance to achieve greater credibility of risk assessment of GMOs, not only for the risk assessment component itself, but also for all other components of governance. These should include:

- Harmonisation between government departments in the approach to risk analysis, taking into account the National Strategy for Biotechnology for South Africa (South Africa 2001) and including policy issues such as the approach to precaution.
- Policy on training, recruitment and remuneration of risk assessors (South Africa 2003).
- An additional step could be considered in the iterative process of risk analysis as described by Codex for development of risk assessment policy that could give direction according to national strategy and good governance policies.
- The majority of the criteria of good governance could be grouped as communication related, transparency, participation, openness. Therefore, improved communication is critical.

Although the credibility of the South African governance of GMOs could be improved, it has certain strengths that could be applied to other risk analysis systems. Functional separation of the risk assessment and decision making as contained in GMO legislation could be followed as an example to ensure scientific integrity; however, implementation of new legislation with respect to risk assessment such as for pesticides should be critically considered with the necessary awareness of good risk governance to ensure credibility of decisions.

A limiting factor that could bear on credibility of any system is availability of experienced risk assessors as peer reviewing of information is critical. The use of regional or sub-regional independent experts could be considered while in the meantime, educating and training of local candidate risk assessors should be a priority.

In general the robustness of the governance of GMOs is reflected in the track record of safety since 1990, as no significant impact from accidents or adverse effects on humans, animals or the environment have been recorded. Trust and confidence will depend largely on the introduction of more democratic governance for both GMOs and other food safety matters.

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Table 3-1a: South African GMO risk governance: Scores for credibility criteria and sub-criteria. (NI: no improvement needed; SI: some improvement needed; MI: much improvement needed; DNK: do not know)

CRITERIA	SUB-CRITERIA	NI	SI	MI	DNK	TOTAL
1	**Legislation**	4	11	3	1	19
1.1	Following the latest international model of Risk Analysis	4	12	3	3	
2	**Effectiveness**	0	10	8	1	19
2.1	Clear roles in the legislative processes	7	11	5	1	
2.2	Evaluation of future impact	2	13	7	2	
2.3	Past experience, where possible	3	14	4	3	
2.4	Clear guidelines	3	13	7	1	
3	**Accountability**	3	8	6	3	20
3.1	Clear roles in the legislative processes	4	12	4	3	
3.2	Clear roles in the executive processes	3	12	5	3	
3.3	Clear roles for risk assessors	4	10	5	3	
3.4	Parties to assume responsibility for their roles	1	8	9	5	
4	**Independency**	7	4	4	4	19
4.1	No pressure on risk assessors from policy makers	10	5	3	5	
4.2	Risk assessors acceptable to all parties	7	8	3	5	
4.3	No pressure from stakeholders on risk assessors	9	7	3	4	
5	**Scientific excellence**	2	9	7	1	19
5.1	Enough suitably qualified specialist risk assessors	3	10	8	3	
5.2	Peer-reviewed assessments of scientific information	4	13	4	3	
5.3	Best use of available information systems	1	13	6	4	
5.4	Consulting with international organisations	0	13	3	8	
5.5	Networking with national food safety authorities	1	9	6	8	
5.6	Consulting with independent experts	1	13	4	6	

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5.7	Risk assessments: international standards/guidelines	5	11	3	5	
5.8	South Africa accredited laboratories	2	11	7	4	
5.9	International standards	4	12	3	5	
6	**Ethical conduct**	7	5	2	5	7
6.1	Risk assessors do not have a conflict of interest	9	8	2	5	
6.2	Risk assessors have confidentiality clearance	8	4	1	11	
7	**Openness**	1	12	5	1	19
7.1	Interaction with stakeholders	4	11	8	1	
7.2	Decision making	3	8	12	1	
8.	**Participation**	3	10	4	2	19
8.1	Inclusive approach	3	10	9	2	
9.	**Transparency**	1	12	5	1	19
9.1	Clear procedures	3	16	4	1	
9.2	Communicating uncertainty in risk assessment	2	10	8	4	
9.3	Risk assessors' names and qualifications known	4	7	5	8	

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Table 3-1b: South African GMO risk governance: Scores for statements on credibility (%)
(AC: GMO Advisory Committee: EC: GMO Executive Council)

NO.	STATEMENTS	TOTAL RESPONSES	AGREE	DISAGREE	UNSURE
10	**Policies and Procedures**				
10.1	RISK ASSESSMENT of GMO's is deemed to be a purely scientific activity	24	84	16	0
10.2	RISK ASSESSMENT should be conducted independently from risk management (including from political influences)	24	92	8	0
10.3	The role of the AC is to review food/feed safety data of new GMOs and make recommendations to the EC	23	100	0	0
10.4	EC members do not have a role as reviewer of risk assessment data/information	24	67	20	13
10.5	The role of the risk managers, including the EC, is to consider managerial risk options regarding risk assessments as proposed by the AC	24	92	4	4
10.6	Any uncertainty / disagreement/need for more information regarding scientific issues should be referred back to the AC for advice before final decisions are made at EC level	24	100	0	0
10.7	The AC should be more pro-active by not only advising on proposals for specific activities or projects but also make proposals in this respect	22	91	9	2
10.8	Lack of policies on some regulatory matters	24	63	8	29
10.9	The AC should initiate new policies pertaining to assessments, e.g. guidelines for risk assessment requirements	24	92	4	4
10.10.	The function of the AC should include the development of guidelines for regulatory risk assessment requirements	24	96	4	0
10.11	Case-by-case assessments could result in uncertainty in regulatory requirements	24	50	46	4
10.12	Guidelines for regulatory requirements of GM food and feed safety should have more detail	24	71	13	17
10.13	Too many separate application forms	24	29	33	38

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10.14	An EVALUATION step to consider socio-economic effects and benefits, should be included in the pre-regulatory assessment, before the managerial decision making step	24	75	17	8
10.15	The AC should receive more legal status as an independent advisory body	24	42	25	33
11	**Scientific excellence**				
11.1	Peer-reviewing of information is very important	24	100	0	0
11.2	A single multi-disciplinarian cannot replace a team of specialists	24	100	0	0
11.3	Risk assessors should be involved in research to remain in touch with science	24	79	17	4
11.4	The AC specialists should be included in the government team to international meetings/conferences	24	92	4	4
11.5	South Africa should keep a roster of all details of potential risk assessors for GMOs	24	88	4	8
11.6	PhD-degree qualification with at least 3 years' experience in the relevant discipline	23	87	13	0
11.7	MSc-degree qualification with at least 5 years' experience in the relevant discipline	24	75	21	4
11.8	To be nominated as a member of the AC, the specialist should have conducted at least 10 GM food/feed safety assessments	23	39	39	22
12	**Communication (transparency, openness, participation)**				
12.1	RISK ANALYSIS policies should be developed in collaboration with stakeholders	24	100	0	0
12.2	Stakeholders communication in risk analysis of GMOs in important	24	100	0	0
12.3	Stakeholder participation in the scientific reviewing of company information is not acceptable	24	42	29	29
12.4	Stakeholder participation regarding the evaluation of the potential risk in the context of socio-economic impact is invaluable	24	71	17	12
12.5	Commencement of risk assessment of new GMOs should be announced in the media	24	38	54	8

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12.6	The risk assessment report of the AC should be made available to the applicant for comments to be considered by the EC	24	92	8	0
12.7	The risk assessment report of the AC should be published for information	24	62	25	13
12.8	The final approved report of the EC, including risk analysis decisions as well as socio-economic and benefit considerations, should be published on the internet/media for public information	24	75	17	8
12.9	There should be an opportunity for objections/comments to decisions of the GMO Council	24	84	8	8

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CHAPTER 4: IMPROVING SOUTH AFRICA'S GMO RISK GOVERNANCE BY CONSIDERING NEW ASSESSMENT APPROACHES: BIOFORTIFIED SORGHUM CASE STUDY.

ABSTRACT

Applicants who apply for regulatory approval of genetically modified products in South Africa are concerned that the requirements for regulatory approval of GM crops are becoming more stringent and protracted, resulting in increased costs for research, development and commercialisation. Lack of clear risk assessment approaches reflected in legislation lead to demands for information that is not necessarily relevant to risk assessment. An analysis of South African GM regulatory instruments and proposals regarding risk assessment was conducted with an improved approach to risk hypothesis and steps in problem formulation in mind. A better understanding of comparative risk assessment in the context of the proposed risk hypothesis and problem formation approach may result in more realism regarding the inclusion or exclusion of particular studies. The South African regulatory assessment for approval of a permit to conduct contained research with biofortified sorghum is evaluated with a perspective on the proposed approaches. Implementation of the proposed approaches may require changes in the governance structure.

KEY WORDS: Safety assessment, comparative risk assessment, problem formulation, genetically modified organisms.

4.1 INTRODUCTION

The advent of molecular genetics and modern biotechnologies has brought new knowledge, new beneficial applications and updated regulatory systems to ensure comparative safety to humans, animals and the environment. It has also brought polarised debates and trade barriers. The focus of debate has centred on genetically modified (GM) crops, while biosafety requirements have become more demanding as crop technologies have become more complex.

Increased biosafety requirements, delays in decision making and rising costs of compliance with regulations are being experienced in many countries, although modern crop biotechnologies have been identified as one of the solutions to increase food production to ameliorate food insecurity in developing countries (Pretty et al. 2010). Jones (2011) and Beachy (2011) complained about excessive regulatory requirements, resulting in multinationals maintaining their monopoly while no new products have been released to the market from universities for more than 10 years, in part 'because of the time and cost necessary to bring the new product forward' (Beachy 2011, p.5). 'Unfortunately, this situation is 'influencing policies in developing countries and retarding the deployment of solutions to the problem of food availability and quality' (Jones 2011, p1814).

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South Africa follows a cautious approach to the regulation of GMOs. The current GM governance framework is mainly through the GMO Act (No. 15 of 1997), as amended in 2006 (South Africa 1997). It now complies with requirements of the Cartagena Protocol on Biosafety (CPB) (Secretariat of the Convention on Biological Diversity 2000), and confirms special conditions for environmental risk assessment (ERA) and environmental impact assessment for transboundary movement of living modified organisms. The GMO Act is administered by the Department of Agriculture, Forestry and Fisheries (DAFF). The importance of protection of the environment echoes the concern of the Department of Environmental Affairs (DEA) (South Africa 2004). The GMO Act is based on a permit system, application for which is assessed by a scientific advisory committee and an official GMO Executive Council (EC) that makes decisions. South Africa has not been isolated from international trends. Constant objections to, and appeals or litigation against, government decisions, and requests by the EC for additional information, have delayed permit decisions (DAFF 2006-2012). Applicants have voiced their concerns over the delays, while results from an initial survey showed certain areas in the regulatory system contributing to the problems experienced (described in 4. 2.1, 4.2.2). All new applications for permits are subject to risk assessment, followed by decisions made by the regulatory authorities. Ambiguity in regulatory approaches to risk assessment and decision making are likely to contribute to delays. This paper strives to outline 'best practice' approaches applying to risk assessment which it is hoped will assist the South African regulators, reviewers and applicants to undertake their duties more effectively and efficiently. The indication of problem areas resulting from two limited surveys, as well as the example of repeated delays on an application for experimentation with bio-fortified sorghum and the eventual termination of the South African leg of the project, suggested that an analysis of risk assessment approaches would be helpful in identifying areas of possible conflicting approaches and information required for implementation of risk assessment analyses, between regulators themselves, as well as among regulators, reviewers and applicants.

The research reported and discussed in this article is based on findings in a very dynamic environment of governance that continues to change. It appears that an intention by the South African government to improve on the reported system is already in process. However, the information reported here could be a further stimulus to direct changes to improve governance.

4.2 SURVEYS ON OPINIONS OF STAKEHOLDERS AND SCIENTISTS

Two preliminary surveys were conducted by way of questionnaires in 2008 and 2009. These studies are described in Chapter 3. One study focused on scientists from industry, public research and academic institutions; and the second aimed at key scientists responsible for submitting agricultural GM applications. Evaluation of elements of good risk governance covered ethical conduct, accountability, independency, participation, openness, transparency, excellence, and effectiveness. Response numbers were low: 24 for the first questionnaire and six (all permit holders) for the second.

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The limited number of responses precluded the use of statistical analyses to rate the most important problem areas in regulatory decision making. Yet, the key issues that were highlighted, were regarded as sufficiently important to justify looking in more depth at South African risk assessment and decision making processes. By analysing the two sets of responses, the key issues are summarised below.

4.2.1 Aspects of the regulatory structure

- Risk assessment and decision making should be functionally separated.
- Independence between risk assessment and risk management is necessary, and risk assessors must also be independent from officials and industry.
- More stakeholder participation is needed in drafting policies and application forms.

4.2.2 Aspects affecting risk assessment

- Effectiveness, including guidelines, needs much improvement.
- Assessments must remain science based.
- Apparently extreme precaution is a major contributor to delays.
- Excellence in risk assessment needs much improvement.
- More transparency is required in application forms and procedures.

The responses could be summarised as 'some to much improvement is necessary'. Aspects of regulatory structure and the precautionary approach are not discussed in this paper. The aspects affecting risk assessment, which are the focus of this paper, relate to poor communication regarding policies, approaches, guidelines, application forms and procedures. Insufficient communication on these matters may cause delays in and even denial of approval of permit applications.

4.3 DELAYS

The exact number of years taken to receive approval for general release of GM crop plant products, all from multinationals, is impossible to establish because the minutes of the GMO EC meetings have been available only since 2006, whereas the first application for general release was submitted in 1995, before the current GMO Act came into force. Delays in more recent South African national and academic research applications show worrying results (Thomson, Shepherd & Mignouna 2010). An example is the delay in permit approval for a sorghum study (Table 4-1). Containment and trial release applications have been held up for several years, with many referrals for more information, and resulted in appeals. According to some researchers, planting seasons have been missed because of these delays, funding has stopped and some researchers have resigned.

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Reasons for non-approvals varied, but were often socio-economic and trade related. No details of the decision are given. These requirements may not have been foreseen at the time that the research commenced. A trend towards more stringent assessment requirements occurred over time, which might be ascribed to consumer concerns and greater activity of anti-GM groups (Wolson 2007; Paarlberg et al. 2000). Guidelines for direct consideration of socio-economic issues are still to be developed, and could be very complex because of the diversity of the South African population and economics, including small-scale farming practices. The influence of trade-related issues resulted in long delays in approval for commodity clearance from about 2006 until 2012 (DAFF 2006-2012).These delays were partly caused by opposing inputs from grain farmers and grain importers, and partly by the Department of Trade and Industry wanting to draft a trade policy framework. Two cases that point to environmental concerns are the applications for experimental work on sorghum and cassava, as well as food/feed risk assessment interpretations affecting the *Bt* potato (SpuntaG2) decisions (Thomson, Shepherd & Mignouna 2010). The latter case is presently (2012) sub judice because of an appeal by the ARC against the EC refusing a permit for general release.

It could be asked why most requests originating in South Africa for GMO permits resulted in non-acceptance and consequent appeals, whereas all applications from multinationals were eventually approved. One reason could be that the focus of multinationals in South Africa is on major commercial crops: maize, soybeans and cotton on which they have gained much experience in regulatory issues worldwide and normally follow requirements of countries with the most stringent requirements, particularly European countries. Other crops (potato, sorghum, grape, cassava, sugarcane) are the focus for improved traits in South Africa. There is relatively less experience in these crops at both the regulatory authority and local applicant level, as will be discussed in the sorghum case study. This paper provides an analysis of recommended approaches to risk assessment and suggests some improvements that would make the regulatory process more efficient and effective, and could reduce appeals against decisions by the EC.

4.4 ASSESSMENT OF SOUTH AFRICAN GMO LEGAL INSTRUMENTS

National legislation and legal instruments provide the goals, scope and boundaries for risk assessments and risk management (Table 4-2). An analysis of the South African legal instruments indicates some causes of the problems, in particular shortcomings in communication resulting in negative consequences to applicants of GMO permits.

4.4.1 The GMO Act

The GMO Act is the central piece of legislation (South Africa, 1997 as amended in 2007). There are several changes from the 1997 Act that may be regarded as contentious.

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- The preamble sets a balanced approach, namely, 'to promote the responsible development, production and use of GMOs'. This is in alignment with the National Biotechnology Strategy for South Africa as the latter promotes biotechnology (South Africa 2001).
- The amended act defines biosafety as level of risk management to 'avoid potential risk' (Section 1(c). This is contradictory to use of 'limit' or 'reduce harm' terminology.
- Section 7 states 'consensus by all' council members (this means unanimity and failure to reach consensus will mean a refusal of the application. This implies that if one government department of the six is not represented at the meeting or opposes approval, the application is refused.
- Some of the terms provided by the CPB (Secretariat of the Convention on Biological Diversity 2000) require clear definition, such as 'adverse', 'loss or damage', 'delayed', 'not lower than the level of protection'.

Although the GMO Act is administered by DAFF, no mention is made of any agricultural matters such as comparative agronomic approaches or familiarity with agricultural practices except that an assessment of animal health is now included. The Regulations give some guidance on the steps in risk assessment but no approach is identified (DEA n.d.). The act does give scope to applying a problem formulation approach if contradictory terminology is corrected.

4.4.2 Application forms

There have been no changes at the time of the study to the GMO application forms for general release, commodity clearance and trial release permits under the GMO Act since they were first brought into practice in the early 1990s, except in 2010 for requests for additional information on endogenous allergens. However, this does not mean that the required information and data are still the same. It is not possible to confirm that additional questions from the regulator have increased the requirements since the first GMO was approved. The questions are open ended, and do not indicate an approach to be followed for the risk assessment. This leaves the applicant free to decide on any approach. In an interview with a senior member of the DAFF, it was explained that a wide range of approaches was welcomed (Director: Biosafety, personal interview, 4 March 2010).This loose basis for assessment may promote divergent interpretations between government departments, between reviewers and between the applicant and the EC.

Aspects such as socio-economic considerations still need to be addressed in detail.

4.4.3 Food safety

South Africa's GM-food safety requirements are according to Codex Alimentarius guidelines, and the DEA guideline to environmental risk assessment (DEA n.d.). Socio-economic goals such as national policies and

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strategies need also be taken into consideration. Some of these could include food security, job creation and agrarian sustainability (DAFF 2012).

4.4.4 Environmental safety

A number of contentious issues are noted in DEA's environmental legislation (South Africa 2004) as well as the ERA framework for GMOs (DEA n.d.).

- Reiteration of inconsistent use of terminology and interpretation of ideal level of risk as zero (DEA n.d.), whereas in scientific terms zero risk is non-existent (Wolt 2008; Querci et al. 2008).
- GMOs are grouped as 'other threats' to the environment under environmental legislation. Should the Minister of DEA have reason to believe that a GMO may pose a threat to the environment, the Minister (of DEA) 'must convey his or her belief ... before the application for the relevant permit is decided'. This applies to trial release or general release (South Africa 2004, Chapter 5, Part 3 (78)). It could be interpreted that DEA's position overrules those of other government departments. However, an ERA can only be conducted on approval of a permit; accordingly, a 'stalemate' situation could exist.
- No mention is made of socio-economic benefit assessment or cost-effectiveness.

4.4.5 South African GMO guidelines

In addition to food safety, the guidelines include directions for environmental and occupational safety requirements (DAFF Guidelines). Requirements for ERA are described in checklist format. Use of terminology such as 'harm' concurs with the description in this paper. However, no specific and detailed approach to ERA is indicated. On the other hand, DEA's framework guideline, described above, has a stronger message because of the pertinent legal position that the minister of the DEA is taking. Accordingly, DAFF is in a far weaker position than DEA in consensus decision making.

4.5 CASE STUDY: SORGHUM

The case of the sorghum application for a permit to conduct research in a greenhouse could shed some light on the ways in which decisions are made by the South African regulatory authorities (DAFF 2006-2012) (Table 4-1).

Sorghum is the world's fifth most important cereal crop and staple food for consumers in India, Nigeria and many African states (Andersson & De Vincente 2009). Sorghum, however, is low in several vitamins (OECD 2010) contributing to Vitamin A deficiency. The Grand Challenges in Global Health Initiative, funded by the Bill & Melinda Gates Foundation (close to US$17 million) for development of more nutritious sorghum (increased levels of lysine, vitamin A, iron and zinc) for the arid and semi-arid tropical areas of Africa, is called the African

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Biofortified Sorghum Project (ABS Project). Consortium partners include the South African Council for Scientific and Industrial Research (CSIR), Agricultural Research Council (ARC) and University of Pretoria (CSIR 2009).

Sorghum originated in north-east Africa. Three cultivated species and five races exist. Cultivated sorghum, *S. bicolour* subsp. bicolour, may intercross regularly with its wild progenitors. Johnsongrass, *S. halepensis*, is considered one of the world's most noxious weeds, and introgression by pollen flow between domesticated sorghum and conspecific weedy wild species is well documented (Andersson & De Vincente 2009).

The time lines and EC decisions are listed in Table 4-1. The applicant applied for contained use trials, classified as Containment Level 2 (CL2) with GM sorghum containing high concentrations of lysine. The EC required upgrading of the greenhouse facilities to comply with Containment Level 3 (CL3). The CSIR greenhouse was upgraded and a new application for greenhouse trials was submitted. The application included an argument that CL3 for research with indigenous crops is unprecedented and would set an 'incorrect precedent, hampering future research and improvement of indigenous crops' in South Africa (CSIR 2009; ABS Project).

EC declined the second application in February 2007. The applicant appealed against this decision. An appeal panel was constituted in June 2007. An appeal finding was made in favour of the CSIR. The minister issued a letter 15 months later, notifying the applicant of approval, subject to use of CL3 and new information to be submitted on the medium- and long-term goals. It took another nine months to finalise the permit. The total time taken for approval of the permit was four years (DAFF 2006-2012; CSIR 2009). By that time the donor funding had been suspended and research taken elsewhere (CSIR 2009). Of particular interest is the decision or comments in the minutes that 'the Council also considered the potential field trial release and concluded that it is unlikely that such an application would have been favourably considered'.

The conclusions made from the sorghum case study are:

- The long delays in decision making had detrimental effects on South Africa's national research.
- A precautionary approach by regulatory authorities by requiring a high level of containment is acceptable in theory according to the tiered step approach (Raybould & Cooper 2005; Romeis et al., 2008). That provides for worst-case hazard and exposure at lower levels of 'tiers' to more realistic scenarios at higher levels of 'tiers' (Romeis et al. 2006, 2008). Here, clearly scientists from the consortium that prepared the submission differed from government officials in their opinions on the required containment level of control.
- The permit application was for contained experimentation in greenhouses and not for field trials. The comment on future applications for permits was not a point for consideration. It is unclear whether advice was obtained from the AC or any experts on sorghum for this untimely decision. The deduction is that the EC was unaware at that stage of scientific approaches such as problem formulation in environmental risk assessment.

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- An interpretation of the EC decision on possible adverse effects on the environment with field trials is that, consistent with the extreme position taken in the debate on the precautionary principle, a 'perception' of harm is sufficient reason not to conduct a risk assessment, but instead to demand a high level of containment (CL3). This is described as a 'better safe than sorry' approach (Wingspread 1998). This could be explained by the grouping of GMOs by some sociologists with AIDS as a diffuse source of risk with long-term and extensive implications (Vlek 2010) or as a risk of uncertain probability and uncertain damage such a polar ice sheets (Renn & Klinke 2001).

A common mistake is to equate hazard or exposure with risk (Poppy 2004). Many examples are quoted to illustrate the point (Poppy 2004, Johnson et al. 2006). One such an example is a study by Schmidt and Bothma study (2006). The objective of the was to investigate (1) the crop-to-crop gene flow in *Sorghum bicolour* subsp. *bicolour;* and (2), on the basis of the experimental data, estimate proper distances or buffer zones to avoid gene flow between sorghum crops and their wild relatives (exposure). Of particular importance is the claim that the study suggested a risk to the environment from the release of sorghum. However, this study was planned on a very artificial scenario as it used a male-sterile (cms) inbred as recipient and a male-fertile isoline as pollinator, both flowering at exactly the same time and pollen competition being absent. For the objectives of this study, no information emerged that was not already common knowledge among plant breeders and biologists, including the fact that some crossing between sorghum species is a demonstrated phenomenon. What the study did not reveal was the probability of pollen flow from cultivated sorghum to wild *S. halepense* under conditions of natural pollen pressure in the wild species, and production of viable seeds to give viable species hybrids. Data from the study do not support the conclusion that such outcrossing will be significant and thus presents a risk. A detailed scientific analysis of the report by Schmidt and Bothma (2006) is presented in Table 4- 3.

The contents of the dossier submitted in the permit application for containment trails with GM sorghum are unknown (Confidential Business Information) and one cannot assume that the mentioned study was included or that it erroneously influenced the decisions of the EC regarding possible future 'risk to the environment '.

4.6 RISK GOVERNANCE AND RISK ASSESSMENT

The concept of risk analysis in risk governance received impetus from the publication of the so-called Red Book on the USA system (NRC 1983) and this eventually resulted in greater recognition from international bodies such as the Codex Alimentarius Commission (CAC 2011) in food safety matters. The risk analysis paradigm proposed by Codex has three main components, related in an iterative process of risk assessment, risk management and risk communication. An additional step, risk assessment policy, includes framing the risk issue on hand. This step is an interaction between risk management and risk assessment, which forms the first step in assessment of the risk issue (CAC 2011). These components of governance apply to both food and environmental risks. Risk

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assessment, as such, includes four steps: hazard assessment, hazard characterisation, exposure assessment and risk characterisation (CAC 2011). Risk characterisation is a cross-cutting step between risk assessment and risk management that follows the assessment of risk, according to the risk assessment/risk management paradigm developed by the National Research Council of the USA (NRC 1994). This step is also called risk evaluation, according to the SAFEFOODS proposal (Koenig et al. 2010). With these components in mind, the place for risk assessment of GM food and environmental risk assessment within risk analysis paradigms and according to approaches described in this paper could be visualised.

4.7 APPROACH: COMPARATIVE RISK ASSESSMENT

4.7.1 Substantial equivalence and comparative risk assessment

The toxicity of foods cannot be assessed as easily as chemicals such as pesticides, as they are highly complex, containing many substances. Feeding laboratory animals at high levels will result in nutritional imbalances. 'Substantial equivalence' forms the core of the comparative risk/safety analysis. (OECD 2003; WHO 1991, 1993, 2000; FAO/WHO 1996) The description of substantial equivalence left a great deal of scope for individual and national interpretations and was replaced with a comparative risk/safety assessment, but the basic concept behind it remained untouched (Kuiper et al. 2001; Kok et al. 2008: CAC 2009; EFSA 2008; FAO/WHO 1996; WHO 1991, 1993, 2000; OECD 2003).

Comparative assessment is an approach which is the starting point of a risk/safety assessment of GM organisms (Kuiper et al. 2001). ERA and food/feed assessment follow the same approach of comparison (Craig &Tepfer 2007; Craig et al. 2008). Risk assessment begins with knowledge of the parent crop, donor organism, the DNA with the novel gene(s), the modification process, the GM crop plant, and the receiving environment. The basic elements of the assessment plan for identification of hazards include a comparative analysis of the GM plant with the conventional counterpart, which includes molecular, compositional, phenotypical and agronomical analysis. Wholesomeness studies with appropriate animals are included as an additional measure to confirm the nutrient value of the rDNA plant products. The risk is characterised by an assessment of intended and possible unintended differences between the GM crop plant and the conventional counterparts (OECD 2003; Kok et al. 2008; EFSA 2010, 2011).

4.7.2 GM food safety

The steps in food safety/ risk assessment are summarised in Figure 4-1. Hazard identification of GMOs intended

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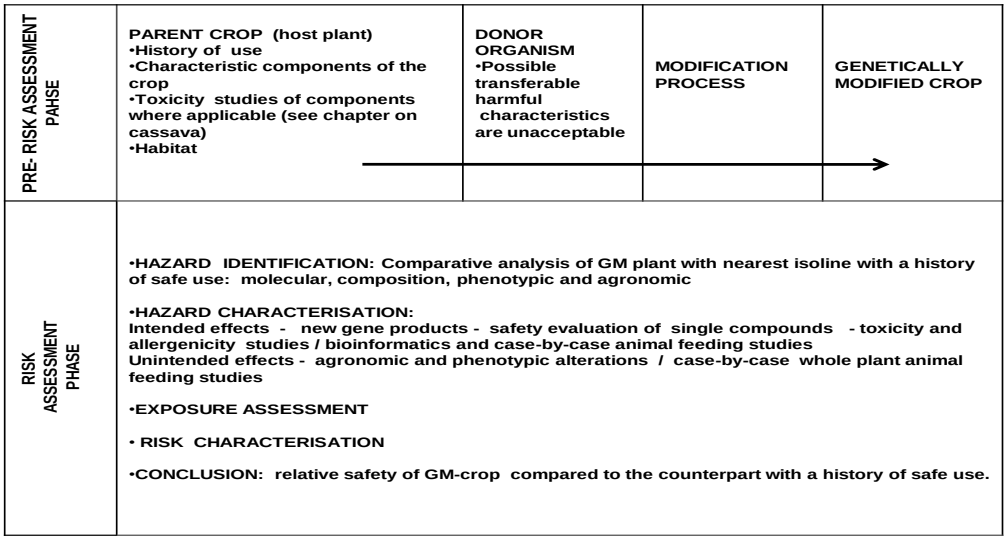

Figure 4- 1: Summary of the steps in GM food safety/risk assessment (CAC 2009)

for use as food or feed consists of a comparison of the GMO with a conventional food plant that has a history of safe use (Constable et al. 2007; Kok et al. 2008; CAC 2009; EFSA 2011). Intended and unintended differences are further researched.

The comparison step is a starting point for a safety assessment. The concept of 'history of safe use' and 'familiarity' invokes precepts of safety, something we are familiar with. Safety assessment is a subjective judgment of acceptable risk, which is value laden and has to be understood in the context of society, culture, politics and economics. It is important to realise that a given level of risk could not be expected to be uniformly deemed safe because of different norms of acceptability of risk in different societies (Wolt 2008).

Objections to this comparative approach suggest that it is not sufficiently objective, and is not meaningful for collective norms because people get used to unacceptable risks, or are shy of new risks, regardless of risk magnitude (Renn & Klinke 2001). The comparative approach is also criticised by those who consider GM foods as substantially different from non-GM foods so that a full 'safety' assessment should be conducted. Substantial equivalence is a so-called 'pseudoscience; the degree of difference between natural food and its GM alternative are not clearly defined and toxicological testing of food from GM crop plants should be done' (Millstone, Brunner & Mayer 1999). Criteria to establish 'biologically significant' and 'not significant' are still being debated (Hilbeck et al. 2011). Raybould (2007, p.590) concluded that critics of the concept of substantial equivalence have misunderstood the concept and fallen into the 'trap of the deficit model' of thinking that more science will automatically lead to better decisions, and that non-scientific judgments have no place in risk assessment. A

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deficit model has been likened to a 'bucket approach' rather than a 'searchlight' approach (Popper 1972; Raybould 2010b, pp.123-133), described in section 4.8.1 below. The concept of substantial equivalence between GM products and their conventional counterparts is intended to demonstrate that GM products fall within the range of natural biological variation, that is, relative and not absolute safety. Raybould's argument is that one should be careful that 'non-targeted approaches simply replace clear risk hypotheses about how transgenic plants may harm assessment endpoints, with null hypotheses of no difference' (Raybould 2007). In a targeted comparative assessment, intended and unintended effects are taken into account rather than trying to identify every possible hazard associated with a particular food (CAC 2009).

A safety assessment of expressed substances is of particular importance. This includes, *inter alia,* donor organism information regarding the genes coding for known toxins or antinutrients that should not be transferred to the rDNA plant, as well as non-protein substances that have not been safely consumed in food. Toxicity and allergenicity of the novel protein are specific assessment requirements for which a variety of tests are recommended by Codex Alimentarius (CAC 2009). This is supplemented with bio-informatic analysis to check for homology with known toxicants and allergens. Tests are often conducted with surrogate proteins produced at high levels in bacteria (e.g. *E. coli*. Arguments have been raised against basing assessments on proteins and not the whole plant (Hilbeck et al. 2011). However, phenotypic and compositional assessment complemented with studies in target animal species to evaluate the nutritive value and performances are instruments that indicate effects on essential endpoints for human safety, but also on environmental safety. No further testing is required if results are of no concern.

Toxicology feeding studies with animals fed on r-DNA plant products are assessed case-by-case. Note should be taken of the disputed value of sub-chronic toxicity in mammalian feeding studies. Strong views are expressed that the need for these studies should be determined on a case-by-case basis when substantial differences are observed in the comparison studies (EFSA 2011; Querci et al. 2008). Applicants often compromise by including 28-day rodent toxicology studies as a substitute for 90-day studies.

Arguments against including chronic and other toxicological studies with whole plant material are that retrospective assessment of data from chronic toxicity studies with rodents and dogs (Betton et al. 1994; Box & Spielmann 2005; Baetcke, Phang & Dellarco, 2005) demonstrated that in many cases the 'lowest and most conservative safety endpoint '(NOEL) came from sub-chronic studies (Munro et al. 1996). Studies to determine the toxicity of chemicals are normally conducted according to the internationally accepted OECD guidelines for testing of chemical substances. Decisions made from these studies are based on results from tests designed with at least three different animal species. In general, additional chronic toxicity studies with GM plants may not add value to the toxicological assessment.

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4.8 APPROACH: PROBLEM FORMULATON FOCUS ON ENVIRONMENTAL RISK ASSESSMENT

Concerns for the environment are related to effects of the GMO plant (stressor) caused by gene flow, horizontal gene transfer, persistence and invasiveness; effects such as weediness; and effects on non-target and target insects/organisms. The assessment of environmental risk fits in the wider environmental risk analysis comprising risk analysis, risk management and risk communication.

More recently, an approach of 'problem formulation' in environmental risk assessment in general received prominence (USEPA 1998) and is now proposed for assessment of GMOs (Raybould 2006, 2007, 2010a, 2010b; Johnson et al. 2007; Fitzpatrick et al.2009; Nickson 2008; Wolt et al. 2010).

4.8.1 Theories about assessment of risks

Two opposing theories of the growth of scientific knowledge need some description when considering ERA. Raybould (2010b) explained them by the metaphors 'bucket and searchlight' (adapted from Popper 1972).

It is commonly considered that the more science is generated, the better and more correct decisions are made, described as the deficit model (Lawton 2007) or the bucket theory (Raybould 2010b). Arguments against this approach are:

- Collecting data to completely understand a natural phenomenon is not the purpose of risk assessment. It causes unnecessary delays and increases associated costs (Raybould 2006, 2007, 2010a, 2010b; Craig & Tepfer 2007).
- Science can make predictions about consequences of certain decisions, but cannot determine whether those are desirable (Lubchenco 1998). If decision makers are uncertain about what is valuable and what is harmful, scientific research will not solve the problem; it may make it worse (Raybould 2010b).

The searchlight theory is in essence a sharp focus in the assessment of those things that are valuable and that one wishes to protect from being harmed. A clear operational definition of harm should relate to stated objectives or management goals of instruments of policy and provide the scope and boundaries of risk assessment (Fitzpatrick et al. 2009). Definitions of harmful effects are of critical importance in risk assessments (Raybould 2007, 2010b). These definitions are formulated upfront in the 'framing step' of the risk analysis. Then follows explicit formulation of hypotheses about how harm may arise, how it should be tested, and the risk characterised (Suter 1990, 1996; Nickson 2008; Raybould 2006, 2007, 2010a, 2010b). Hypotheses of no harm are referred to as 'risk hypotheses' (Raybould 2006, 2007, 2010b). Raybould (2010b) describes a null hypothesis when a) a risk is not characterised and when research simply analyses effects without specifying harmfulness; and b) how harm may arise is not tested.

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4.8.2 Essence of the process in environmental risk assessment

In a paper by a panel of six scientists from five universities and research institutes, a plan is described to assess the potential environmental risks of gene flow from ABS to wild sorghum in Africa (Hokanson et al. 2010). Their argument was that many GM crops being developed to solve agronomic or nutritional problems in developing countries may be grown near centres of origin and diversity of the crop. Lack of experience in assessment on all sides, including regulators, reviewers and applicants, could be problematic. Greater understanding to manage 'gene flow' problems in centres of biodiversity is possible with the advantage of increased benefit to those most in need by following a problem formulation approach (Table 4-3). Applying this approach to problem formulation would narrow down the focus to essential endpoints in the research, excluding unnecessary research and irrelevant conclusions.

A summary of the phases for ERA as promoted by the USEPA (1998) is illustrated in Figure 4-2. The phases have been elaborated on by several authors (Johnson et al. 2006, Nickson 2008; Fitzpatrick et al. 2009; Raybould 2006, 2010; Wolt et al. 2010). Three phases are identified; problem formulation, analysis and

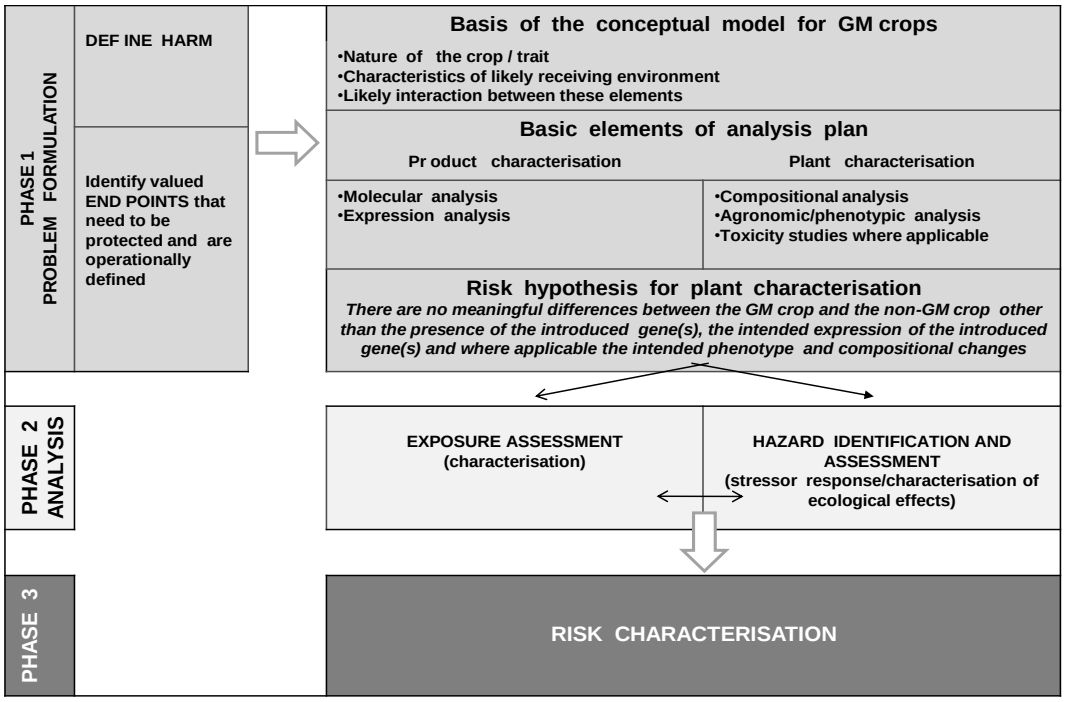

Figure 4- 2: Adapted schematic of problem formulation in the context of the risk assessment process for environmental risk assessments (USEPA 1998) and basic elements of the conceptual model and analysis plan for environmental risk assessment of GM crops (Nickson 2008)

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risk characterisation (USEPA 1998). This may be an iterative process when more questions are asked and new hypotheses tested. The problem formulation phase is relevant for the purpose of the discussion on the environmental risk assessment of sorghum. EFSA (2010) and UNEP (1995) have developed almost similar models for ERA.

4.8.2.1 Problem formulation phase

The starting point of a scientific approach to risk assessment consists of three steps for a case-by-case assessment in the problem formulation phase (Figure 4-2, Table 4-3).

Step 1: *Key issue identification*: Risk managers, risk assessors and relevant stakeholders should agree in a participative manner on the essential issues particularly related to the specific new application for a permit. This step should be strongly guided by national strategies and policies for example on food security and the role that biotechnology could play. The framing step is essential in the analysis to identify key issues and to direct the assessment. These entail decisions about what needs to be protected and how harm may arise as described above. A definition for harm relating to sorghum gene flow is for example loss of valuable genetic diversity in the crop or compatible species The defining of assessment endpoints follows, which depend on the management goals of legislation (Suter 1990). Endpoints are different from goals, as endpoints should be accessible to prediction and measurement, for example extinction or abundance of the wild sorghum population (USEPA 1998; Suter 1990).

Step 2*: Conceptual model*: Questions are defined that describe plausible sets of scenarios that warrant detailed assessment. This includes information on the nature of the stressor, its proposed use, reasonable pathways where exposure occurs and potential resultant responses by the assessment endpoints.

Risk hypotheses are then defined to propose answers to reasonable questions about how the assessment endpoints will respond to the stressors

Step 3: *Analysis plan*: This step narrows down the data needed and the approach to be taken for data acquisition and synthesis. The endpoints to be measured are selected and the hypotheses are prioritised

4.8.2.2 Analysis phase

The next phase is testing risk hypotheses for hazard identification (stressor response) and exposure assessment. During this phase the two components of risk, exposure and effects (stressor response), and their relationships between each other and the ecosystem are characterised base on the information needs identified in the problem formulation phase. Two profiles, one for exposure and one for stressor response are then described (Figure 4-2).

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4.8.2.3 Risk characterisation phase

The mentioned two profiles are integrated through a risk estimation process resulting in a risk description. Such a description includes the environmental adversity and uncertainties and lines of evidence. The outcome characterises the risk and forms the basis on which decisions by risk managers are based (Figure 4-2).

4.8.3 Environmental risk evaluation, management and communication

Risk assessment as described in section 4.8.2 is followed by scientific risk evaluation (Johnson et al. 2007; Renn & Dreyer 2009), and followed by managerial decision making. Scientific research clarifies the implications of taking particular actions, but cannot decide which actions should be taken, as these are the responsibility of the risk manager (Raybould 2010a). These actions could be on threshold values, monitoring and implementation (Johnson et al. 2007). Matters regarding precaution, prevention and concerns (Ely et al. 2009) are basic managerial considerations.

4.9 CONCLUSIONS

A benchmark of effective risk governance is the lack of delays in issuing of permits, and the lack of unjustified declining of GMO permits. At present, risk governance in South Africa is not effective. There appear to be several reasons, one of which is that the approach to risk assessment procedures as explained in this paper is not being followed. Because of the lack of clarity on risk assessment approaches, there is a trend towards increased regulatory requirements. Additional requirements could be formal or *ad hoc*, although the latter cannot be easily identified because of the confidentiality of information. A few examples of the extended time taken to reach decisions and issue permits are found in the minutes of the GMO EC. Risk assessment of sorghum is used as a case study in this paper because of the EC's reluctance to consider the actual risks arising from concerns of gene flow.

A framework for environmental risk assessment, as well as food/feed safety assessment based on problem formulation, is proposed here. In agreement with a number of authors (Craig & Tepfer 2007; Johnson et al. 2006; Nickson 2008; Fitzpatrick et al. 2009; Raybould 2006, 2010a, 2010b; Wolt et al. 2010), the merit lies in:

- A focused approach.
- Requiring only data that are related to the risk.
- Less confusion in regulatory decision making.
- Avoiding unnecessary delays in decision making.
- Benefits reaching those in need sooner.

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Implementation of such a proposal would require revision of the GMO Act, especially for environmental risk assessments, by eliminating the use of terminologies that are not expressions of scientific assessments of risk, for example 'avoid' and 'threat'. The assessment of sorghum starting with a problem formulation, which includes defining 'harm', 'analysis plan', and 'risk hypothesis', illustrated by Hokanson et al. (2010) (Table 4-3), is proposed as the starting point in the way forward for ERAs. There are a number of challenges that will have to be addressed. A team of experts in crop biology should be included in the process of problem formulation for each crop where there is potential for outcrossing. This should be done in a participative manner. A challenge would be to define 'harm' and for the team to concur on 'assessment endpoints'. Such challenges may be better considered in a regional centralised way because of limited regulatory and, perhaps, national research expertise. The need for an additional step in South Africa's risk governance that provides for development of policies on assessment approaches, interaction with scientists and framing of the risk approach is a matter of urgency.

4.10 PROPOSALS

Proposals for the way forward are made:

- A national policy on risk assessment approaches is required to give direction for research assessments. The policy should make provision for risk-benefit assessment instead of only risk assessment.
- The balance between national biosafety strategies and policies to achieve sustainability in food production, national economic growth, job creation and agrarian development versus protecting the environment should be regarded as priority as these give direction to risk assessment.
- The South African biosafety regulatory framework should be improved to meet requirements of the proposed risk assessment approaches.
- It is important that South Africa decides on approaches to risk assessments that are firmly described in policies, guidelines and application forms.
- Training of risk assessors, risk managers and also the applicants should be prioritised.
- A framing step in iterative risk analysis to ensure scientific participation must be included.
- All aspects of good governance must be improved to restore credibility of South African risk assessment governance.
- Sub-regional, regional and international consultation should be implemented in order to exploit scarce skills and improve risk assessment throughout the region.

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Table 4-1: GM-sorghum: Protracted decision making by South African government.
(DAFF 2006-2011; CSIR 2009)

Application for contained use: Sorghum with increased levels of lysine **(Minute reference17/3/1-CSIR-06/005).**
1. Application submitted in May 2005 by the Council for Scientific and Industrial Research (CSIR 2. More detailed information was requested by the Executive Council (EC) on 15 June 2006, but then decided the applicant did not give new information and the real benefit could not be identified. Upgrading from Containment Level 2 (CL2) to Containment Level 3 (CL3) was required. Upgrading was approved on 4 September 2006. 3. CSIR resubmitted application on 15 September 2006. 4. EC declined the second application on 30 January 2007 because 'escape from CL3 would have major environmental impact'. 5. On 30 January 2007 the EC, in 'deliberating on the matter, also considered the potential field trial release and concluded that it is unlikely that such an application would have been favourably considered'. 6. The applicant appealed against the EC decision to decline the contained use application on 1 March 2007. It also sought lowering of CL3 to CL2 as 'research with indigenous crops is unprecedented and will set an incorrect precedent hampering future research and improvement of indigenous crops in South Africa'. 7. The appeal panel was instituted on 15 June 2007. 8. On 11 September 2008 the minister of agriculture issued a letter stating approval of contained greenhouse experiments (CL3). Additional requirements were included in the permit (additional filters and long term planning). 9. In July 2009 a final confirmation was received from the registrar to proceed with CL3 greenhouse experiments.

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Table 4-2: Contested study in policy-relevant science around gene-flow in sorghum-queries (Schmidt and Bothma 2006)

- Hybrid sorghum seed production is based on use of a cytoplasmic male-sterile (cms) inbred, designated as A-line, and a fertility restorer pollinator (Rf) inbred, designated as R line where the Rf gene overrides the cms cytoplasmic sterility gene. The cms parent line is maintained by crossing it with a pollen-fertile isoline, designated as a B line that does not restore fertility in the cross. The study used two isolines, A and B, genetically identical except for the cms gene.
- Pollen flow data are readily available and safe isolation distances for certified seed production established at 350 to 750 m for South African sorghum seed production stages: pre-basic to basic to certified seed (SANSOR, 2011) standards being applicable to cultivated and wild species. What new information does the study convey?
- The use of cms male-sterile recipient plants creates an unnatural situation as it removes normal pollen pressure and competition, sorghum being primarily self-pollinated that places wind-blown pollen at a competitive disadvantage.
- The researchers did not understand or anticipate that cms sterility reverts back to fertility at a low rate, and did not take precaution to remove the fertile plant before pollen shedding. The outcome was a high incidence of unexpected fertilised seeds at 104 m distance, as well as apparent similar contamination of plants at 117 m, 130 m and 158 m distances, and most definitely also of plants at 91 m, 78 m and 65 m, as is evidenced in graph 5
- However, the most serious flaw in the study was not to do the logical pollen flow analysis, namely flow of S. bicolour subsp. bicolour pollen to a wild relative such as Johnson grass, *S. halepense*, taking into account pollen pressure and competition in *S.halepense* florets, and resultant sterile triploid plants.
- South Africa has been planting cultivated grain sorghum on 70 000 to well over 100 000 hectares in areas where *S. halepense* occurs at negligible, minor or significant levels, and the authors did not submit evidence of discovery in South Africa of natural hybrids out in nature between *S. Bicolour bicolour and S.halepense*.
- The authors concluded that crop-to-crop pollen flow in *S. Bicolour* subsp *bicolour* occurs to over 100 m (barring the anomaly mentioned above), supporting a well-known fact. The extrapolation of this to a likely risk of transgenic genes flowing to wild relatives and that transgenic traits could favour survival of hybrids with wild relatives is not supported by any data in the study.
- The triploid progeny of Johnson grass crossed with sorghum hybrids are normally sterile.

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Table 4-3: A plan to assess the potential environmental risks of gene flow of ABS to wild sorghum in Africa (Hokanson et al. 2010) (Only one identified harm with four scenarios, four hypotheses and an experimental plan recorded. Original references are not included as the table serves only as demonstration.)

Harm	Risk scenarios	Hypothesis	Experimental plan
Harm 1. Loss of valuable genetic diversity in the crop or crop or compatible species	Scenario 1: Loss of allelic diversity in the wild sorghum due to a 'selective sweep'. A selective sweep following the movement of transgenes into the wild populations would likely leave the populations more genetically uniform in parts of the genome closely linked to the transgenes under strong selections. This requires a substantial advantage for plants with the ABS transgene.	Hypothesis: ABS* traits will not increase survival or reproduction of sorghum.	A thorough comparison of ABS and non-GM sorghum for characteristics related to survival and reproduction, disease and insect susceptibility, nutritional composition, and known toxicants.
	Scenario 2: Loss of allelic diversity due to 'genetic swamping'. Genetic swamping' whereby the wild species become genetically inextinguishable from the crop plant ('extinction by assimilation') is often cited as a risk from gene flow, but circumstances that would lead to such swamping are likely to be rare. Genetic swamping from crop sorghum to wild sorghum does not occur currently; therefore, harm via this route would require a substantial increase in hybridisation frequency associated with ABS*.	Hypothesis. ABS trait will not change the hybridisation frequency of sorghum.	

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	Scenario 3: Loss of abundance of wild sorghum due to 'out breeding depression'. In certain circumstances, populations may decline if there is a reduction in the ability of hybrids to survive and reproduce following hybridisation. If the ABS transgenes reduce survival and reproduction, populations of wild sorghum could decline following hybridisation with ABS.	Hypothesis. ABS traits will not reduce the survival or reproduction of sorghum.	
	Scenario 4. Loss in abundance of wild sorghum due to increased bird preference. Higher levels of tannins in sorghum seeds can make them less palatable to birds. If the level of tannins decreases in ABS compared with those in other cultivated sorghums, birds may preferentially feed on the wild sorghum with the ABS traits over other non-sorghum seed sources. It is difficult to predict how this change in bird behaviour could affect the dynamics of wild sorghum populations. It could potentially decrease the abundance of wild sorghums.	Hypothesis. ABS trait will not decrease tannin levels (increase bird preference) in sorghum.	

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CHAPTER 5: FOOD SAFETY: IMPORTANCE OF COMPOSITION: CASSAVA (*MANIHOT ESCULENTA*, CRANTZ)

A paper in much revised form has been accepted for publication in the Journal of Agricultural and Food Chemistry, http://pubs.acs.org/journal/jafcau

ABSTRACT

The importance of food composition in the safety assessment of genetically modified (GM) food is described with cassava (*Manihot esculenta*, Crantz) as an example, a crop containing cyanogenic glycoside (CG) toxicants. Despite its widespread consumption, cassava cannot be regarded as a crop with a history of safe use. A new safety tolerance level for chronic CG dietary exposure should be established. Genetic modification of cassava is being applied to improve its safety and nutritional value. Targeted compositional comparison should be done between the GM crop with improved safety and nutritional qualities and the 'unsafe' near isogenic cassava line, under a variety of environmental conditions to assess the improved qualities and possible unintended effects. Because the impact of the genetic modification may not be adequately observed in the comparative analysis, the compositional data should be augmented by animal feeding trials, and administration of dose range concentrations of GM cassava or non-GM cassava prepared in a formulated diet. This analysis could be repeated with processed cassava meals representing the variability CG concentrations owing to preparation methods.

Key words: Genetically modified food, food composition, comparative approach, animal feeding studies, safety tolerance, cassava, cyanogenic glycoside

5.1 INTRODUCTION

The introduction of food from genetically modified (GM or GMO) crops (also described as recombinant deoxyribonucleic acid (rDNA) crop plants) increased interest in the composition of food as an important criterion for determining food safety. The compositional approach has improved the comparative assessment of food as a means of safety and risk assessment.

The safety of new foods developed by conventional modification technologies and methods such as embryo rescue, somatic hybridisation, induced mutagenesis (chemical or irradiation) and conventional breeding has not been subjected to the same extent of intensive compositional assessment as for GM foods. It has been stated that 'genomic disruption' could be as much as or worse than GM 'disruption' (Committee on Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health 2004).The compositional

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analysis of conventional food is carried out mainly to determine its nutrient value where labelling is required, but it is rare that conventional foods are subjected to safety assessments (WHO 2000).

The comparative risk assessment approach for safety and nutritional assessment of products from GMOs has been developed by several international bodies, including work of the first and second ad hoc Inter-governmental Task Force on Foods derived from Modern Biotechnology in 1999 to 2003 and 2004 to 2009. The purpose of the task force was to develop standards and guidelines for safety assessment of biotech foods (CAC n.d.). This approach to GM crop assessment has been applied for more than a decade. Experience gained and information gathered in safety/risk assessment of GM food from crop plants could be considered a benchmark for contemplating the future role of comparative safety assessment of GM crops.

There is a role for GM crops among other agricultural practices in addressing a diversity of future challenges. Future demands on global agriculture production will require solutions to feeding a projected increase in world human population from 7 million in 2012 to 9.2 million by the middle of the twenty-first century (Dellink et al. 2012). The FAO estimated that food and feed production must increase by 70 -100% to meet the demand (FAOSTAT). Malnutrition in a number of countries, limits on land and water resources, climate change, future capacity of fossil fuels and fertiliser stocks, exposure to hazardous chemicals, and biodiversity loss are all concerns that need policy development and research (Dellink et al. 2012; Pretty et al. 2010).

Cassava, *Manihot esculenta* (Crantz), is one of a number of crop plants that is receiving a great deal of attention from international bodies and research groups because of its importance in food security, despite the presence of high levels of the toxic cyanogenic glycosides (CG), and also because it is a crop with potential for genetically improved safety and increased nutritional value (Ganjewala et al. 2010). Cassava is the major food and feed crop for nearly a billion people and their animals, is produced in tropical and sub-tropical parts of the world, and ranks eighth among the major food crops, based on consumption per capita per day (FAOSTAT). It is the fourth most important crop grown in developing countries (FAOSTAT). The knowledge and needs for improvement of cassava are of great importance.

A challenge in the near future is the safety assessment of crops with improved safety and enhanced/improved nutritional quality from programmes involving research on cassava. The safety assessment of cassava as a possible future GM crop is considered in this study according to the internationally accepted comparative compositional safety assessment approach to illustrate the importance of composition.

5.2 CONVENTIONAL FOOD SAFETY AND NUTRITIONAL LANDSCAPE

Historically, knowledge of food safety and nutritional values has developed through 'trial and error' by selection and preservation of plant variants with desirable traits and human preference for taste and colour (Committee on

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Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health 2004). Humans are aware of crop plant toxicants from traditionally gained knowledge and experience in cultivation and food preparation.

Of particular interest in food safety is documented scientific knowledge of toxicants and anti-nutrients present in crop plants, for example toxic amino acids, lectins, proteinase inhibitors, antigenic proteins, alkaloids, fibrous polysaccharides, saponins, and condensed tannins (Duffus & Duffus 1991). Ganjewala et al. (2010) quote the CG toxicants as a specific concern, being produced in more than 2 600 plant species, which include crop plants such as barley, sorghum and cassava. CG toxicants may have various functions: chemical defence, plant-insect interactions (Zagrobelny et al. 2004) nitrogen–storage compounds (Busk & Moller 2002), evidence of chemo-taxonomical (Vetter 2000) relationships and phagostimulants, to name a few (Gleadow & Windrow 2002). Standard practices for preparation of food containing high levels of toxicants and antinutrients serve as a general guide to ensure safety of food (OECD 2009). It is normal practice in many countries that plant breeders and agronomists monitor levels of natural hazardous substances. Preparation of the crop into various forms of products may reduce the levels of toxicants (Nambisan 1994). The methods used, however, may not always be successful in reducing toxicant levels sufficiently but may even increase the level (Nambisan 1994; Saka 2012).

The International Codex Standard for edible cassava flour is based on hydrocyanic acid (HCN) concentration of not more than 10 mg/kg (FAO/WHO 1995). This conclusion is based on acute toxicity observations, as no adequate quantitative toxicological and epidemiological information was available for HCN. Information from chronic studies with CGs and all their metabolites is needed to confirm safe levels for daily exposure over a lifetime. The Codex standard for classification purposes of raw 'sweet' cassava' is <50 mg/kg HCN (FAO/WHO 2011a) and for raw 'bitter' cassava is 50 mg/kg HCN (FAO/WHO 2011b). Levels as high as 2000 mg HCN equiv/kg fresh weight (or 2000 ppm) have been reported (Cardoso et al. 2005). The tuber parenchyma is more cyanogenic than the cortex (peel) of the root and leaves (Cardoso et al. 2005). Concentrations may vary among cultivars from 1 to 2000 mg HCN equiv/kg fresh weight (Cardoso et al. 2005; Nyirenda et al. 2011).

The improvement of nutritional quality of crop plants is an important research focus because of inadequate quantities of nutrients in the normal diets of many people, especially in developing countries where crops such as cassava are the main food source. Cassava roots, valued as an energy source in human and animal diets, are deficient in protein, whereas the leaves are a better protein source, but have less favour. Efforts to improve protein content are on-going (Stupak et al. 2006). The leaves are also a source of ß-carotene, vitamin C, and minerals (iron and calcium) (Uusiku et al. 2010; OECD 2009). Roots are the preferred food, but have a low content of ß-carotene. When prepared according to different methods, the levels of nutrients could be further depleted (Failla et al. 2012). High ß-carotene transgenic cassava roots may provide a solution for vitamin A deficiency (Spencer & Palmer, 2012). Further research is required to study malnutrition and adverse health

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effects such as neurotoxicity in cassava-based diets (Spencer & Palmer 2012). The presence of CG and the thyrotoxic action of the CG metabolites thiocyanate and/or cyanate are of concern in malnutrition (Spencer & Palmer 2012).

The collection of baseline information on the composition of conventional crop plants such as cassava therefore remains an important consideration, especially for compositional comparisons with the GM derivative.

5.3 UNINTENDED COMPOSITIONAL DIFFERENCES

The unintended differences in constituents of crops are a function of genetic variables, environmental factors and agricultural practices (Committee on Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health 2004). Pleiotropy plays an important role in possible interactions between all these variables. Comparative compositional analysis can identify possible unintended effects.

All methods of crop improvement have potential to cause unintended compositional changes, as demonstrated by an advisory group for the USA (Committee on Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health 2004). The group contended that it was unlikely that all methods of GM, non-GM or conventional breeding will have equal probability of unintended effects. They identified methods of induced mutagenesis as being the most genetically disruptive technique and, therefore, the most likely to display unintended phenotypic changes. This was followed by biolistic transfer, and then by Agrobacterium transfer of DNA from distantly related species. Agrobacterium transfer of rDNA from closely related species was ranked less likely to cause unintended changes than any of the above methods, including conventional pollen-based crossing of distantly related species and/or embryo rescue. Unintended effects have been reported from non-GMs at the point of commercialisation, although this is rare (Cellini et al. 2004). There have been examples showing that the formation of increased levels of new metabolites has led to unintended effects.

Hybrids of *Solanum tuberosum* and *S. brevidens*, in addition to the usual steroid glycoalkaloids (solanine and chaconine), produced the toxic demissidine, which was not present in the individual parents (Laurila et al. 1996). Trace amounts were reported of the unintended metabolite cis15-octadecadionic acid, an isomer of linoleic acid not usually present in nonhydrogenated soybean oil, but present in hydrogenated soybean oil and other food sources (Kitamura 1995; National Academies of Sciences 2004). A number of examples of increased levels of toxicants have been reported apparently owing to environmental factors or genetics, for example psoralins (furocoumarins) in celery (Diawara, Trumble & Quiros 1993; Diawara et al. 1995). Increased glycoalkaloid content in GM and conventionally bred potatoes was reported (National Academies of Sciences 2004) and average daily intake levels were determined (Kuiper et al. 2001).

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Plant breeders traditionally eliminate observed off-types during the evaluation process. However, agronomic/phenotypic assessments are not food safety assessments. Compositional analysis of conventionally produced food is required only for food labelling. For example, in South African legislation, the onus is on the seller to ensure food safety (South Africa 2007). Food quality guidelines for example for potatoes prescribe grading according to the amount of 'green' (South Africa 1990), but quantifying the parameters that would designate a food 'unfit for human consumption is a controversial issue.

5.4 SAFETY/RISK ASSESSMENT OF GM FOOD

The assessment of GM derived food to determine whether it is suitable for human and/or animal consumption is conducted in four steps: hazard identification, hazard characterisation, exposure assessment, and risk characterisation (Secretariat of the Codex Alimentarius Commission 2011). Any assessment starts with a description of the recombinant plant, the donor and host plant(s) and its use, and the recombination method (CAC 2009).

5.4.1 Steps in food risk assessment

A comparative approach has been recommended by expert international bodies (WHO 1991; WHO 1993; OECD 1993; FAO 1996; OECD 1996; WHO 2000; CAC 2009) in which 'substantial equivalence' has to be a starting point of the assessment. It entails comparative analyses between the crop test plant and a suitable comparator of molecular, compositional and phenotype/agronomic data (Kok et al. 2008).This approach is described by OECD (1993) as the most appropriate strategy for the safety/nutritional assessment of GM food. It focuses on the determination of similarities and differences between GM food and the conventional counterpart. It forms a key step in the process of safety assessment (Kuiper et al. 2001). It is regarded as a safety assessment based on comparison with 'safety information of the comparator', described in more detail in the following sections. In some types of GM cassava in development, it is the opposite: the purpose is to produce a product 'more safe' and nutritious than the comparator.

The next step is hazard characterisation for assessment of a) intended differences for example the DNA, RNA, new proteins, and intended compositional changes; and, b) unintended differences observed in the compositional and phenotypic comparisons. The following two steps – exposure assessment and risk characterisation – lead to a conclusion on the safety of the GM food.

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5.5 CONSIDERATIONS FOR COMPOSITIONAL ASSESSMENT OF FOODS FROM GMOs

5.5.1 Comparative approach

The comparative approach was considered suitable for GM food because of valid reasons that safety/risk of food would be difficult to assess according to toxicological principles only (CAC 2009; FAO 1996; WHO 1990; WHO 1993; WHO 2000; OECD 1993; OECD 1996). Rodgers (1996) listed a number of differences between chemical substances and food that showed the limitations in assessing a complex mixture of food/feed components with specific nutritional function within a specific confined dose range. The conventional toxicological approach for chemical substances is to administer or feed animals with the test material at a range of doses over a period of 90 days or in chronic studies over a life span of two years for rats and 18 months for mice. The highest dose in the dose range should show an effect in about 10% of animals in order to determine a no-observed-effect level (NOEL). Generally two to three species (rat, mouse, dog) are included in the testing programme. When the species behave similarly, compared to the controls, much more information on the mechanism and metabolism is needed to confirm any relevance to humankind before extrapolation to human beings can be made with any confidence (Wilson 1988). The OECD Guidelines for Testing of Chemicals (OECD Guidelines for Testing of Chemicals) are recognised by regulatory authorities as references and serve to harmonise regulatory toxicological requirements for chemicals. These guidelines have not been followed by some scientists, resulting in grossly incorrect interpretation and extrapolation to human beings (Seralini et al. 2012).

The nature of food being complex, satiety at high levels, palatability, acceptability (loss of appetite) over a lifespan and nutritional imbalance at high doses are all factors that may compromise interpretation of results from animal species (CAC 2009; FAO 1996; WHO 1990; WHO 1993; WHO 2000; OECD 1993; OECD 1996). The protocols for toxicology studies with GMs are adapted for assessment of possible unintended changes in crop composition resulting from the method of genetic modification. Such feeding studies are designed for a limited dose range of the crop components to be evaluated because of the above limitations.

Studies with GM ‘improved’ compositional characteristics, for example reduced or zero levels of CGs, would only be possible if the toxicant level has been reduced to be within the recommended safety level. For cassava and other crops containing CGs, at least the protein concentration levels of GM cassava should be within the profile of a standard diet to avoid confounding the outcome of study results. The reasons are explained later in this paper.

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5.5.2 History of safe use

The concept of 'food safety is not absolute, since it is a judgment; it is value laden ... [that is] understood within the context of society, culture, politics, and economics' (Wolt2008). Even with a concept of safety, risk is not negated as there is 'always a degree of risk' (Wolt 2008; Querci et al. 2008). Safety in this context is illustrated by a study on farmers' 'perception' of the toxicity of and reasons for farming with cassava (Oluwole et al. 2007). A percentage of farmers interviewed in Tanzania stated that cassava could be eaten raw. This group had never seen anybody die of eating raw cassava and did not ascribe any adverse effects to consumption of cassava, except for one farmer, who noticed minor acute ailments. The levels of cyanogenic compounds ranged from 8 to 1064 HCN equiv/kg dry weight cassava. Preference for bitter cassava is because of higher yield, resistance to pests (Bellotti & Riis 1994), and reduced theft of produce (Koch et al.1994). According to Oluwole et al. (2007), most of the farmers from Nigeria and Tanzania plant cassava for subsistence only. Cassava is preferably harvested close to markets to prevent increasing levels of CG that apparently result from damage causing oxidative stress (Zindenga 2012).The levels of cyanogenic compounds in certain areas of countries such as Mozambique are of concern (Burns et al. 2012). Programmes to raise awareness are in place for example in Nigeria (Integrated Cassava Project).

OECD (1993) describes safety vaguely as 'reasonable certainty' of no 'harm'. The definition of 'harm' should be considered with great caution because of different perceptions. The role of scientists in interacting with regulators and society to define harm needs consideration. Constable et al. (2007) list possible items in each of these categories: history, safety and use. A critical item in this list is food composition, confirming the importance of this analysis. OECD has prepared a number of consensus documents that contribute to a better understanding of 'history', 'safety 'and 'use' of a number of crops (OECD Consensus documents for the work on the safety of novel foods and feeds) The compositional components to be considered include proximates (analytical determinants of major classes of food components) and nutritional components, toxicants, antinutrients, secondary metabolites, and other characterising components.

In studies with cassava to improve food safety and nutritional value, the conventional crop comparator is the starting point for improvement, as, despite its widespread consumption, it cannot be regarded as having a history of safe use. This is in contrast with currently available GM foods, where comparative safety assessment is based on the assumption that the conventional crop is 'safe'. For a crop such as cassava, the use of the conventional crop as a comparator to identify unintended effects in the GM derivative through comparative compositional studies has serious limitations. A different application of the comparative approach will have to be followed, as described in this paper.

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5.5.3 Components to be analysed

The assessment of food/feed safety according to the Codex Alimentarius Commission (2009) should be included in any overall risk assessment. The risk hypothesis should focus on the important components that are characteristic of the specific crop, following a 'searchlight' approach rather than 'filling a bucket' approach (Popper 1972; Raybould 2010). OECD aims to reach consensus on 'searchlight' components of interest. The proposed important compositional components could be useful not only for GM compositional purposes, but also for conventional modification methods.

OECD consensus documents for safety of food and feed components are being developed. The comparators agreed on by members (as well as invited non-members) tend to address questions on the suitability of comparators, cultural difference, preparation differences, consumption patterns for different regions, and analytical methods, and include valuable information on history of safe use (OECD 2009).

Cassava is used as an example for choices of comparators. The concentrations of important components of cassava should be compared in the roots, the main source of energy for many people, and cassava leaves, a source of protein. According to the OECD consensus document, the proposed constituents to be measured in fresh leaves for human food include proximates, fatty acids, amino acids, minerals (calcium, phosphorus, magnesium, iron), vitamins (ß-carotene, ascorbic acid, thiamine, riboflavin and niacin), cyanogenic glycosides, HCN, tannins, and phytic acid. Those proposed for fresh roots include all of those for leaves except tannins and phytic acid, and also starch. The choice of constituents for analysis is based on a large concentration of starch in the roots, which are an important source of energy where cassava is a staple food. The protein content of roots (crude protein: 1.5-4.7 g/100g dry matter) is small, though it still forms a valuable source of protein, particularly in Africa. Fresh leaves contain much higher concentrations of protein (14.7-36.4 g/100g dry matter). Cyanogenic glycosides (CG) and hydrocyanic acid (HCN) are obvious choices for safety assessment, as levels as high as 2561.7 mg HCN /kg dry weight has been reported (Chavez et al. 2005).

Processed cassava products are not included in the current OECD document for comparative analysis, because of the wide range of processing and preparation methods and products consumed. Yet different processing methods can profoundly affect the levels of CGs and HCN present in the final product (Nambisan 1994; Saka 2012). The time of harvesting is at 12 months' maturity, since most of the nutritional data are available at this age of the plant (OECD 2009).

Conventional varieties or hybrids that are grown commercially in the various geographic areas are normally included in comparative studies with the GM crop derivative. The purpose is to review differences between the test substance and the comparator substance of the near isogenic line against the background of the range of values found in the edible varieties of the crop. Differences, whether genetic or environmental in origin, could be

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clarified in this way. If the observed difference is within the biological range of the commercial varieties of the crop, there should not be a safety concern (OECD 1997). However, this assumption is rendered invalid in the case of cassava, where serious health concerns have been raised that relate to conventional cassava varieties.

5.5.4 Genetic and environmental variability

Compositional data are available for major commercial crops such as maize. The information on maize components shows the impact of genetics and the environment on the nutritional and metabolite components (Reynolds et al. 2005; Harrigan et al. 2007a; Harrigan et al. 2007b). This information is valuable as the comparison is between the test crop and the near isogenic lines. A database has been developed from comparative compositional studies with the major crops covering data from different environments and illustrating the variability (South Africa 1990). Cassava is known to survive under extreme environmental conditions (Pretty et al. 2010; Burns et al. 2010). It has been called the drought, war and famine crop (Burns et al. 2010). However, cyanide content and nutrient composition of cassava are reported to vary with environmental conditions and agricultural practices, such as drought and soil nutrient supply, and between cultivars (Burns et al. 2012). The OECD consensus document for cassava indicates the ranges of constituents. This is the first international source of a set of compositional data for cassava obtained from peer-reviewed publications (OECD 2009). However, regular updating of the information would contribute to its validity.

5.6 ASSESSMENT OF METABOLIC PATHWAYS

Morandini et al. (2003) describe the complexity when permanent changes in the biochemical pathways may affect other pathways essential for producing critical nutrients. The assessment of possible changes in plant metabolic pathways should receive more attention in future. The following cases would fall under this kind of assessment.

- Stacking of traits, at least where interactions in metabolic pathways are possible. This needs to be assessed case by case. Stacking is a fast growing practice that is evident from the increase in hectares from 32 million in 2010 to 42 million in 2011 (James 2011).
- Nutritionally enhanced/improved crops, for example cassava with increased concentrations of ß-carotene and minerals, as well as protein content (Sayre et al. 2011).
- Crops with reduced levels of toxicants, for example reduced CG levels in crop plants (Ganjewala 2010).

5.7 CASSAVA STUDIES: CYANOGENIC GLYCOSIDES

Progress has been made in unravelling the biosynthesis of CGs and their catabolism, which is important where compositional assessment of cassava with reduced levels of toxicants is to be considered in a safety study.

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Several reviews have documented the important findings from such research. A short overview of current knowledge of CG biochemistry is provided by Ganjewala et al. (2010) (Figure 5-1).

CGs in cassava (the main one is linamarin) are derived from only two amino acid precursors, namely L-valine, and L-isoleucine (Burns et al. 2012), though L-leucine, L-phenylalanine, L-tyrosine and a non-protein amino acid cyclopentenyl-glycine are reported in other crops as precursors of CGs. Three steps in the biosynthesis have been identified. In step one, the precursor amino acid is converted to aldoxime by N-hydroxylation of the parent amino group. An enzyme from the cytochrome-P450 family is involved. In a second step, aldoxime is converted to cyanohydrins catalysed by another cytochrome-P450 enzyme, and in the third step, glycosylation occurs by a soluble enzyme UDP-glycosyltransferase. Recent studies suggested that the three enzymes are organised as metabolon, which is defined as a 'supramolecular complex of sequential metabolic enzymes and cellular structural elements' (Srere 1985), ensuring channelling of precursor/substrates and intermediates. Ganjewala et al. (2010) list a number of published research papers on gene identification, and characterisation in the biosynthetic pathway.

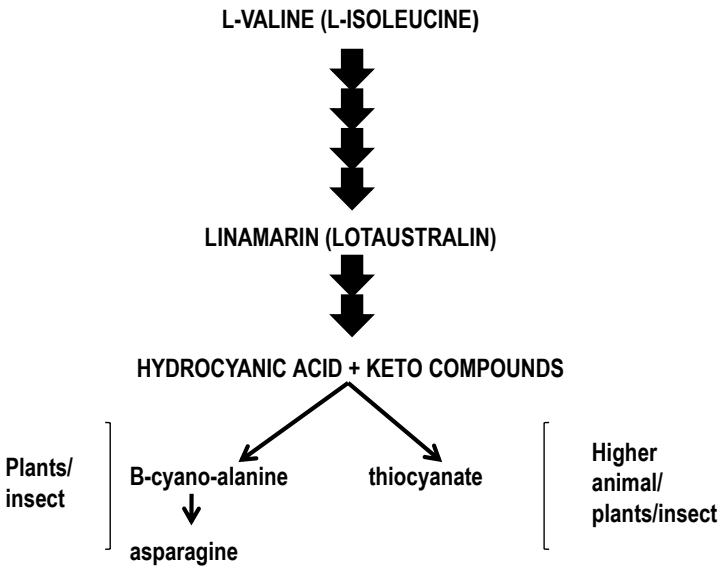

Figure 5- 1: Schematic pathways of biosynthesis and catabolism of cassava cyanogenic glycosides

The CGs are catabolised to HCN. The most important enzymes involved in the catabolism are ß-glucosidases and hydroxynitrilelyases. The nitriles dissociate into a sugar, a keto-compound, and hydrocyanic acid (HCN) at

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pH above 6.At low pH the nitrile degradation is catalysed by a lyase enzyme, resulting in the release of HCN. HCN is detoxified by two separate routes. The first route leads to formation of asparagine. The second route leads to formation of a thiocyanate. Genes encoding some of the enzymes of CG catabolism have been cloned and characterised. Detection of CGs has been made possible by chromatographic procedures and enzyme immunoassay methods, however with some limitations (Ganjewala et al. 2010).

Ganjeala et al. (2010) conclude that despite the progress in unravelling the biochemistry of CGs, more knowledge is required of the regulatory mechanisms that control CG metabolism.

Knowledge gained on the CGs would facilitate the selection of appropriate comparators for comparative assessment once the cassava is ready to enter the regulatory process for approval. The effects of such genetic modification on all possible biochemical pathways involving important food and feed constituents need to be considered.

5.8 NON-TARGETED TECHNIQUES: GENOMICS, TRANSCRIPT PROFILING, PROTEOMICS AND METABOLOMICS

Analytical methodologies, particularly analytical techniques such as chemical analysis and profiling, are still being developed. The types of analysis include DNA sequence analysis; gene expression analysis (mRNA); protein analysis; specific organic compounds, and trace elements. These types of methodologies have opened the door for in-depth comparative studies to gain a better understanding of the genomic and environmental effects on composition of crop plants.

These technologies are non-targeted, but facilitate the simultaneous measurement of thousands of biological variables in test material. The use of metabolomics has been advocated as an approach to expand the range of metabolites that can be measured for potential unintended effects (Davies 2010).The value of these technologies is in principle large; however, at this stage interpretation of the vast amount of information is a challenge. The methodology still need be standardised and validated, and is qualitative and not fully reproducible.

Ricroch et al. (2011) conducted a survey of publications on studies with transcriptomic, proteomic and metabolic studies of ten crop plants, comparing GM (25) with non-GM (19) crop varieties, with or without intentional metabolic changes. Indications are that:

- Gene expression profiles of GM-crops are comparable with those of non-GM crops (Coll et al. 2009).
- Natural variation explains most transcriptomic changes among maize plants (Coll et al. 2010).
- Micro-array analysis reveals that plant mutagenesis may induce more transcriptomic changes than transgene insertion (Batista et al. 2008).

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- Transgenesis has less impact on the transcriptome of wheat grain than conventional breeding (Baudo et al. 2006).
- Transcriptome and metabolome profiling of field-grown transgenic barley lack induced differences, but show cultivar-specific variance (Kogel et al. (2010).

The current results from 'omics' studies with single traits confirm the hypothesis that transgenic modifications are less disruptive to the genome than conventional genetic modification methods. Harrigan & Chassy (2012) challenge the likelihood that metabolic profiling would provide 'immediately interpretable data in safety assessments that would otherwise enhance rigorously quantitative assessments' (p.342). The complexity of CG biosynthesis, dynamics of protein regulation and the environmental effects on CG levels in cassava may render great difficulties in interpretation of results from comparative studies with the current 'omics' techniques.

5.9 DISCUSSION AND CONCLUSIONS

Compositional analysis has a significant role in both conventional and GM crop safety assessments. The importance of compositional comparison as one of the three pillars – molecular, agronomic/phenotypic, composition – of safety analysis may increase in future when complex compositional issues are to be considered. Cassava is a specific example because of the complexity of the biosynthesis and catabolism of the CGs. The OECD consensus documents fulfil an important need in providing information on the 'history of safety use' and choice of food/ feed constituents to be analysed for crops in the mainstream of commercialisation in general. However, there are a number of matters that need to be considered to improve on the approach in order to include crops such as cassava in a comparative safety assessment. The comparator in this case is the 'unsafe' cassava, with the 'improved' cassava. The determination of comparative safety of the 'improved' cassava requires that a safe limit should be developed for the toxicant.

As first line in the safety/nutritional assessment of improved cassava crops comparison with the components of the near isogenic line under various environmental conditions is the obvious step to confirm the purpose of the genetic /conventional modification. The results may still be difficult to interpret because of the complexity of the CG biosynthesis and the remaining CG levels (supposed to be below the safety guideline levels). The effect of the genetic intervention, should unintended effects have resulted, need be further investigated. The second line of the assessment could then be animal feeding studies, as described in this paper. Further confirmation of safety could be comparative studies with representative cassava prepared food /feed products.

A tolerance level for hydrocyanic acid, a metabolic product present in cassava flour, based on acute toxicity information by Codex Alimentarius, is not sufficient guide to safety assessments. Before any comparative compositional studies are considered, a safety guideline level(s) for CGs and their metabolites needs first to be

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determined based on long-term exposure studies. This is an important safety measure because long-term exposure to these toxicants may indicate a lower tolerance level than for acute exposure. Long-term exposure considerations are important because cassava is the staple food of a large proportion of the world population. Indications of neurotoxicity, thyrotoxicity and possibly other toxic symptoms are being investigated, but are difficult to interpret because of the complexity of additional factors resulting from malnutrition. The nutritional factors causing malnutrition will have to be simultaneously addressed, because of interaction between the toxicant and the nutritional status of the crop. Without such knowledge, confirmation of safety of GM cassava would be questionable in a comparative approach.

More information on the presence of the CG 'defence' mechanism, apparently in all parts of the plants, and active under all possible environmental conditions, would be useful. The biosynthesis of the toxicants involves amino acids that are major elements of 'normal' metabolic pathways. An understanding of the regulatory systems involved in changes in metabolic flux through these pathways in roots and leaves under different stress conditions could help elucidate changes that might occur through other interventions such as GM techniques. This information is important in a safety assessment.

A 'safety profile' of conventional raw cassava, including a new 'safety guideline value' for CG and its metabolites, could serve as a benchmark for compositional comparison purposes. Such a profile should include data on the composition (nutrients, antinutrients, metabolites, toxicants and allergens) of cassava illustrating genomic variability, environmental factors and farming practices that all have effects on crop composition particularly on the levels of the CGs and their metabolites. This option could be useful to assess crop composition from GM as well as conventional plant breeding practices as a benchmark for improvement of cassava.

A safety profile at the level of processed products, for example cassava flour, including a new 'safety guideline value' for CG and metabolites for processed products could serve to provide further assurance of the safety of products from GM cassava. This is not in accordance with current GM assessment requirements and is complicated by the multitude of processing methods in common use.

That 'safety' is a perception has been proved by the high levels of the toxic cyanogenic glycosides present in cassava, a crop that has been consumed for many years by many people. Data are lacking on the long-term exposure. The importance of compositional analysis, whether for products derived from conventional breeding practices or from GM technology, is illustrated by the assessment of the composition of cassava by means of comparison between the 'new' crop and the 'unsafe' comparator. The development of a safety guideline level based on long-term studies with isolated cyanogenic glycosides and their metabolites is imperative in a compositional safety assessment of cassava. Knowledge of the interaction between environmental influences and the constituents of the comparator, such as low levels of protein and other nutrients is important in the

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interpretation of the results from comparative studies. It may be necessary to complement such studies to provide additional confirmation of safety because of the lack of a suitable ‘safe ‘ comparator with a) animal feeding studies with a suitable ‘safe comparator’, and b) comparative compositional analysis of representative cassava food/feed products.

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CHAPTER 6: AN ANALYSIS OF THE PRECAUTIONARY PRINCIPLE: POSSIBLE UNINTENDED CHANGES IN ENDOGENOUS ALLERGENS IN GMOs

ABSTRACT

A clear understanding and a way forward for South Africa when dealing with the precautionary principle in decisions on genetically modified organisms (GMO) is prevalent. The precautionary approach of the Cartagena Protocol on Biosafety, if incorporated into legislation of countries as a precautionary principle (PP), could cause great difficulty in GMO decision making. The debate on the shortcomings in precautionary-based approaches to evaluate and manage risk is still raging and explained in this chapter. No consensus seems to be possible on the interpretation of the PP, as the buck is passed on to political decision making and, eventually, to court rulings. The current debate on the inclusion of possible unintended changes in endogenous allergens of GMO crops in risk assessments, illustrates the diversity of views on the PP and the difficulty in decision making. The chapter focuses on the debate, an analysis of the PP, acceptable solutions and a way forward for South Africa. A case study on the assessment of possible unintended effects of endogenous allergens illustrates consideration for application of the PP. It is proposed that African countries, where food security is a priority, and South African GMO amended legislation, should up–front, capture in policy, necessary guidance to decision makers on values of critical and beneficial importance when considering precautionary requirements both for risk assessments and risk management.

Keywords: Genetically modified organisms, South Africa, risk assessment, precautionary principle, endogenous allergens

6.1 INTRODUCTION

Fierce debates on approaches to the assessment, evaluation and management of genetically modified crops (GMO or GM crops) for safety to the environment and humans are still raging, making it difficult for decision makers to find a clear direction. Decision makers have to steer their way through the challenges of conflicting views. The difficulties for decision makers could even increase with new modification technologies being developed. The core issue of this debate is the understanding of risks, uncertainties and precaution. This paper endeavours to contribute to a clearer understanding of the issues in order to improve rational decision making.

Much has been written on the interpretation and implementation of the PP (Cooney 2004), yet confusion still exists. This observation is especially valid in African countries. The confusion is observed in decisions by governments, such as rejection of donor GM maize, establishing expensive laboratories to detect GM in maize consignments crossing boundaries, trade barriers caused by lack of legislation, increased cost for developers of

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the technology, creation of negative perceptions towards GMOs, indecisiveness on new applications for permits, and many delays with negative consequences to producers and consumers. This paper includes a review of studies on the PP in order to find a way forward with risk governance of GMOs. The PP has been applied mainly to possible environmental risks, but examples are found in GM food safety as well. A case study covering assessment of possible unintended changes in concentrations of endogenous allergens of GM crops is included as an illustration of application of the PP.

6.2 DESCRIPTION OF TERMS

6.2.1 Risk, risk assessment and the risk analysis model

Risk analysis describes a dynamic iterative process composed of risk assessment, risk management and risk communication (CAC 2011). The term 'risk' describes the probability of an adverse (health, environmental) effect (leading to harm or undesired consequence) and the severity of that effect, consequential to a hazard(s) or threat(s) (CAC 2011; UNEP 1995). In scientific terms, zero risk is non-existent (Querci et al. 2008) because human knowledge is always incomplete and some uncertainty is always present (De Bruijn & Ten Heuvelhof 1999). Uncertainty is an inherent and integral element of scientific analysis and risk assessment (UNEP 1995; Wolt & Peterson 2000; Renn 2008; Wolt 2008; Stirling 2001).

6.2.2 Precautionary principle or precautionary approach

'Precaution' is generally recognised, not as a hypothesis, theory or methodological rule, but rather as a normative principle for making practical decisions under conditions of scientific uncertainty (Cranor 2001). A normative principle implies obligations to 'anticipate harm and moral obligations in judging the adequacy of available knowledge' (Levidow, Carr & Wield 2005, p. 263). The implementation of the PP requires different normative commitments and choices (Ahteensuu 2007b, p.1). Ahteensuu (2007b, p.2) describes the PP as a principle of 'practical decision-making which may be justified on the basis of ethical and socio-political grounds and/or as a form of rational action. The obligatory nature of this normative principle has resulted in more than policy design criteria but becomes a 'regulatory philosophy' (Löfstedt 2004, p.23; Löfstedt, Fischhoff &Fischhoff 2002) when included in legislation which, in turn, has to be interpreted by regulators.

Authors such as Recuerda (2008, p.5) analysed the legal interpretations of the United States of America (USA) versus the European systems. The conclusion was that 'principle' had the connotation of legal language, of law, a 'principle of law', which is the status of the PP in Europe, whereas the USA considers it an approach with no legal connotation. The English language version of the Cartagena Protocol on Biosafety (Secretariat of the Convention on Biological Diversity 2000) (hereafter called the CPB) uses the word 'approach', French 'l'approche

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de précaution', German 'vorsichtprinzip' and Spanish version 'principio'. It seems that the words 'approach' and 'principle' are used without clear distinction in different languages.

The conclusion is that the precautionary approach is recognised as a precautionary principle when included in legislation with the obligations as explained by authors such as Levidow et al. (2005) and Löfstedt (2004). Cooney (2004, pp. 5-6) reasoned that the PP would not determine a specific outcome or decision, unless a specific formulation required it and, therefore, the terms 'precautionary approach' and 'precautionary principle' were used interchangeably. This nomenclature is followed in this paper.

6.3 INTERNATIONAL AGREEMENTS AND LAWS OF PARLIAMENT

A precautionary approach was originally developed to provide risk managers with a tool for decision making on environmental threats from processes or substances that had not undergone safety evaluation or regulatory approval (Hathcock 2000, p.255). Cooney (2004) summarised the history of the development that resulted in a number of international agreements (see also Löfstedt et al. 2002).

The CPB (Secretariat of the Convention on Biological Diversity 2000), requires measures to safely manage transboundary movement of living modified organisms and was one of a number of important agreements among nations to consider possible harm to the environment and human health. Countries that became signatories to the CPB were expected to incorporate the CPB into legislation and to adhere to the requirements for environmental safety and human health. A precautionary approach in consideration of risks, articulated in the CPB as well as in other international agreements and environmental law, is the cause of on-going debates on the interpretation and implementation of precaution (Cooney 2004).

The PP was first incorporated in 1994 into the World Trade Organisation's (WTO) Agreement on Sanitary and Phytosanitary Measures (SPS Agreement). Article 5.7 provides for obtaining additional information within a 'reasonable period of time' when existing information is inadequate whereas Article 3.3 allows for more stringent protection than relevant international standards, if there is scientific justification (United Nations, World Trade Organisation online). The Codex Alimentarius Committee standards are accepted by WTO as references.

The establishment in South Africa of SAGENE (South African Committee for Genetic Experimentation) (South Africa 1994) in 1978 is proof of the sincere environmental and human health concern of scientists when progressing with a new technology such as genetic engineering (also known as genetic modification or modern biotechnology). The need for a precautionary approach to possible environmental threats and concern for human health is illustrated by several South African laws. A precautionary approach in managing risks is included in for example South Africa's National Environmental Management Act (South Africa 1998), which provides for 'a cautious approach which takes into account the limits of current knowledge about the consequences of decisions

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and actions' (South Africa 1998, see also South Africa 2004). The Genetically Modified Organisms Act of 1997, as amended, incorporates the requirements of the CPB, and in the regulations to the act, requirements are described for protection of human health and the environment against possible risk from genetically modified organisms (South Africa1997). No mention is made of cost/benefit or risk/benefit, or proportionality of risk in applying the precautionary principle, although the GMO Act does refer to socio-economic 'impact', with the implication that impact could be either positive or negative.

6.4 CORE OF THE DEBATE

As the nature of threats to health and the environment becomes more complex, uncertain and global in nature, the precautionary principle is increasingly being debated (Martuzzi &Tickner 2004). Cognisance has to be taken of the debate. At the core of the debate on the precautionary principle is the degree of scientific uncertainty in risk assessment and what decisions should be made by managers in the face of uncertainty, when to apply precaution, and what precautionary measures should be taken to achieve certain levels of protection (EC 2000).

Klinke and Renn (2002) identified five major noteworthy themes in this debate (Table 6-1). These can be grouped mainly into two very closely related issues: how risks are perceived by different people; and how regulatory authorities deal with them.

6.4.1 Perception of risks and evaluation of uncertainties

There are two camps. One claims that risks are mental constructs, originating in human minds and are only real within a specific group of people. The opposite camp argues that technical estimates of risks are true representations of observable hazards and that the effect is predictable, regardless of the analyst's beliefs. In between these two viewpoints are those who believe that a combination of the two is more realistic (Renn & Klinke 2001; OECD 2003).

The concept of 'sound science' included in international agreements and guidelines (CAC 2009; South Africa 1997) is being challenged. It is questioned (Stirling 1998; 2001; Löfstedt et al. 2002, p.386; Levidow et al. 2005, p.264) whether scientists can conduct objective analysis of risks because they interpret information according to their values (Löfstedt et al. 2002, p. 386) and their scientific knowledge' (Wynne 2001). Anti- commercial sentiment is also often observed in literature on the PP, by remarks on the integrity and independence of scientists, the regulators' public accountability and those with 'financial stake in scientific development' (Feintuck 2005, p.376; Wynne 2001, pp. 445-482; Löfstedt et al. 2002, p. 396).

Charnley (2000 p.3), former president of the of the Society for Risk Analysis, has it that risk analysis is 'threatened by a serious, growing, anti-risk analysis sentiment that is challenging the legitimacy of science in

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general, and risk analysis in particular'. Scientists and managers receive blame for many 'risky' incidents, although there is perhaps an implication here that the PP replaces risk assessment. Berry (2010, p.7) responded on the accusations, 'evaluation of data obtained from scientific investigations is not easy and the process often seems counter-intuitive to the uninformed. Some hold the conviction that ideological motives colour all deliberations – this makes it easy to suggest that in any scientific debate an opponent's reason for holding a particular viewpoint or belief depends on his or her motives rather than their knowledge base. This position may be useful in providing the grounds on which to mount a polemic against any perceived threat (drugs in modern medicine, pesticides in intensive agriculture or genetically modified organisms).' 'The conviction that opinions cannot be based on independent thought, has led to a disregard of professionalism and the development of the view that who pays you determines your opinion – not your science' (Berry 2010 p.7).

The debate also includes evaluation of uncertainty in risk assessment, a topic for the professional community on issues such as the validity of animal models, variability in data and lack of knowledge (EC 2000; Klinke & Renn 2002). Approaches to assessment of GMOs, for example substantial equivalence, and concepts of familiarity and 'food with a history of safe use' are criticised as pseudo-science (Millstone, Brunner & Mayer 1999). As an alternative, a 'holistic' approach is advocated by some (Millstone et al. 1999; Traavik & Ching 2007; Hilbeck et al. 2011). Instead of gaining more knowledge about uncertainties, alternative management strategies could be proposed, for example human interventions that are manageable (Klinke & Renn 2002). Additional and more stringent control to the point of embargos or refusal to avoid any risk as a precautionary measure might be detrimental to progress. Steering direction is difficult in these situations without clear policies at every level of decision making. As an example, South African legislation requires a risk assessment and an assessment of socio-economic effects. The precautionary approach is referred to in South African legislation because the country is a signatory to the CPB. The place of benefit assessment is unknown, as it is not specifically referred to in legislation. Without clear policy on biotechnology, different South African government departments represented on the GMO Council apparently hold different positions, for example the Department of Environmental Affairs in its 'framework' (DEA n.d.) refers to 'null risk', 'avoid' and 'prevent', which describes precaution at its extreme, whereas other government departments do not seem to have any specific published policy. This is very obvious in the recent mandatory GMO labelling requirements that were promulgated by the Department of Trade and Industry without having consulted other government departments on their existing GMO labelling regulations (South Africa 2008).

Apparently, there is no well-established classification of uncertainty in risk assessment (Klinke & Renn 2002). Renn and Klinke (2001) described six groups of risks named from Greek mythology. GMO technology is grouped with disintegrating polar ice sheets because of uncertainty in both probability of occurrence and extent of damage. Vlek (2010a) grouped GMOs with risk such as the AIDS epidemic as a 'diffuse source' with the potential risk of long-term and extensive effects. Conventional agricultural plant breeding is not mentioned or far less

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precise techniques such as induced-mutation breeding where plants or seeds are exposed to ionising radiation on which regulatory control does not exist or is more lenient than for GMOs.

6.4.2 Public interest

Public perception on how uncertainty in risk assessment is handled is a valid issue to some (Klinke&Renn2002) and engagement of interested and affected parties in appraisal is also a matter of 'scientific rigour' (Stirling 2001).Unfortunately, most scientists are not great communicators, resulting in a gap in knowledge transfer to the public at large, while some sensational media contributions have led to misguided public perceptions. The debate also focuses on the legitimate role of public deliberations in risk analysis and management. The International Risk Governance Council's (IRGC) position is that all groups in society have the same right to raise concerns, arising both from intuitively estimated risk (non-factual perception) and from estimations of risk based on systematic observation, empirical data collection and rigorous modelling (IRGC 2005).

The 'contextual variables of risk' as they affect perceptions of consumers are important. (Klinke & Renn 2002, p.1077). One of the many issues is trust in regulatory agencies and risk-handling, often described as credibility (Löfstedt 2004).

6.4.3 The debate in perspective

Risk is a societal construct as well as a physical reality (OECD 2003). Results from the continued debate are observed in changes in the process of risk analysis, critical assessment of approaches to risk analysis and proposals for improved structured communication (Dreyer & Renn 2006; Dreyer et al. 2009). Some valid arguments have been raised. Inclusion of public concern/social criteria needs further research. The inclusion of sociological issues in decision making is anything but simple. There are many aspects to take into account, such as cultural differences, country needs, human nature, philosophies, religions, political issues, or whatever angle of life is approached.

6.5 ANALYSIS OF THE PRECAUTIONARY APPROACH (PRINCIPLE) AND ITS APPLICATION

5.5.1 Definitions

It is to be expected that a normative principle may be interpreted in different ways. This is illustrated by about 19 definitions of the PP (Sandin 1999; Vlek 2010a) (Table 6-2). Central to the PP is the obligation of action to reduce harm to the environment and human health, and the moral obligation that action be taken even if scientific evidence is inconclusive. These obligations are formulated in different ways, namely strong 'obligatory'

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versions and weak 'optional' versions (Table 6-3). The strong form of the PP, for example the Wingspread Statement (1998), is advocated by Greenpeace and UNESCO-COMEST (2005), while an example of a weak form is included in the Rio Declaration (UNEP 2000). The difference between weak and strong precaution lies mainly in the greater emphasis on risk avoidance, providing safety, and the obligation to take safety measures. Variations in the scope of 'precaution' from narrow to broader accounts are reflected in 1) prior risk assessment; 2) what triggers PP; and 3) the scope of action (Stirling 1998; 2001; Levidow et al. 2005).

6.5.2 Cartagena Protocol

The CPB (UN 2000), although based on what is regarded as a 'weak form' of a PP, is still the critical international instrument for making decisions on GMOs. Many debates seem to have ignored the fact that the point of departure in assessing biosafety of LMOs (living modified organisms) is determined in Article 15 of the CPB, which states that 'the focus of the Protocol is on LMOs that may have adverse effects on biodiversity' and 'risk assessments shall be carried out in a scientifically sound manner' (Annex III). Furthermore, the directive for application of a precautionary approach has been set in Principle 15 of the Rio Declaration (UNEP 2000; UNCED 1992), namely 'where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation'. Neither of these approaches demands that all applications of biotechnology or of genetic modification must undergo extensive assessments to comply with the precautionary approach and neither implies that biotechnologies are inherently unsafe. The interpretation of the requirements of the CPB in many aspects has been debated for a number of years. Some of the implementation procedures seem not to be in proportion to the risk or a cost/benefit analysis, for example the need for milling GMO commodities such as maize in the Southern Africa Development Community (SADC). An unforeseen restriction is placed on importation of commodity maize that is an LMO or contains LMOs because of liability and redress clauses that could impact negatively on the owner of the technology.

6.5.3 Critique of the PP

Vlek (2010a) groups the multiple criticisms of the PP into ten objections. Some of the objections are that the PP is vague and broadly ambitious (Majone 2002); that serious or irreversible harm is ill defined (Majone 2002; Peterson 2007); that it is dependent 'on plausibility reasoning' (Gray 1990); that it is a policy of risk avoidance (Baker 2002); that it is too absolute and obligatory, thereby blocking or slowing down technology innovation and progress (Marchant & Mossman 2005); that it demands 'impossible' proof of safety; that identifying the nature and likelihood of possible serious harm may yield high costs of safety tests and long delays in relevant policy decisions (Hanekamp & Bast 2007); and that it can be misused by powerful interest groups (Feintuck 2005).

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Vlek's (2010a, p. 533) conclusion was that the PP has 'an unusually protective inclination towards foregoing an activity or imposing strict(er) safety measures upon it, both of which are induced by large uncertainty about possible disastrous consequences'.

Peterson (2007, p.306) rejected the use of the PP as a basis for decision making, citing examples of decisions on conducting clinical trials, mobile phones and genetically modified foods. He said, 'the precautionary principle therefore replaces the balancing of risks and benefits with what might best be described as pure pessimism' (Peterson 2007, p.306). He argued, 'we need a principle that tells what to do and what not to do for each possible input of qualitative information ... no generally accepted formulation will ever emerge as the PP is not a single well defined idea ... it makes more sense to describe it as a cluster of vague related intentions about risk aversion, burden of proof, irreversible damage and normative obligations' and further 'any reasonable formulation of the PP will imply a value judgment that no rational decision maker would be prepared to accept' (Peterson 2007 pp.306-307. With respect to the burden of proof, Petersen claimed, 'it rests with anyone who makes a claim, regardless of what is being claimed' and concludes, 'There is nothing wrong with the precautionary principle – as long as it is not used for decision-making' (Peterson 2007 p.308).

Berry (2010 p.7) commented, 'convictions with ideological motives colour all deliberations'. In this regard, he mentioned the PP as a good example of only considering results that fit a preconceived viewpoint. He asserts, '[but] it should be made clear when political or socio-economic judgments are being made and the pretence that they are scientific judgment, should be eschewed. It is comforting to pretend that we know more than we think, but damaging to pretend too much'.

In summary, Vlek (2010a, p.532) said that the PP is mostly derogated for its general inclination and motivation, its dependence on plausibility reasoning, its lack of comparative risk evaluation, its lack of explicit decision-making considerations, its openness with regard to legal obligations, and its implied shift of burden of proof of safety.

6.5.4 Decisions by courts

Proof of the difficulty in interpretation of the meaning of the PP concept lies in the opinions of jurists who are grappling with it because of its philosophical characteristic, its inherent uncertainty, ambiguous and arbitrary nature (Marchant & Mossman 2005, p.10). The PP is open-ended and undefined, which 'gives regulators almost unlimited discretion to impose restrictions' (Marchant & Mossman 2005, p. 32). Ultimately the courts will have to flesh out the principle (Marchant & Mossman 2005; De Sadeleer 2009; Peel 2009, Feintuck 2005).

The reality is that prevailing social and political values influence to some degree the trend in case law. UNESCO-COMEST (2005, p.22) advises in legal formulation; firstly, the recognition of a value by a society is worthy of

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protection, and, secondly, the provision of a legislative tool [is] in order to protect this new recognised value'. The assessment of possible unintended effects on endogenous allergens resulting from genetic modification as an additional step in the process of assessment is a case in point, discussed in Section 5.9.

A WTO (WTO online) ruling on GMOs illustrates the application of the PP in international trade. A long-standing dispute existed between the United States of America and Europe over the European Commission's and several European member states' moratorium on approval of GMOs. The moratorium lasted from 1998 to 2004. In 2003, the USA, Canada and Argentina sought legal recourse at the WTO under WTO SPS (Sanitary and Phytosanitary) law based on unjustified and illegal denial of access to European markets (EC Biotech Products case) that resulted in financial losses to USA farmers. The WTO based its final decision in 2006 on failure of the defendant to conduct 'adequate' risk assessment, in terms of SPS article 5.1 and Annex A (4), by not taking into account risk assessment techniques (protocols) of relevant international organisations. Although their scientists' conclusions were based on scientific methods, the WTO panel found that legislators often based decisions on 'unverifiable facts and public fears' (Kogan 2006, p.2). The European Commission's arguments apparently rested on concerns by regulators on 'scientific uncertainty' and thereby ignoring their own risk assessments. The WTO panel rejected the defendant's arguments (Article 5.1 and 2.2). The argument that there was 'insufficient scientific evidence' (Article 5.7) was also rejected as the European Commissions' scientific committees indeed reviewed the relevant information and have not questioned their previous conclusions. Therefore, additional information in this case was not an issue. 'Scientific uncertainty' and 'insufficient scientific evidence' are not the same (SPS Article 5.7). The WTO also concluded that the European Commission had acted inconsistently with its obligation under Annex C (1) (a) and Article 8 because of the undue long delay. The European Commission accepted the ruling. Europe introduced legislation to improve the framework of assessing the application of GM pants and introduced strict labelling and traceability requirements for GMOs in 2003 to accommodate public perception and address fears. An assessment of the WTO panel's decision is not further pursued in this study (WTO 2006 online).

The interpretation of uncertainty, and perhaps consumer perceptions, is further illustrated by the November 2011 ruling of the two highest courts in the European Union, the European court of Justice and the Conseild' Etat of France, against the French ban on planting of GMO *Bt* maize. The ban was based on an EU 'safeguard clause' and legal provision for 'emergency measures' in case of evidence of serious hazards to human health and the environment. The courts ruled that France did not present any such new evidence to substantiate their ban on *Bt* maize. France responded by stating that it will reinstate the ban (EuropaBio 2011). In an October 2011 decision the European Food Safety Authority (EFSA 2011) found that pollen of maize containing the *Bt* gene was unlikely to raise any concerns. Yet, European Union regulators installed a legal requirement that all imported honey must be tested for presence of the *Bt* gene in case it contains pollen.

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In South Africa, appeals against several decisions made by the GMO Executive Council on Bt11 maize general release, biofortified sorghum for greenhouse studies and cassava field trials (DAFF, minutes of the GMO Executive Council) resulted in the Appeal Board ruling in favour of the applicants, although in the latter two cases certain conditions that require more stringent management were added. An appeal against the decision of the GMO Council on limited general release (community trials) of *Bt* potato has been pending for three years now, in spite of the GMO regulations' requirement that an Appeal Board be appointed within 60 days (DAFF, minutes of the GMO Executive Council). In the case of an appeal by Biowatch against the decision to grant general release for *Bt*11 maize, the appeal board ruled against the appeal (Morris et al. 2005). Valuable lessons were learned from this case, one of which was that demands for additional data, as a matter of 'nice to know', illustrating the interpretation of the PP by some groups in the society, could result in costly delays to the applicant, as well as the complainant and government. These are examples of interpretation of the PP in South Africa.

6.6 ACCEPTABLE SOLUTIONS?

6.6.1 Key issues in the PP

Having summarised the issues in the debate, the reality is that clear guidance is needed to facilitate regulatory decisions based on an even-handed approach to precaution. What is known at this stage is that:

- Key inherent problems with the application of the PP and the corresponding precautionary approach were identified by Vlek (2010a), as for example (a) substantive issues such as determining the plausibility, nature and seriousness of possible harm or damage; and (b) procedural issues, for instance optional versus obligatory precaution, and the need for further research and policy development. These are also described as factors triggering recourse, which is the decision to act or not to act, and the measures on how to act (EC 2000).
- The PP applies to serious uncertain risks or threats; it is inclined to be unusually protective or even preventative; the proponent has a large burden of demonstrating the likelihood of safety; and there is the tendency to delay risk-taking until sufficient new information becomes available (Vlek 2010a; Resnik 2003).
- A number of authors have described models for decision making based on assessment of risks in general (Salo 2001; Vlek 2010a, b; Resnik 2003).These rest upon axioms and assumptions that are not always valid in practice such as perceptions of cultural differences.

In trying to find a way forward, the following comments on the application of the PP by Feintuck (2005) are noteworthy. 'The PP is currently applied as a procedural rather than a substantive device and 'substantive content and value-orientation' are necessary. He contended that if the 'PP is devoid of intrinsic values, these may simply be filled by the values of dominant groups' (Feintuck 2005, p.378). Therefore, prior prioritisation of values is necessary. His conclusion, after having studied the development and implementation of the PP, was

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that 'it is a 'complex picture of interaction between science, economics, public policy and law' (Feintuck 2005 p. 377, p.392).

6.6.2 Risk governance of GMOs

The European Commission places the burden of determining an acceptable level of risk for society as a judgment of an eminently political responsibility, 'Decision-makers faced with an unacceptable risk, scientific uncertainty and public concerns have a duty to find answers' (EC 2000). Guidance from the EU perspective is followed by for example the South African regulatory authorities for GMO governance (Table 6-2) (South Africa 2004, Japhta on a parliamentary question on PP).

The International Risk Governance Council (IRGC), a private, independent, not-for–profit foundation, was established in 2003 to support governments, industries, NGOs and other organisations to deal with major and global risks and to foster public confidence in risk governance. Debates within the PP protagonist circles focus on the relative importance of substance versus procedure. At the very least, agreement on the importance of procedural steps in instances of great uncertainty about the available evidence, possible consequences, feasible options and long-term effects and minority views, is important. This organisation developed a framework to assist governments in decision making on all kinds of risks (IRGC 2003).

The IRGC framework (See also Dreyer & Renn 2009) emphasises the importance of stakeholder participation. This is also elaborated on by a number of proponents of the PP (Ahteensuu 2007; De Marchi 2003, Stirling 2001; UNESCO-COMEST 2005). One can conclude that interaction at different levels is required, but it would have specific challenges. Vlek (2010b) suggested that the parties involved might do well to attend carefully to the kind of participants, structure, content and process making up the relevant assessment and management strategy. Vlek (2010b) also warned against individual judgments and social decision making that allow room for prior beliefs and biases, selective information processing, authoritative dominance and groupthink at the cost of minority views. In participative, multi-stakeholder situations, this could lead to disputable judgments, decisions and actions (Feintuck 2005).

The PP is scientifically indefensible. Sociological considerations would not easily disappear. In a democratic political situation, and to improve credibility of risk governance, improved interaction with stakeholders (for example the public, scientists, and the owners of the technology) has to be considered. Much more thought will have to go into defining the nature and substance of such interactions. These may differ between developing and developed countries for many reasons, but in particular policy priorities, such as food security, that express the needs of the population should be discussed. Participation has to be correctly defined, as accountability remains with the regulatory authority.

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6.7 ADVANCED TECHNOLOGIES

Entering the debate on a completely different level, which will have future impact on decision making, are a number of advanced genetic technologies that will have to be considered for inclusion or exclusion as GMOs/LMOs (and therefore included under the CPB) or excluded as non-GMOs. These include cisgenics and intragenics, oligo-nucleotide directed mutagenesis, precise molecular surgery in the plant genome (Fauser 2012), zinc-finger nuclease technologies, RNA-dependent DNA methylation, grafting on GM rootstock, reverse breeding, agro-infiltration, and synthetic genomics (Lusser et al. 2011). Many of these genetic alterations occur in nature (Lusser et al. 2011). Several recent articles have shown that traditional breeding causes more inherent variability than GM (Baudo 2006; Batista et al. 2008; Ricroch, Berge & Kuntz 2011; Kogel et al. 2010). Arguments for less stringent requirements or exemption from regulation are heard frequently (Chassy 2010; Herman, Chassy & Parrott 2009; Parrott 2010; Ricroch et al. 2011; Waltz 2012), as well as the need for policy reform to take into account the new developments (Durham, Doucet & Snyder2011; Canadian Plant Biosafety Office 2002). A case-by–case approach and the introduction of proactive measures by proposing a de minimus approach to regulatory requirements are being given increasingly more thought. This may have a stimulating effect on other governments to reassess their requirements and to reconsider the role of the PP.

6.8 ADDITIONAL STEP IN RISK ANALYSIS

The need for an additional step in the risk analysis process has become of critical importance for South Africa. Policy development is of great importance to give direction in time on matters such as socio-economic benefits and new technologies. This should be done in advance of risk assessment. Codex describes such a step as determination of ‘risk assessment policy’ as a specific component of risk management interaction between risk managers, risk assessors and stakeholders (CAC 2011). However, an additional step may include more than defining policies as the need arises for improved risk assessment.

South Africa, as a developing country that ranks eighth in line in world production of GM crops, may in the near future be approached to consider these advanced technologies. Issues on new developments of GMOs, new techniques, and new problem formulation require considerable scientific capacity that may not be available in small closed systems that are currently functional, for example the South African GMO governance system. This proposed additional step in risk for ‘risk assessment policy’ (CAC 2011) or ‘framing’ step (Dreyer & Renn 2009) should also address the limited capacity in experience and expertise in the fast advancing and diversified field of biotechnology.

Where the application of the precautionary principle is part of risk management, consideration of scientific uncertainty in risk analysis is described as a ‘prudential approach’ that is part of risk assessment policy (EC

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2000). Inclusion of consideration of scientific uncertainty in the proposed step is illustrated in the case study endogenous allergens.

Another additional step, described as the evaluation step or characterisation of the risk may also be important in future. This step follows on risk assessment and brings aspects such as benefits of socio-economic relevance into perspective.

6.9 ASSESSMENT OF ENDOGENOUS ALLERGENS

The following discussion provides an example of the complexity with which decision makers could be confronted with when uncertainty in risk assessment and precautionary management measures are considered.

Codex's guidance for risk assessment of GMOs describes the precautionary process to be followed in the safety/risk assessment of GM products. Codex has not adopted the PP for risk management (CAC 2007). The different steps for assessment, described in Chapter 4, comprise *inter alia,* comparative assessments between GMOs and the near isogenic lines with respect to the components: nutrients, antinutrients and toxicants. The comparison provides for identifying possible unintended effects of concern regarding those mentioned components. Codex (CAC 2009) in a footnote considers that endogenous allergens to be included in the comparative assessment. Identification of possible unintended effects of endogenous allergens poses to be problematic and thereby resulting in some uncertainty. The following description touches on the difficulties in identification of possible changes in endogenous allergen levels and possible options that decision makers may have in applying more precaution in the risk assessment and/or in precautionary risk management. Additional regulatory requirements could result in increasing cost of regulatory compliance with possible negative effects on availability of food. Analysis for possible unintended changes in endogenous allergenicity may be a priority 'value' for some, however, food security may be a major issue valued by others in poor countries.

A scenario of the knowledge gained over sixteen years with GM plants and, with assessment of food allergenicity, may give better perspective on assessment of endogenous allergens of GM plants and options to apply the precautionary principle in managerial measures.

6.9.1 Step: Risk assessment framing

6.9.1.1 Policy development

A precautionary /risk assessment debate may proceed as follows.

Possible questions that could be asked are: Does the case under consideration qualify as a situation of serious uncertainty and an irreversible risk? This question may not be easy to answer and may provoke diverse

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reactions. The next question could be: Are there any assumptions that could be made? An answer would be that hypothetically there would be people allergic to any possible food, whether processed or eaten raw. More questions with some information are given in Table 6-4.

The information is grouped into exposure to and hazard of allergens, as well as variability in humans, the variability in plant allergen levels due to environmental effects, and genetic variability between crop varieties. Important questions relate to the status and validity of detection methods such as serum tests and animal models, as well as use of proteomic studies. The same questions can be asked for endogenous allergens of maize as a specific example in this illustration of decision making (Table 6-5). A general conclusion is that there are a number of issues that would make it difficult to make a decision of absolute safety unless much more information is generated. The shortage of serum donors would be critical in most cases.

More questions are: What tolerance level would be considered once the range of endogenous allergen levels has been determined for each crop plant? How sensitive are the tests and what serum sample size is required? What percentage (or concentration) increase above the range of natural biological variation is acceptable? What percentage of the population should be protected? What levels would cause reactions in patients, from mild to severe? What percentage of severe reactions such as anaphylactic shocks has been documented for the population?

General issues on how allergenicity is handled by consumers and how countries manage allergenic foods are relevant, for example:

- In many countries allergen labelling is required only for the eight allergenic food groups.
- It is difficult to determine the prevalence of allergenicity, as consumers tend to avoid foods to which they are allergic.
- Although allergenicity to some foods such as peanuts and tree nuts could affect up to 1% of the population, none of these foods have been withdrawn from the market.

6.9.1.2 Defining different options

Having in mind the application of the PP as relevant for serious uncertain risks or threats, its uncertain protective inclination, the developer's larger burden of demonstrating the likelihood of safety, and the tendency to delay risk-taking until sufficient new information becomes available (Vlek 2010a), the following possible scenarios for decision making could be:

- Unintended effects have not been demonstrated as yet for endogenous allergens. Variability in plants is large, resulting in exposure of all consumers to a range of allergen levels in plants. Conventional plant

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breeding has been found to lead to unintended effects. Extreme increase in endogenous allergen levels in plants might be detected in the phenotypic and compositional changes as these allergens have specific functions in plants that could interact in different ways with plant metabolism. Small changes should not have an impact on consumer behaviour and there should be no current need for additional assessments. The molecular assessment did not show any issues of concern.

- A more conservative scenario would be to include an evaluation of changes in only the major identified sources of allergens (soybean, peanuts, wheat, etc.).
- An even more conservative scenario of requesting analysis of all crop plants, vegetable and fruits with currently available techniques.

6.9.1.3 Possible policy decisions

- Approve with labelling for allergenicity? The eight important allergenic foods are already labelled. There are existing requirements for labelling of GM foods with increased allergen levels. Allergenicity could be triggered at very low concentrations. Some of the GM-derived foods already on the market did not have any allergenic effects, so would that require an Identity Preservation System (IPS) to manage possible co-mingling and what would be the IPS tolerance levels?
- Approve with monitoring
- Do not approve
- Approve without restriction.

The extreme position would be not to approve the application for a permit as a precautionary measure. Another position would be to make a judgmental decision based on 'weight of evidence'.

6.10 DISCUSSION

Decision makers are confronted with a number of challenges. A study of the literature on natural allergens and GM crop plant endogenous allergens shows that many questions remain unanswered. It seems that some regulatory authorities are over-reacting by asking for more and more information to confirm possible unintended differences between the endogenous allergens of GM and its non-GM near isogenic line. Adequacy of the assessment of allergenicity is debated. Goodman et al. (2008) comment on the validation of the tests particularly available of serum. They contend that the 'extreme precautionary position is not scientifically defensible' (Goodman et al. 2008, p.1071).The current practice is to avoid allergens. Their opinion is that 'we need to know more about endogenous allergen levels and natural variation and have not seen data that demonstrate an enhanced risk to the consumer, based on the observed variation'. To date, no empirical evidence has been presented that South African crops containing current genetic modifications, have up-regulated allergen levels

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and there is no evidence tabled on consumers having shown adverse reactions due to allergens from eating approved GM products. Therefore, the postulated risk remains a hypothetical one. Regulatory authorities have to make decisions, while scientists continue to debate at a technical level. Before requesting additional studies, policies on risk to consumers should be placed in the broader context of the country's needs such as food security. The example shows the need for proactively considering the approach to be followed. These should be included in a 'risk assessment policy' step that does not exist in many risk governance situations. Consequences for additional precautionary requirements that are not well thought through are far reaching. Regulating these issues has implications for sustainable development particularly for developing countries, including national research, careers of young scientists, but above all, on poverty reduction and the livelihoods of the poor and marginalised.

6.11 CONCLUSIONS AND RECOMMENDATIONS

The debate on the PP illustrates the diverse opinions on the safety requirements for GM crop plants. The problems inherent in the application of the precautionary approach are clearly demonstrated by the example of endogenous allergens described in this chapter. Some consider GM crops irreversibly harmful, while others view them as representing only a continuum of existing knowledge and agricultural practices. Regulatory authorities appear hesitant to formulate decisions that strike an appropriate balance between risk and benefit, and that take into account comparative risk. The key problem with the PP is that it is a normative principle, ill-defined and vague. Future developments such as a range of new molecular breeding techniques, leading to differences in what is to be regarded as a non-GMO and what is not a GMO, would require much more in depth consideration

The following recommendations can be made for South Africa:

- Regulatory decisions must give consideration to the objectives of the National Strategy on Biotechnology (being revised as a bio-economy strategy).
- There needs to be a clear national policy for a harmonious approach between different government departments represented on the GMO Executive Committee, on biosafety and precaution.
- Such a national policy should facilitate the local development and application of GM crops with relevance to African farmers that will contribute to food security.
- An additional step in risk governance is proposed to accommodate communication in development of policies and guidelines, including approaches to sound science-based risk assessment and the PP, as well as governing emerging new genetic technologies in South Africa. At this proposed step, clarity on socio-economic issues that could impact on risk assessment should be considered as guidance for judgements on uncertainty matters e.g. possible unintended effects. Guidance should include the extent of scientific

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detailed requirements for the specific risk assessment. This proposal is envisaged to facilitate a more harmonious national system for biosafety assessments.

- A new dispensation in South African risk governance of GMOs should be considered that require benefits of modern biotechnology (including genetic modification) are given adequate consideration and applied to the advantage of the population.
- National regulators, scientific advisors and biotechnology applicants will be increasingly confronted by new biotechnologies and possible new additions to biosafety regulations. Conflict can be reduced by means of capacity building and improved communication.
- The GMO Act of 1997, as amended in 2006, is in need of updating as it makes reference to eight government departments (presently six) to be represented on the GMO Executive Council, but several of these departments have since been merged or reshuffled. This would also enable re-consideration of certain unacceptable text such as 'avoiding risks' and impractical requirements such as decision making based on consensus. Inclusion of an additional step, described as risk assessment policy (framing) to improve credibility of risk analysis, should be seriously considered.
- South Africa, as leader in Africa with 14 years of experience of growing GMO crops and a biosafety framework, should start to play a leading role in Africa, instead of leaving it to other states to draft disharmonious policies that will prevent regional agricultural trade from flourishing in a continent exposed to food shortage and famine.
- Strong policies are needed that focus firmly on critical issues such as food security that is critical to the wellbeing of all in developing countries.

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Table 6 -1: Definitions and guideline description of the Precautionary Principle

Codex Alimentarius Commission (CAC 2009) 'Precaution is an inherent element of risk analysis. Many sources of uncertainty exist in the process of risk assessment and risk management in food related hazards to human health. The degree of uncertainty and variability in the available scientific information should be explicitly considered in the risk analysis. Where there is sufficient scientific evidence to allow Codex to proceed to elaborate a standard or related text, the assumption used for the risk assessment and the risk management options selected should reflect the degree of uncertainty and the characteristics of the hazard'.
Rio Declaration, Principle 15 (UNCED 1992; UNEP 2000); Cartagena Protocol on Biosafety to the convention on biological diversity (Secretariat of the Convention on Biological Diversity 2000) 'In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as reason for postponing cost-effective measures to prevent environmental degradation'.
GMO Act (15 of 1997) as amended in 2006 (South Africa 1997) (DAFF 2004; Japhta 2004). • Proportional to risk • Non-discriminatory • Consistent • Based on cost-effect assessment • Subject to review. Capable of assigning responsibility for producing scientific evidence.
UNESCO-COMEST (UNESCO-COMEST 2005, p.14) 'When human activities may lead to morally unacceptable harm that is scientifically plausible but uncertain, actions shall be taken to avoid or diminish harm ... Morally unacceptable harm is ... (1) threatening to human life or health, (2) Serious and effectively irreversible, (3) Inequitably to present or future generations, (4) imposed without ... consideration of ... human rights ... 'The judgment of plausibility should be grounded in scientific analysis ... Uncertainty may apply to, but need not be limited to, causality or the bounds of the possible harm. Actions are interventions that are undertaken before harm occurs that seek to avoid or diminish the harm. Actions should be chosen that are proportional to the seriousness of the potential harm, with consideration of their positive and negative consequences and with an assessment of their moral implications of both action and inaction. The choice of action should be the result of a participatory process'.

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Wingspread Statement on the Precautionary Principle (Wingspread1998) 'Where an activity raises threats of harm to human health or the environment precautionary measure should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent of the activity, rather the public, should bear the burden of proof '.

Table 6-2: Accounts of the precautionary principle (Levidow, Carr & Wield 2005; Stirling 2001)

NARROW ACCOUNTS	BROADER ACCOUNTS
Prior risk assessment	
The burden of evidence is inherently shifted, from demonstrating risk, to demonstrating safety	The burden of evidence depends on the questions asked: asking the right questions needs stakeholder involvement
Trigger for PP	
PP can be triggered only by an objective scientific evaluation, indicating reasonable grounds to expect potentially dangerous effects (or established scientific uncertainty)	PP can be triggered also by initial suspicions about risk. PP can justify measures to control undesirable effects (including potentially dangerous ones)
Scope of action	
Analyse policy options: regulatory action versus inaction – e.g. through a cost-benefit analysis	Provide the means to demonstrate that alternative solutions are less harmful Establish a dialogue on social issues, e.g. what options are desirable and feasible.

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Table 6-3: Controversial issues in risk management (Klinke & Renn 2002)

1.	Realism versus constructivism
2.	The relevance of public concerns revealed through studies of perceptions as criteria for risk regulation
3.	The appropriate handling of uncertainty in risk assessments
4.	The legitimate role of 'science-based' versus 'precaution-based' management approaches
5.	The optimal integration of analytical and deliberative processes

Table 6.4: Endogenous food allergen information

Exposure to all food allergens: Plant tissues can express at least 100 000 discrete proteins to which humans could be exposed. Conventional breeding results in transfer of hundreds of genes between different sources. They are not all potential allergens. A weight of evidence approach described by Codex Alimentarius (CAC 2011) is currently the accepted way of confirming food allergens of genetically modified foods specifically novel proteins. Exposure is a prerequisite for sensitisation. The threshold for sensitisation needs further research (EFSA 2010). A risk factor is the abundance of the protein in food. Many food allergens account for 1% of the protein in high-protein allergenic foods. Lipid transfer proteins and parcalbumins are less abundant (Goodman et al. 2008). Cross-reactive allergies occur e.g. Spaniard sensitivity to apples (Mal d 3 a lipid transfer protein) is different from Dutchmen (Mal d 1) because of birch pollen exposure in Holland (Fernandez-Rivas et al. 2006).GM production for 2010 is 1 097.9 million hectares (James 2011).
Human hazard: The prevalence of food allergenicity is unknown, but it is estimated that the eight most common allergens affect up to 3% of the adults and up 6 % of infants of the population (Sampson 2005; Zuberbier et al. 2004). Common allergenic foods that account for over 90% of reported food allergies are peanuts, soybean, tree nuts, wheat, cow's milk, egg, fish and crustaceans (Bush & Hefle 1996; Hefle, Nordlee &Taylor1996). These require labelling by many countries. Less common allergic foods of plant or animal origin are buckwheat, lupin, peas, psyllium, rice, apples, cabbage, celery, chocolate, melons, papain, potato, tomato, and molluscs (Bush &Hefle1996).

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Variability in humans: Each of the allergenic foods contains multiple allergens, some regarded as principal allergens when 50% of an allergic population expresses allergic symptoms, although some of the minor allergens may cause more severe reactions, depending on the sensitivity of the persons (Bush&Hefle1996).Human biological variability is high, as human sensitivity to different allergens of a species differs. It is not predictable who will become allergic and to which foods and which proteins in foods. (Goodman et al. 2008). There are stable and abundant proteins that do not cause allergy as well as moderately abundant proteins that do cause allergy. (Goodman &Tetteh 2011). Sensitivity reactions vary between mild rashes to anaphylactic shock to the same concentration allergen in different people (Anderson 1996). There is a wide variation in IgE binding to different varieties of the same species of non-GM crops (Sten et al. 2004).
Natural variability of plant allergen levels: Natural variability is a result of genetics, environmental factors, post-harvest conditions. Food processing and interactions with the food matrix also affect the allergic potential. (EFSA 2010). Natural variation of expression levels of various allergenic proteins for most crops has not been documented (Goodman &Tetteh 2011).
Status of detection methods: Specific serum screening to confirm allergenicity may not be possible for many food allergens because of difficulties in identification of sufficient number of donors, cross-reactivity and other problems (Goodman & Tetteh 2011; EFSA 2010) The number of sera samples needed is dependent on the required degree of protection to the population. Animal models are in general considered not validated and inconclusive for assessment (EFSA 2010, Ladics et al 2010). Sufficient sensitivity and specificity to guarantee absence of false negative and false positive results are not yet possible (EFSA 2010). Analytical and profiling techniques/in vitro protein analysis and proteomics methods are to be assessed for accuracy, sensitivity, specificity and feasibility before being routinely used for allergenicity assessment (EFSA 2010).

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Table 6-5: Exposure and hazard considerations for endogenous allergens of maize

Criteria	Maize
Characteristics of the allergen	The main allergen of maize is a lipid transfer protein (LTP), Zea m 14, a true pan-allergen. It is a potentially severe food allergen (Pasterello et al. 2000; Asero et al. 2001). LTP maintains its structure after cooking at high temperatures (Pastorello et al. 2003). Large numbers of allergens have been identified (Pastorello et al. 2009). Cross sensitivity with other fruits and vegetables (Pastorello et al. 2000)
Exposure: the food basket of the country and exposure to consumer of the country	Maize is a staple in Africa. The average consumption is about 500g per person per day
Hazard classification: not a common food allergen	Prevalence is unknown. Not many incidences have been reported and reported incidences are particularly in a region in Italy (Pastorello et al. 2000), in Mexico (Zavala et al. 2006) and ad hoc reports in the literature (Bock 1987; Tanaka, El-Dahr & Lehrer2001). There may be more, but due to consumers' habit of avoiding allergic foods, reporting is unreliable. South Africa and the rest of Africa have no available information
Allergen Labelling requirements	Not for maize

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Environmental and hybrid variability of principal allergens	Grain from specific hybrids varied up to 10-fold in relative abundance from irrigated test plots and nearly 20-fold in non-irrigated plots. For two hybrids the LPT concentrations differed nearly 10-fold between irrigated and non-irrigated plots. (Ariyarathna, Pramod & Goodman 2009). Environmental and hybrid variability is high (Goodman RE. Personal communication. email message on 26 April 2011 address rgoodman2@unl.edu) The population has been exposed for many years to fluctuating concentrations because of environmental influences
Availability of serum for routine testing	Serum tests would be very difficult to conduct because of scarcity of allergic consumers (Goodman &Tetteh 2011)
Level of sensitivity	Two patients reacted to 100mg of raw maize and nearly half (unknown, not quoted) to =1.6 g of raw maize (Venter, Skypala & Dean 2008; Scibilia et al. 2008)

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CHAPTER 7: A MODEL FOR GMO RISK GOVERNANCE

7.1 INTRODUCTION

This chapter serves to formulate a proposal for improved risk governance of GMOs. The results from the various investigations as described in different chapters are summarised in order to follow the rationale for the critical elements in the proposed governance model.

Chapter 2 covered governance models in general and for specific countries and regions. In Chapter 3, criteria for good governance were analysed and additional opinions were obtained from applicants of areas of most concern. In Chapters 4, 5 and 6 some of the concerns identified in Chapter 3 were investigated in depth.

7.2 COMPARISON BETWEEN SOUTH AFRICAN RISK GOVERNANCE AND MODELS OF RISK GOVERNANCE

The characteristics of three risk governance models in a continuum of development towards improved democratisation are described in Chapter 2. The frameworks of governance of a number of countries illustrate features that are commendable. The framework and functioning of the European Food Safety Authority (EFSA) is an example of a risk assessment model that concurs with most of the requirements for good governance. Its independency in risk assessments, self-tasking to fulfil a need for guidelines, and scientific excellence in performance, as illustrated by the scientific reports and transparency in activities, are a few of the criteria for good governance that set an example for the development of new models. The model developed by the United Kingdom (UK) is an example of increased communication and scientific excellence (independent expert teams). Argentina has developed a platform for stakeholder participation, the elements of which could be further investigated. The model described for Australia and New Zealand seems to be too complex for a developing country with little capacity. The Common Market for Eastern and Southern Africa (COMESA) is considering a model to overcome shortage of capacity by centralising independent risk assessment. The model for pesticide assessment in operation in Central Africa needs improvement in too many aspects of good governance and is not recommended. These models have elements that could be incorporated into an ideal model for South Africa.

An ideal South African model for GMO governance of risks is based on improvements to the current framework, which is characteristic of the decisionist model. The need for and kind of improvement identified in this study, as well as relevant country frameworks, serve to design a framework according to the transparent model, which is the most advanced for democratic decision making (Ely et al. 2009) and specifically the proposed framework for improved risk analysis of food as develop by a consortium of specialists for Europe (König et al, 2010).

GMO legislation complies mainly with the requirements of the decisionist model, which is functional separation between the risk assessors and risk managers. The risk assessors are independent members of the GMO

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Advisory Committee (AC), not government employees, but from universities and research institutes. However, the implementation of the act tends to lean towards a 'technocratic' model because regulatory authorities (risk managers with the specific function of decision making in the context of this study) are responsible for departmental risk assessments in terms of each department's mandate.

The current system lacks the elements of the more advanced transparent risk governance model that, in addition to improved independency, is in need of improved risk communication, described as transparency, participation and openness.

7.3 IDENTIFYING ELEMENTS FOR IMPROVEMENT OF SOUTH AFRICAN RISK GOVERNANCE

South African governance was analysed according to criteria for good governance. The results are summarised in Table 7-1 and Table 7-2. .A focus for detailed analysis of some of the critical issues was identified in this study. Obvious reasons for concern for effectiveness and accountability were unclear role descriptions. It was found that effectiveness needed a great deal of improvement. It could be a consequence of long delays in issuing permits. The main cause for delays was identified as the consensus approach applied as unanimity in Executive Council (EC) decision making, possibly because of excessive precaution in certain cases. The respondents to the questionnaire were of the opinion that guidelines and guidelines in risk assessment and decision making were required to improve effectiveness. The interpretation of the precautionary principle in decision making was identified as a possible matter of concern. Consequently, research was undertaken into a better understanding of the principle and its interpretation by the regulatory authorities. Because approaches to risk assessments could also have been a cause of delays, case studies that involved environmental risk and food safety/risk assessments were included in the research.

Three studies were conducted to identify reasons for delays. The first study, that of sorghum, was chosen as example of environmental risk assessment because of exceptional long delays in the regulatory decision making. The conclusion was that, apparently, the assessment was not conducted according to the requirements of a risk assessment, described as formulating the problem, risk hypothesis, and endpoints in the assessment plan. Risk was described erroneously by not considering all factors to identify the risk. The conclusion was that there was no policy or guidance on approaches to be followed in environmental risk assessment. This was confirmed by the lack of a consistent and correct description of 'risk' in the GMO Act and the Framework Guideline of the Department of Environmental Affairs.

The second study was an analysis of cassava information to propose a method for assessment of crops with high concentrations of natural toxicants. The approach differs from the proposed comparative analysis between

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the test plant and the near isogenic line with a 'history of safe use'. The significance of timely consultation on approaches to safety/risk assessment of crops needs the attention of decision makers.

The third study included an application of the precautionary principle to endogenous allergens. The justification for not proceeding with the GM potato case was that its present sub judice status, because of an appeal, prevented the use of confidential information. Therefore, the decision was reached to continue with a case study on maize. The analysis of the case showed the complexities that decision makers encounter specifically where possible uncertainties are identified in risk assessment and the benefits of the product are of importance in developing countries.

All three case studies point at a serious deficiency in timeous communication. Communication includes *inter alia* approved policies and approved guidelines. The studies showed lack of consensus on approaches to risk assessment and in applying precautionary decision making to uncertainties in risk assessments. One of the reasons for inconsistency could be the absence of national policy and, consequently, no coherence in a national strategic plan, which, in any case, does not provide guidance to a better understanding of 'risk'.

Alternatively, legally binding structures for communication, such as a framing phase for risk assessments, could enhance coherence because of the inclusion of scientists of competent standing, transparency in procedures, and sound science, as well as accountability in an open framing process that should increase credibility of governance.

7.4 A GOVERNANCE MODEL FOR SOUTH AFRICA

7.4.1 The model

The proposed model is constructed on the existing decisionist model. An additional phase (step) in the procedures is recommended that would provide for timely communication. Communication should have framing for risk assessments as purpose. Framing would not have much value if policy and guidelines are not available. Therefore, to develop the necessary 'tools' for risk assessment in a much more transparent milieu and striving for scientific excellence would require expertise, whether from national or international resources.

The decisions of the EC were often based on socio-economic and trade considerations. No details of decisions are available and, therefore, these could not be investigated in this research. However, such scientific information would be of great value in the evaluation of the risk and the benefits of the product. An additional phase (step) is therefore included in the proposed model to accommodate such considerations.

A proposed model is illustrated in Figure 7-1. The model includes a risk assessment framing body (RAFB). A chairperson, independent of government and industry, should be considered to ensure continued independency.

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Government departments on RAFB are to be represented in their individual capacity, and not as council members, to ensure individual contributions. Experts in applicable fields of interest are included to contribute to high-level discussions and to build capacity. A specific requirement is knowledge and understanding of the concept of 'risk'. Policy and guidance on socio-economic and benefit issues should be addressed beforehand by experts, preferably at the RAFB intervention. The clarity on the socio-economic policy and guidelines should improve the evaluations to be made by a possible risk evaluation committee of the EC.

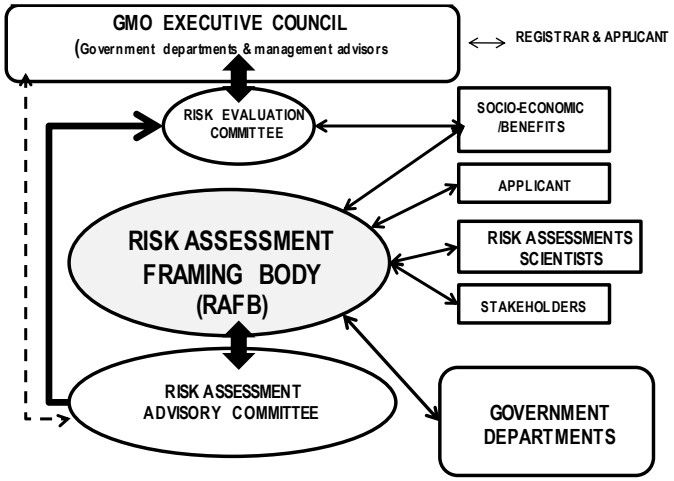

Figure 7- 1: GMO risk governance model for South Africa

7.4.2 The role of decision makers

The exclusive tasks of risk managers are defined as decision making, implementation and monitoring (Renn & Dreyer 2009).The role of risk managers as decision makers, in the framing step, should be within the perspective that' tasks [are]undertaken jointly by assessors and managers…with inputs from a wide range of stakeholders' (Ely et al. 2009,p. 47).Knudsen commented that there should be a strict separation between the role players, particularly the interface group, and the scientists and stakeholders (Knudsen 2010).

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7.4.3 Role of risk assessors

The need for more experienced risk assessors can be addressed in various ways, but has to be guided by 'needs assessments' and policy on adequacy of risk assessors. The GMO Act provides for two positions from the public sector on the AC. This creates an opportunity for the national research institutes to develop expertise in risk assessment. Training of the advisory committee members, as well as members of the EC, was suggested as a remedial action. However, training needs to be in the approved principles of risk assessment to be determined by official policies. The advanced governance transparent model suggests that policy development occurs through participation of various role players. In this case, expertise in risk assessment approaches and exposure on international fora such as the Organisation for Economic Coordination and Development (OECD) would be essential.

Peer reviewing is considered of great importance by the respondents to the questionnaire. The system could be improved by regrouping the AC according to the EFSA example of panel groups. The ecologist should be replaced by an eco-toxicologist as the environmental risk assessment is based on risk criteria, and not on scientific criteria. The case study with cassava shows the importance of specialisation in crop composition analysis and the application of existing approaches to new challenges in future. A need for more specialist inputs into phenotypic and agronomic contribution would become more important when more complex risk assessment is to be conducted and interpretation and the essential role of plant breeders are recognised.

7.4.4 Scientists

Studies showed that scientists are the most credible of the interviewed groups for conveying correct information (Aerni, 2002, 2006). This is an important 'perception' to build trust in governance and, therefore, the inclusion of expert scientists should be strongly considered as additional resource to contribute to risk assessments as in the case of the UK 's expert groups (Atkins & Norman2009) and recommended for EFSA (Kuiper & Davis 2010). However, the value of additional scientific expertise should be exploited beyond risk assessments and should include participation in policy development, guideline development, capacity building and framing. The goal should be the establishment of a platform of expertise for South African GMO risk assessments. The case studies on sorghum and cassava provide justification for inclusion of scientists from public and academic institutions as well as international specialists.

7.4.5 Stakeholder participation

Stakeholder participation is a new concept that has not been thoroughly researched. The European Commission is currently investigating participation according to a structured approach (Knudsen 2010, p. 1654; Kuiper &Davis 2010).

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7.4.6 Functions of the risk assessment framing body

7.4.6.1 Policy development:

The following should be considered:

- Role description and Independency;
- Procedural policies;
- Risk assessment approaches;
- Application of the precautionary principle;
- Application of socio-economic principles and benefit assessment;
- Scientific excellence – peer reviewing, guidelines, capacity building, platform for excellence;
- Capacity building – training, experience, national and international interactions;
- Policy on international participation such as OECD and conferences;
- Stakeholder participation;
- Risk communication – transparency, openness; and,
- Guidelines for implementing policies and legality of guidelines.

7.4.6.2 Framing

This is described in detail in Chapter 2.

7.5 IMPLEMENTATION

Incremental implementation is recommended:

- Firstly: Development of policies and guidelines by risk assessors, risk managers and identification of experts/specialists for establishing a platform of expertise;
- Secondly: Implementation of policies and guidelines in the framing of risk assessments;
- Thirdly: Amendment of legislation to reflect the intention of 'risk' and the inclusion of the additional phases in the process of risk analysis; and,
- Fourthly: Implementation of amended legislation.

7.6 CONCLUSION

The proposed risk governance model, when fully implemented, should contribute to satisfy the required improvement of credibility of governance. The governance model is briefly described, as well as, the roles of

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decision makers, risk assessors, scientists and stakeholders. The inclusion of additional scientists in various capacities could be a critical factor to improved trust in risk governance. The important concept of conducting 'risk assessment', as opposed to scientific research investigations, is a critical issue that may need a change in mind set. Scientists have an important role in capacity building and framing of risk assessments, and to be able to fulfil in these needs they have to be in touch with international trends in risk assessments concepts, approaches and methodologies.

Incremental implementation of the model is the obvious way to go because of considerable changes proposed to the current system. Awareness of democratic principles in governance, such as 'independency'' as described in this study may receive resistance because of present fixed departmental mandates. However, a need for change has been identified to improve the credibility of the system.

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Table 7-1: Summary of results from two questionnaires and focus of research

QUESTIONNAIRE 1: CREDIBILITY			QUESTIONNAIRE 2: DELAYS		RESEARCH
CRITERION	**DESCRIPTION**	**RESPONSES**	**DELAYS RESPONSES**	**REMEDIAL RESPONSES**	
Effectiveness	Roles defined Guidelines Planning Experience	Effectiveness and accountability need much improvement	Excessive Precaution	Training Guideline	• Principles and approaches to • Food safety/risk assessment • Precautionary decision making • Environmental risk assessment
Accountability	Roles defined	Roles are unclear	Council		
Independency	No pressure from policy makers and stakeholders	Independency needs some improvement	Unanimity		
Scientific Excellence	Enough risk assessors	Not enough	Shortage of risk assessors	Training Guideline	To be identified
	Peer review	Some to much improvement	-		
	Networks/ info systems Consultation	Some to much improvement	-		
	Guidelines	Some to much improvement	need		
Openness	Stakeholders Decision making	Some improvement	-	-	To be identified
Transparency	Procedures / Communicating uncertainty / Names known	Some improvement	-	-	
Participation	Inclusive / exclusive	Some improvement	-	-	

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Table 7-2: Summary of results from two questionnaires and focus of research

STUDY	JUSTIFICATION	RESULTS of study	REASONS FOR DELAYS	REMEDIATION	Proposal
Environmental risk assessment: sorghum	Trial release permit not approved, appeal, delays, research terminated	Questionable application of risk assessment approach	No policy, no guidelines No communication?	Transparent policy and guidelines development before commencement of risk assessments including scientific research inputs/consultations/ training in risk assessment	New phase (step) to be included in risk analysis for risk assessment framing, determining of needs for improved risk assessment and risk management decisions and addressing identified needs, e.g. policies and capacity building
Food safety/risk assessment: cassava	Crops with high levels toxicants and no regulatory requirements for assessment of food safety /industrial use	No guidance available	No policy, no guidelines No communication?		
Precautionary Principle: endogenous allergens of maize	Permit for *Bt* potato not approved because of various reasons and also including endogenous allergens. .	Unclear rationale for inclusion all crop endogenous allergen assessment in regulatory requirement	No policy, no guidelines No communication?		

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CHAPTER 8: GOVERNANCE OF TOXICOLOGICAL ASSESSMENT OF PESTICIDES

ABSTRACT

The purpose of the study was to design a model for South African (SA) governance of toxicological assessment of new pesticide molecules based on principles of good risk governance. Such a need was identified because of outdated legislation on pesticide registrations, no legal obligation to the health department to conduct assessments, and apparent shortage of regulatory toxicologists. The methodology followed in the study was, firstly, by comparing the historical development of governance of toxicological assessments since the early 1900's until 2011 against risk governance models, and secondly, to obtain the opinions of some stakeholders on acceptable models. The analysis indicates that functional separation between toxicological assessment s and registration is important to ensure independency and peer reviewing of assessments that would improve credibility. A SA model is proposed to include the existing arrangements with veterinarians identified as the most suitable discipline for toxicological assessments. An important feature is inclusion of a body for risk assessment policy development and reporting to provide for an interface between independent toxicological assessments and regulatory authorities, as well as improved communication with stakeholders. A proposal is made for establishing a center of excellence that should include the existing veterinary facilities at the University of Pretoria and the Agricultural Research Council.

Keywords: Veterinarians, toxicologists, pesticides, risk assessment body, risk policy development and reporting body, toxicology review body

8.1. INTRODUCTION

In South Africa, the Department of Agriculture, Forestry and Fisheries (DAFF) regulate the registration of all pesticides by stipulating inter alia the requirements for efficacy, quality and safety (South Africa 1947). Act 36 of 1947 required the registration of remedies per definition, including pesticides and livestock (excluding substances prescribed by veterinarians). Veterinary medicines are registered under the Medicines and Related Substances Act (South Africa, 1965, as amended). The safety of agricultural remedies (pesticides), stock remedies and veterinary medicines is considered with respect to human and animal health. The environmental risk of pesticides was weighed up on an ad hoc basis, as national facilities were not available for clearing the environmental risks (Wiese & Bot 1971) until environmental legislation was promulgated in 1998, and environmental authorities took on the responsibility of the assessments. The DAFF evaluates data submitted by applicants to determine statutory maximum residue levels (MRLs), but the legal responsibility for regulating MRLs for pesticides rests with the South African Department of Health in terms of a reactive food safety act

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(South Africa 1972). This implies that the Health Department considers recommendations made by an authority responsible for the toxicological assessment of pesticides.

Since the promulgation of the act that regulates pesticides, a great deal of development has occurred in the formulation of governance models, as is described in this study. Therefore, there is a need to analyse the governance of pesticides to make proposals for improvement, should it be deemed necessary. The focus of the analysis is on the toxicological assessment of new molecules, which forms part of the safety requirements for registration of new pesticides.

The proposed governance model is based on:

- Literature studies on food safety governance
- An analysis of the historical development of almost a century of South African governance of toxicological assessment of pesticides
- The perceptions of stakeholders based on a questionnaire on criteria for good governance of pesticide risk assessment
- Analysis of the South African risk governance of genetically modified organisms

8.2. METHODOLOGY

8.2.1 Models for analysis of risk governance

The evolvement of frameworks for risk/safety assessment of food described by Millstone (2007) and applied as the basis for proposals of improved governance of European food safety (Dreyer et al. 2009) forms the reference for assessment of South African frameworks and proposals for improvement. Three models have been identified on the continuum of democratising decision making on risks (Millstone 2007; Dreyer & Renn 2009). The earliest model (technocratic model) does not permit separation between science and decision making (risk assessment and risk management) and operates independently of social, cultural and economic conditions. Functional separation between the policy makers and risk assessors is not clearly defined in many countries, leading to possible political influences. This has changed to some extent since the mad cow disease debacle in Europe (Vos & Wendler 2006; Dreyer & Renn 2009). In the decisionist model, the next model in the continuum, functional separation between risk assessment and risk management is prominent. With the third model (transparent or democratic model), 'other legitimate factors' (Millstone et al. 2008, p.7) such as socio-economic considerations in a holistic concept of risk governance, are included in addition to risk assessment and risk management. This model is motivated by institutional and legal arrangements of governance within environments that keep on changing. The cyclical nature of the framework of the transparent model is conducive to iterative development and adjustments on demands from the environments (Millstone 2007).

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A European project, the SAFE FOODs project, funded by the European Commission's Sixth Framework Program for Research and Technology Development, needs special mentioning as it describes the details of the most advanced model for food risk governance to be implemented in Europe. This framework is referred to in more detail in Chapter 2 (2.4.1).

8.2.2. History profile of South Africa's pesticide governance

A profile over a period of about 94 years of the history of governance of toxicological assessment of pesticides serves as a reference for the assessment of the changes in institutional arrangements. The analysis includes the history of pesticide legislation. The profile is divided into three consecutive phases and stretches from the first recording of government's responsibility to regulate pesticides in 1917 until a recommendation report on the institutional capacity of agricultural and stock remedies by a ministerial task team in 2011.

8.2.2.1. History of pesticide legislation

The Fertilizers, Farm Feeds, Agricultural and Stock Remedies Act, Act 36 of 1947 (South Africa 1947), replaced the Fertilizers, Farm Foods, Seeds and Pest Remedies Act of 1917. The latter act was intended to regulate sales of pesticides by the Agricultural Department in order 'to deter the sale of under grade remedies, thus protecting the farmer from potential commercial exploitation' (Wiese & Bot 1971, p.50). Act 36 of 1947 was regarded by Van Dyk, Wiese and Mullen (1982, p.39) as 'sophisticated and in some cases advanced'. This act, which at the time of publication is still operative, specifically requires proof of efficacy, quality and safety to human beings and animals. It does not require socio-economic or benefit assessments, a trend in new legislation such as the Genetically Modified Organisms Act (South Africa 1997, as amended)

Several acts of parliament (medical, dental, pharmacy, public health) administered by the Health Department provided for control of pesticides where human health could be compromised (Wiese & Bot 1971; Van Dijk, Wiese & Mullen 1982). In 1972 the Foodstuffs, Cosmetics and Disinfectants Act (South Africa 1972a), a reactive act, was promulgated to replace legislation pertaining to food safety with regards to pesticides in food. The Hazardous Substances Act (South Africa1972b), administered by the Health Department, covers the regulation of pesticides and other hazardous substances in order to safeguard human beings against harm other than food safety issues.

Phase A: **1917–1969**

The Agricultural Department functioned as the Department of Agricultural Technical Services, which included the agricultural/animal research institutes. The agricultural research and development leg of the department became an independent Agricultural Research Council in 1990.

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Several authors reported (Wiese & Bot 1971, Van Dyk, Wiese & Mullen 1982) on the registration procedures and assessment of the applications for registration. The registration procedure was to submit, under cover of a completed registration form, two samples of the remedy, experimental data to support efficacy, pharmacological and toxicological date, methods of micro and macro analysis and, where applicable, residue and phytotoxicity data. The toxicological data consisted of results from acute, chronic and generation studies with rodents. Potential carcinogens and teratogens were not accepted for registration.

A technical advisor was responsible for scrutinising applications for efficacy and 'undue hazards' (Wiese & Bot 1971, p.54). He or she solicited comments from colleagues (not defined) who were not attached to the pesticide industry and, if necessary, communicated directly with the applicant to request further data (Wiese & Bot 1971, p. 51). The recommendations were considered at monthly meetings of the Standing Advisory Committee on Pesticides (Committee), consisting of representatives from the Agricultural and Health Departments, before registration by the officer in charge. In the case of new pesticide molecules, the applicant could obtain an 'idea' of possible acceptability before commencing with efficacy trials by submitting the toxicological data and proposed use to the Committee (Wiese & Bot 1971, p.54).

The technical advisors of Agricultural Department played an active role in advising on the experimental work. The department, through its technical services, reserved the right to conduct its own experimental work prior to registration (Wiese & Bot 1971, p.51). The purpose of the 'work' is not qualified. It is assumed to be efficacy trials of various natures such as treatment of grain in bulk storage as well as residue studies as a requirement for registration. Such results were published in recognised scientific journals subsequent to use by the applicant (Wiese & Bot 1971).

Phase B: Interdepartmental Advisory Committee for Safeguarding Man against Poisons, 1969 to ca 2002

The Standing Interdepartmental Advisory Committee for Safeguarding Man against Poisons (INDAC) came into being in 1969 on recommendation by a committee of enquiry appointed by the minister of health in 1967 to identify shortcomings in coordination between the Health Department and the Agricultural Department and its plant protection research and the veterinary institutes (the research arm of the agricultural department). The main function of INDAC was to advise the registrar of pesticides on matters related to the toxicity of agricultural and veterinary remedies (Wiese 1976). It also acted as an important policy-making body that influenced research work on certain problems (Van Dyk, Wiese & Mullen 1982, p.39). It did not control research work, although it exerted 'considerable pressure through its members on the agencies who could undertake the required research' (Van Dyk, Wiese & Mullen 1982, p.56). Arrangements for toxicological assessments changed in the mid-1970s when a scientist was appointed in the Health Department who was responsible for the toxicological assessment of pesticides.

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The members of INDAC were appointed by the minister of agriculture (South Africa 1992) from scientists and advisors in the Agricultural Department, Health Department, and departments of Environmental Affairs, Water Affairs and public agricultural/veterinary research institutes, as well as the Faculty for Veterinary Sciences (University of Pretoria). They represented veterinarians, toxicologists, chemists, pharmacologists and entomologists (FWJvR: letter of appointment 1 April 1992). Several chairpersons came from the Plant Protection Research Institute (now Agricultural Research Council)

During this phase INDAC played an active role in peer-reviewing data for the registration of new pesticide molecules, developing guidelines and regulatory requirements, and setting up training courses as well as surveys on pesticide levels. The Working Group on Pesticide Residues was appointed in 1972 to coordinate research and specifically to monitor persistent pesticide residues. Guidelines for toxicity assessment, including those for synthetic chemicals, technical, botanical and biopesticide products, were prepared by members of INDAC. The relationship with stakeholders was limited to formal consulting with the organised agricultural pesticide industry, the Agricultural and Veterinary Chemicals Association of South Africa (AVCASA online).

This position in the Health Department was filled successively by veterinarians and pharmacologists. A need was felt for specialised training in 'regulatory toxicology'(Table 8-1) and subsequently a pharmacologist was commissioned by the Health Department for postgraduate training at a recognised toxicology centre in Europe (University of Surrey, online). Such training was not available in South Africa because of limited demand (Toxicology Society of South Africa (TOXSA) online).

The entry standard for example for a postgraduate degree at a recognised training centre for toxicologists in Europe is a medical degree, veterinary degree or a 'good' honours science degree with 'strong' biological, biochemical or chemical content. Descriptions of 'good' and 'strong' are not provided (University of Surrey online). Three areas of professional toxicology are described as (Eaton & Klaasen 1995, pp.13-14):

Table 8-1: Specialisation field in toxicology

Descriptive toxicologist: He or she is directly concerned with toxicity testing, including effects on humans, industrial, environmental. Appropriate toxicity tests are designed to yield information to evaluate the risk
Mechanistic toxicologist: He or she identifies and understands the mechanisms by which chemicals exert toxic effects
Regulatory toxicologist: This person is responsible for decision making based on the data provided by descriptive and mechanistic toxicologists

The following information is from the author's experience while employed by the Health Department. Two to three scientists were responsible for reviewing the data and preparing reports. This included a special arrangement

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with a scientist who had resigned from the Health Department. In all cases, Health Department scientists submitted the final recommendation. The number of new applications received and reviewed fluctuated, apparently because of the influence of the world economic climate. It was estimated that four to six weeks per application for registration was the average for completion of a report. Regulatory toxicological requirements for food safety followed the guidelines for testing chemicals devised by the Organisation for Economic Cooperation and Development (OECD online). The format of the reports to INDAC needs mention as it was developed over time in agreement with INDAC's requirements for transparency (FWJvR, 2012, personal communication 1 November).

The last appointment of members took place in April 1992 for three years. No more meetings of INDAC were called after *ca* 2000 (FWJvR 1992, letter of appointment).

Phase C: 2002 to 2011 Ad hoc arrangements

After the termination of INDAC, the Health Department continued to supply toxicological assessments and recommendations to the registrar of pesticides. However, resignations in Health Department followed, which resulted in the cessation of toxicological assessments in October 2005 and the accumulation of dossiers for applications of new molecules. The Health Department made a temporary arrangement in March 2007 with the Veterinary Clinical Committee (VCC) of the Medicines Control Council (now being changed to the South African Health Products Regulatory Authority, or SAHPRA) to address the backlog. This was a peer-reviewed process whereby veterinary pharmacologists/toxicologists, clinicians and a regulatory toxicologist contributed to the assessment. The ad hoc arrangement by the Agricultural Department with an independent scientist continued during this phase and provided for conditional registration.

Registration of medicines has entered a new dispensation, described in Section 8.4.4.1 (South Africa 2009). A draft amendment to the act that regulates medicines was considered to include the Health Department's directorate for food control in SAHPRA (South Africa 2012). The implications for toxicological assessment for food safety are still to be clarified.

Proceedings were brought against the minister of agriculture by AVCASA, which incorporated the South African Animal Health Association and CropLife South Africa (Mabesa 2012, personal communication 1 August) to address the long delay in registration of agricultural remedies and stock remedies. A ministerial task team was appointed to make recommendations to the minister according to the terms of reference drafted by AVCASA. The team reported to the minister in 2011.

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8.2.2.2 Questionnaire

The opinions of respondents on good governance were gained during Phase C of the history profile. Good governance entails a number of criteria. Those focused on independency, excellence in performance transparency, openness and participation, (CEC 2000, 2001; CAC 2011). The opinions were grouped on criteria for matters pertaining to:

- Risk management (policies and procedures)
- Risk assessment (excellence in performance)
- Communication (transparency, participation, openness)

Response percentage was judged according to the percentage of agreement in column 2 (AGREE) of Table 2: (80 per cent and above – very good agreement/little uncertainty/; 60 to 79 per cent good/moderate agreement, some uncertainty; and, up to 50 to 59 per cent average agreement/uncertainty).

The address list was established from contact details of academics, researchers, pesticide chemical industry scientists (CropLife SA), members of TOXSA, stakeholders involved in the organic and biopesticide agriculture industry (farmers, merchants, distributors) and the Chemical and Allied Industries Association (CAIA).

Respondents expressed their opinions from personal experience, which were categorised as perceptions. Literature data and interviews with some respondents as well as the personal experience of the author while employed by government formed the basis for evaluation of the results.

8.2.3 Limitations in the study

Limitations in this study revolved around the lack of published and accessible government information. A request for information to determine the workload was rejected on advice from a government legal unit, because of the confidentiality of applications for registration of pesticides. Non-confidential information reported in this study is from personal experience of the author, who was responsible, as the regulatory authority, for toxicological assessments and as consultant during most part of the governance of pesticides since 1988. The organised pesticide industry did not provide any information on the statistics of number of applications for registrations per year. There is no detailed data on the chemical pesticides industries' website (Croplife online). The websites of government departments do not contain relevant pesticide data either.

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8.3 RESULTS

8.3.1. History profile of South Africa's pesticide governance

Three phases were identified with reference to the evolving models of risk governance:

Phase A: 1917 to1969: Technocratic governance

Phase B: 1969 to ca 2002: INDAC Technocratic progressing into decisionist governance

Phase C: 2002 to 2011; Ad hoc arrangements: decisionist governance

8.3.2. Questionnaire

8.3.2.1. General

A total number of 44 (8%) responses were received from a possible 544 contact names captured in the database. Sector responses could not be compared in several cases, because the areas in which some respondents operated overlapped. Though exact figures could not be obtained, it appeared that roughly 50 per cent of the respondents were from the synthetic and organic pesticide industries. The apparent small number of replies from CropLife SA, the organised pesticide chemical industry, should be interpreted as collective responses on behalf of the company. The rest of the respondents were academics and former individual regulatory authorities. Stakeholders with relatively more experience of the regulatory system were from the organised pesticide industry and a few from universities. The organic/biopesticide industry respondents included farmers, distributors and merchants, of whom only a few had direct experience of the regulatory requirements. A few respondents were former government officials, now consulting mainly for industry. CAIA expressed no interest in participation.

Limitations in this study were that the views and perceptions of only a small part of the target audience had been measured. However, these were considered representative of the agricultural pesticide industry, synthetic as well as organic/biopesticide, and could be regarded as an indication of the path to further investigation in order to draft proposals for improved governance

8.3.2.2. Improvement of governance

The questionnaire statements concerned the three phases of the risk analysis paradigm: risk management (policies and procedures); risk assessment (excellence); and risk communication. The purpose was to obtain respondents' perceptions of the concept 'good governance'. Good governance is explained in Chapter 2.

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8.3.2.2.1. Risk management step: policies and procedures

The focus was on accountability described by the roles of decision makers and risk assessors (reviewers) and on independency of these role players. Knowledge of the regulatory system and legislation was a requisite to be able to respond to the statements. The results are summarised in Table 8-2, statements 1.1 to 1.9. The respondents' knowledge of legislation pertaining to pesticide registration seemed to be limited (1.2), although there was good agreement that the legislation should be amended to be in line with international trends, for example Codex Alimentarius (1.1). However, they were uncertain whether to include an evaluation step for considering socio-economic effects (1.8). This is a recommended step whereby benefits and risks can be evaluated (Dreyer et al. 2006). The respondents were also uncertain about the roles of decision makers and risk assessors (1.3, 1.5, 1.6). Independency in risk assessment was viewed as very important (1.4), though it remained uncertain whether the risk assessment group should have independent legal status (1.9). As far as functions of this group were concerned, it was agreed that toxicological assessment and exposure assessment (MRL) should both be conducted within the same group (1.7).

8.3.2.2.2. Risk assessment step – toxicological assessments

This section (Table 8-2, statements 2.1 to 2.9) focused on scientific 'excellence'. This includes peer reviewing and availability of qualified and experienced toxicologists. Respondents felt strongly about the importance of peer reviewing (2.1) and that a multi-disciplinarian could not replace a team of specialists (2.2). They were uncertain whether risk assessors should be involved in research in order to remain in touch with scientific developments (2.3); however, most respondents were of the opinion that risk assessors should stay abreast of development by attending conferences and meetings, and accompany government to such meetings (2.4). The majority (83%) of respondents believed that there is a general shortage of educated and experienced toxicologists (2.5). The need to establish a database of toxicologists was considered important in order to address the critical shortage of expertise (2.6). Pooling resources for assessing chemical substances was also identified as an intervention step (2.7).

8.3.2.2.3. Communication step

Criteria for good communication include participation, transparency, and openness. The results from statements on communication are summarised in Table 8-2, statements 3.1 to 3.8. Various forms of communication were considered important by respondents, for example participation in policy development (3.1), communication with stakeholders throughout risk analysis (3.2), and in particular the availability of the specialist toxicological reports to stakeholders for comments (3.6). Stakeholders' participation in the evaluation of socio-economic impact was considered important (3.4). Publication of the final managerial decisions, including the risk analysis and socio-economic and benefit considerations, was regarded as important (3.8). Publication of the toxicology report (3.7)

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and commencement of a risk assessment of a new pesticide (3.5) were of lesser importance. The majority did not approve scientific reviewing by stakeholder participation (3.3).

8.3.2.2.4. Structure for good governance.

The results are summarised in Table 8-2, statements 4.1 to 4.10

No definite opinion was expressed regarding responsibility for toxicological assessments (4.1, 4.2, 4.6, 4.8). The Department of Science and Technology (4.3, 4.4) and the Department of Trade and Industry (4.5) were considered least acceptable, with low scores of less than 50%. A general suggestion for improvement for South Africa was to consider international options for toxicological assessments (4.10). The option that only pesticides already approved by developed countries should be registered received a negative response (4.9).

8.4. DISCUSSION

8.4.1 Application of different models: policies and procedures

In Phase A, South African legislation for pesticide registration and the implementation of assessment of pesticides could be grouped with the technocratic model. Legislation did not change through the consecutive phases; accordingly, no provision for improvement was made for a more credible system. The Health Department realised its responsibility towards human safety by being the main role player in initiating the creation of INDAC. However, this arrangement with different role players was not captured in legislation and resulted in confusion in Phase C.

Implementation of toxicological assessment progressed towards a decisionist model (Phase B) when the Health Department took responsibility for toxicological assessment of pesticides, thereby increasing the distance of separation from the decision maker. Independency, as an important criterion of credibility, is also possible within a government department, as in a number of developed countries, for example in Europe (Vos & Wendler 2006) and Australia (AVPMA online), where risk assessors function independently of the risk managers within the same government department. Examples of a decisionist model include the European Food Safety Authority (EFSA) as described in Chapter 2, and as articulated in the South African Genetically Modified Organisms Act (South Africa 1997).

INDAC served as an important scientific advisory body, though not a true peer reviewing body for toxicological assessment because of the diverse disciplines represented. The arrangement with the Health Department had the potential to increase the time of completion of assessments, leading to a disadvantage from the point of view of applicants. In Phase 2, national research had a prominent role in place, in relationship with other government departments' needs for investigation into environmental pollution and pesticide residues in meat, dairy produce

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and fresh produce (Van Dyk, Wiese & Mullen 1982). In Phase 3, the arrangement with the VCC represented the decisionist model with clear separation from the decision maker (Agricultural Department) and no influence from the pesticide applicant.

The third model in the continuum of the development of governance has not yet been attained in South Africa. This seems to be the case in many countries. Millstone et al. (2008) investigated interactions between scientists and regulators, as well as stakeholders, in a number of countries. They concluded that among those that were investigated, the transition to a more transparent model varied. The SAFE FOODS Project of the European Commission recommended a model transparent structure (König et al. 2010), the implementation of which is being considered by EFSA (Kuiper & Davis 2010).

8.4.2. Risk assessment step: toxicological assessments

Guidance from responses to the questionnaire indicates strong support for peer reviewing and increased confidence in a multidisciplinary team than a single person responsible for the toxicological assessments.

The arrangement in Phase C could be recommended as an example for 'peer reviewing' in the South African situation. Whereas INDAC members represented a diverse group, the members of the VCC were veterinarians from various specialisations, including toxicology and pharmacology, as well as a regulatory toxicologist. Experience included membership of the international Joint Food and Agriculture /World Health Organisation (FAO/WHO) Expert Committee on Food Additives (JECFA).

An ideal peer review group would consist of experts qualified in regulatory toxicology (Table 8-1). Regulatory toxicology is a postgraduate qualification, focused on regulatory requirements, and based on advanced knowledge of chemical/physical characteristics of the new molecule and its metabolites, as well as toxicological effects on laboratory animals (rat, mouse, dog, rabbit, and guinea pig). This composition is confirmed by the contents of the Organisation for Economic Cooperation and Development (OECD, Guidelines for Testing of Chemicals online). The areas of specialisation include pathology, clinical chemistry, haematology, biochemistry, genotoxicity (in vitro and in vivo assays), neurotoxicity, immunotoxicity, endocrinology and special studies to determine the mode of action and relevance to human beings. Toxicokinetics, as well as residue studies in food producing animals, is also an important requirement.

Veterinarians specialised in laboratory animal toxicology are the most suited to toxicological risk assessments. However, there are constraints in the South African situation. There is a great shortage of veterinarians in general (Professor GE Swan 2012, Dean of the Faculty for Veterinary Sciences, University of Pretoria, electronic communication 24 July) (South Africa, 2012 Parliamentary Speeches and Statements). Recruiting foreign scientists suited to conduct toxicological assessments could be contemplated. Alternatively, the formation of

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supporting groups to a veterinary toxicologist, consisting of veterinarians / human medicine specialists in one or more of the above disciplines, could be further investigated. Preparation of review reports by scientists with training and experience in regulatory toxicology would be an essential attribute to the review process. Postgraduate education is recommended. On-going mentorship could be borne in mind with experts from relevant disciplines in South Africa.

The establishment of special courses in South Africa for training regulatory toxicologists needs to be considered in the light of an estimation of the needs. From the history of toxicological assessments by government, two to three scientists should be an adequate number to prepare review reports at two-monthly intervals for peer reviewing by a panel of experts. Should the demand increase, it would be possible to have more frequent review meetings. The training of industrial scientists needs be assessed, having in mind the complexity of the kinds of questions from the expert review team and the availability of international networks of multinational companies.

Independent scientists and scientists from academia and from South African research institutes should be considered for the peer review group. Should a government official be included in the team, the qualification as described would be required. It would be advisable to place such a government scientist(s) at a South African university or National Research Institute. Mentorship is possible in a science milieu and the applications for new molecules often pose difficult challenges, for which the presence of peer scientists is important. An example is the arrangement that Denmark has for novel product assessment with an academic institute (Danish government official, 12 May 2011). Consultation with scientists in specialised fields could be included through virtual conferences as an additional resource of expertise.

These proposed arrangements for South Africa would each require consultation and agreements between the government departments, and amendments to legislation. The burden and responsibility of assessment of these extremely hazardous substances should not be left to the judgment of a single individual. Should these not be successful and peer reviewing is not possible, then government may have to weigh up options such as:

- Consider virtual meetings with pools of national expertise as well as international.
- Sign mutual agreements with countries with reputable pesticide registration systems.
- Accept only those pesticide products that have already been approved by a number of developed countries.
- Accept the toxicological assessments only of the expert bodies of Codex Alimentarius Commission.
- Consider the OECD agreement arrangements (OECD 2006).

Challenges with protracted decision making are related to several issues. Lengthy administration because of bulky dossiers could be replaced by applications on CDs. The number of meetings per year could be increased and virtual communication is a possibility. Answers to additional questions to applicants depend on the

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applicant's network to supply answers without too much delay. In some cases, exceptionally good explanations to questions from reviewers were received, including those of expert review committees from other regulatory authorities. Incompleteness of dossiers should be addressed as the first step in any review process practised by all reviewers. In all cases, improved procedures and training remain important.

8.4.3 Communication step

Several aspects of communication need improvement. A requirement of good governance is transparency, participation and openness in decision making. A number of aspects to communication motivate in-depth research, as pointed out by respondents to the questionnaire on good governance. Only one aspect is described. It concerns structuring such an opportunity between risk assessors, risk managers and relevant stakeholders with the focus on risk assessment.

There should be an additional stage in risk analysis, described as a step for risk assessment policy development (CAC 2011, Dreyer & Renn 2009). A need for interaction between scientists and policy makers is critically important, specifically when an independent peer review group is contemplated for risk assessment (Dreyer & Renn 2009) in order to improve communication. This step should be an opportunity for applicants to communicate issues regarding their products. Inclusion of other stakeholders should to be investigated in great detail to find a structured way forward. Policies on socio-economics and benefits are important matters, but ought to be addressed by the decision makers or as an additional evaluation step, which is not discussed in this study (Wentholt et al. 2009).

8.4.4 Options for a toxicology peer review centre of excellence

The conclusion from this study is that an independent peer review body under the auspice of the Agricultural Department should be considered. The options to think about are existing bodies/institutes with potential capacity to accommodate a peer review panel.

8.4.4.1 The existing Veterinary Clinical Committee of the Medicines Control Council

The arrangements for registration of medicines are currently being reconsidered. The amended Medicines and Related Substances Control Act (South Africa 2008) provides for the establishment of a South African Health Regulatory Authority (SAHRA) as an organ of state, outside the public sector (Section 2(1) of the act), but accountable to and reporting to the minister of health (Section 2(3) of the act). The intention is to take over responsibility of regulatory oversight of foodstuffs as defined in terms of the Foodstuffs Act (South Africa 1972). The chief executive officer of SAHRA will appoint suitable qualified staff and may contract other suitable qualified

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persons to assist the authority in carrying out its functions (Section 3(5)). Implementation of SAHRA is under way and the creation of peer review groups is possible under Section 3(5).

The current VCC is responsible for a number of advisory functions for registration of veterinary medicines. It is a functional committee consisting of veterinarians, toxicologists and pharmacologists. It is accountable for the clinical and toxicological assessment of all veterinary medicines and, since 2006, as an interim measure, for the toxicological assessment of pesticides. Dismantling this group would constitute a serious loss to the country. It is trusted that it will not happen when SAHRA starts to operate. However, the shortage in experienced veterinary toxicologists, inadequate remuneration of experts, priority for veterinary medicine registration (the VCC's principle responsibility is towards the registration of medicines) and time limitations of academics could become major constraints. Still, because of the credibility of this group, the possibility of negotiating a memorandum of understanding with SARHA should be investigated.

8.4.4.2 Platforms of excellence: university faculties and research institutes

The tendency in research and development is to establish platforms of excellence, for example the Agricultural Biotechnology Cluster at the ARC, Onderstepoort (ARC online). The potential for platforms and partnerships exists in South Africa because of the number of medical schools and in particular the Faculty for Veterinary Science of the University of Pretoria and the Animal Toxicology Centre of the ARC at its Veterinary Research Institute.

8.4.5 Proposed structure for independent toxicological assessment of pesticides

The scenario for good governance of pesticide risk assessment, according to the transparent model, should include two permanent bodies with supporting groups, as sketched here, taking into account constraints and opportunities (Figure 8-1).

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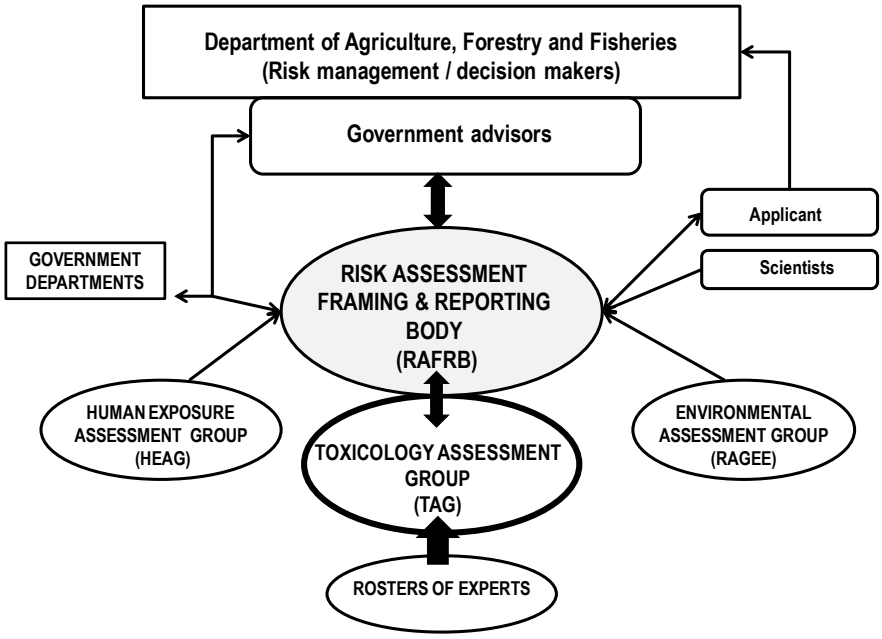

Figure 8- 1: Diagram illustrating the interaction among the pesticide Risk Assessment Framing and Reporting Body (RAFPB) and various bodies and groups.

Risk Assessment Framing and Reporting Body (RAFRB):

a) The purpose of this body would be to give direction to risk assessments through developing policy; framing risk assessment; and presenting risk scenario options to DAFF and its government advisors. Policy development and framing should be performed by the relevant regulatory authorities, members of peer review groups, and relevant stakeholders. The RAFRB body should inter alia consider policy on risk assessment approaches and recommend interactions at national and international levels to achieve excellence in execution of risk assessor functions as well as those actions necessary to ensure sustainable risk assessment duties such as development of institutional memory.
b) Consolidated reports on risk assessments to be presented to the government advisors should be strictly the responsibility of relevant members of the peer review groups and the chairperson of the RAFRB.

Toxicology Assessment Group (TAG): TAG should be an independent group that reports to RAFRB. It should be responsible for peer reviewing toxicological assessment of pesticides that may enter the food/feed chain, as well as causing harm to human health. The scope of this group should include new synthetic pesticides molecules, new phytopesticides and biopesticides. It should also be responsible for reassessing existing pesticides as well

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as toxicological matters that are identified by risk managers as being of concern. Such a group should be recognised by all relevant government departments by means of a memorandum of understanding. Membership should consists of one or more technical advisors (qualified in regulatory toxicology) appointed by government and seconded to a toxicological research institute acknowledged by government; and independent scientists, including veterinary toxicologists/pharmacologists, animal/human pathologists, a specialist in genotoxicity, and a specialist in toxicokinetics and biotransformation of chemical substances.

Risk Assessment Group for Ecotoxicology/Environmental Fate (RAGEE): RAGEE should report to RAFRB on pesticides (synthetic chemicals, phytopesticides and biopesticides. The members are to be appointed in collaboration with the Department of Environmental Affairs.

Human Exposure Assessment Group (HEAG): HEAG should report to the RAFRB. Their responsibility should be to determine maximum residue limits (MRL) as well as occupational health risks. Scientists from the agriculture and health governments should be considered for inclusion in this group.

Roster of experts

Two groups of experts could be considered, a) for chemistry and physics, statistical analysis as well as risk modelling, and b) experts in biopesticide- and phytopesticide-related sciences to assist in specific specialisations

Government Advisors: No details of this group are proposed except that the model described for Argentina (Chapter 2.6.4) could be considered.

Quality assurance and control and product labelling as well as assessment of formulations are not discussed in this study.

A vision for the future includes the establishment of a platform of expertise working toward a centre of excellence.

8.5. CONCLUSION AND PROPOSALS

8.5.1 Conclusion

An analysis of current South African governance of toxicological assessments of new pesticides molecules indicates that much improvement is required to comply with international principles of good governance. South African legislation is outdated as no provision is made for independent, peer reviewed toxicological assessment of pesticides. Independency implies clear roles for and separation between risk assessors (reviewers) and the decision makers (risk managers). The ideal peer review group of scientists in the case of toxicology of pesticides conducted with animal species should comprise veterinary toxicologists. This is a very scarce skill. Therefore, 'supporting' scientists with related scientific qualifications and with postgraduate training specifically in regulatory toxicology should be considered to be on the review panel with veterinarians.

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Communication is an important aspect in good governance because of the requirements for transparency, participation, accountability and openness in assessments and decision making. This could be provided for by means of a structured risk assessment policy and communication step that includes members from government departments, the proposed toxicology assessment body, research institutes and stakeholders.

A model is proposed that meet the requirements of good governance for South African risk governance, particular the toxicological assessment of new pesticides molecules. Such a model could initiate a platform of expertise and steer in the direction of a centre of excellence.

8.5.2. Proposals

The following proposals are made:

- That legislation for a structure for toxicological risk assessment of pesticides according to requirements of good governance should be advocated.
- That an institutional arrangement should be considered for the toxicological assessment of pesticides consisting of two bodies and their supporting groups. It could be created under the auspices of DAFF: a toxicology policy development and communication body; and an independent peer review body for toxicological assessment of pesticides in line with South Africa's needs for registration of pesticides.
- That education and training of regulatory toxicologists should be captured in policy to ensure sustainability of service in toxicological assessments
- That a platform of excellence should be considered to nurture scientists in toxicological assessment of pesticides
- That a needs assessment regarding the number of 'supporting' toxicologist should be carried out to assist the review panel in preparation of assessments

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Table 8-1: Reponses to statements: pesticides (%)

NO.	STATEMENT	TOTAL RESPONSES	AGREE	DISAGREE	UNSURE
1	**Policies and procedures**				
1.1	South African legislation should be amended to be in line with accepted international guidelines for risk analysis	43	67	23	9
1.2	The act that regulates registration of pesticide (1947) is vague on who should be responsible for the toxicology assessment of pesticides	43	53	28	19
1.3	Risk assessment is deemed to be a purely scientific activity	43	56	35	9
1.4	Risk assessment should be conducted independently from risk management (including from political influence)	43	93	7	0
1.5	The managerial decision making body does not have a role as reviewer of risk assessment data/information	43	56	23	21
1.6	The toxicology assessment group should be mandated to initiate new policies pertaining to assessment e.g., guidelines on risk assessment requirements	43	58	21	21
1.7	The function of the toxicology assessment group could be expanded to include exposure assessment determinations (MRL*)	43	74	14	12
1.8	An evaluation step to consider the socio-economic effects and the benefits should be included in pre-regulatory assessment (new chemicals), before the managerial decision making step	43	56	35	9
1.9	The toxicology assessment group should receive legal status as an independent advisory group	43	53	26	21
2	**Scientific excellence**				
2.1	Peer reviewing of information is important	42	93	7	0
2.2	A single multi-disciplinarian cannot replace a team of specialists	42	88	7	5
2.3	Risk assessors should be involved in research to remain in touch with science	42	55	38	7

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2.4	The risk assessors should be included in the government team to international meetings/conferences	42	69	21	10
2.5	South Africa does not have enough adequately trained toxicologists	42	83	2	14
2.6	South Africa should keep a database of all details of potential toxicologists	42	95	0	5
2.7	South Africa should pool resources of assessors of the toxicology of chemical substances	42	93	0	7
3	**Communication (transparency, openness, participation)**				
3.1	Risk analysis policies for pesticides should be developed in collaboration with stakeholders	41	83	10	7
3.2	Stakeholders communication in risk analysis of pesticides is important	42	93	2	5
3.3	Stakeholders participation in the scientific reviewing of company information is not acceptable	42	60	26	14
3.4	Stakeholder participation regarding the evaluation of the potential risk to pesticides in the context of socio-economic impact is invaluable	41	63	22	15
3.5	Commencement of risk assessment of new pesticides should be announced in the media	41	59	37	5
3.6	The reports of the toxicology specialist group should be made available to the applicant for comments	42	100	0	0
3.7	The reports of the toxicology specialist group should be published for information	42	57	33	10
3.8	The final approved report of the management– decision making group, including risk analysis decisions as well as socio-economical and benefit considerations, should be published on the Internet/media for public information	42	64	26	10
4	**Structure**				
4.1	Department of Agriculture responsible for independent toxicology assessment of all synthetic chemical pesticides as well as phytopesticides	41	49	37	15
4.2	Department of Health responsible for independent toxicology assessment of all synthetic chemical pesticides as well as phytopesticides	41	29	56	15

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4.3	Department of Science and Technology responsible for independent toxicology assessment of all synthetic chemical pesticides as well as phytopesticides	41	12	71	17
4.4	Department of Science and Technology responsible for independent toxicology assessment of all chemicals	41	20	63	17
4.5	Department of Trade and Industry responsible for independent toxicology of al chemicals as part of the new international labelling requirements	41	12	71	17
4.6	An interdepartmental authority/agency to be created for toxicological assessment of all chemicals in South Africa	38	37	50	13
4.7	A semi-autonomous authority/agency to be created for toxicological assessment of all chemicals in South Africa	42	36	48	17
4.8	An authority/agency to be created to take responsibility for all safety assessments	41	46	39	15
4.9	Due to number of constrains in toxicological assessments, only pesticides already approved in some developed countries should be approved for use in South Africa	41	32	63	5
4.10.	South Africa should not reinvent the wheel but consider internationally available option for toxicological assessments	41	80	15	5

*MRLs: maximum residue limits

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CHAPTER 9: SUMMARY, CONCLUSIONS AND PROPOSALS

9.1 INTRODUCTION

Governance of food/feed safety/risk and the risk to the environment take place at different levels, international, regional and national. Framework conditions of regulation are developed through exposure to new experience and interactions at all levels. This chapter summarises the results from the desk research on risk governance of genetically modified organisms (GMOs or GM) with reference to crop plants developed for food, feed and industrial use. It also includes an application of good governance principles to institutional arrangements for toxicological assessments of pesticides in South Africa.

This study was prompted by the need to identify the reasons for protracted decision making in regulatory approval of GMOs and to contribute to improvement of governance. These delays have far-reaching impacts on research, development and production of GMOs. The production of GM crops is considered one of the agricultural practices that could contribute to sustainable food supply to feed a fast growing world population. Therefore, it is important to have a look at possible causes for delays and to suggest proposals for improvement of governance.

The aims of the study were:

- To contribute to the improvement of risk governance of GMOs in South Africa; and,
- To contribute to the improvement of governance of toxicological assessments of new pesticide molecules in South Africa.

The objectives were:

- To analyse South Africa's current governance of risks regarding GMOs according to principles for good governance (Chapter 3);
- To analyse those governance criteria identified as important causes for improvement (Chapters 4,5 and 6);
- To propose improved institutional arrangements for risk governance of GMOs based on criteria of good governance and the results from the analysis of causes for improvement (Chapter 7); and,
- To propose a model for governance of toxicological assessment of new pesticides molecules with reference to the proposed South African model for GMOs (Chapter 8).

The methodology used in the study (Chapter 2) was to investigate and analyse models for good governance and the implementation by different countries as they have developed over years.

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9.2 ANALYSIS OF GOVERNANCE OF GMOs IN SOUTH AFRICA

'How credible is governance of GMOs in South Africa as perceived by scientists with knowledge of the system?' This was the question asked on governance of GMOs in Chapter 3. The results from a questionnaire survey showed that, in general, 'some to much' improvement was necessary. Criteria for ethical conduct and independency in risk assessments needed 'no to some improvement'; criteria related to risk communication, including transparency, participation and openness in decision making needed 'some improvement'; and criteria for excellence in performance, accountability and effectiveness in operation needed 'some to much' improvement.

On further probing into the perceptions of the target group, it appeared that although the regulatory system provided for functional separation between risk assessment (by the scientific Advisory Committee, AC), and risk management (by the GMO Executive Council, EC) the decision makers would conduct risk assessments. This is an indication of unclear roles when evaluated according to governance models described in the continuum of improved transparency and democratisation. The respondents to a second questionnaire confirmed the concern for government's unanimity. A deficiency was inadequacy in specific issues such as peer reviewing, improved guidelines, training, international exposure and a sufficient number of risk assessors. Risk communication at the various steps in the process was identified for more attention. These critical issues need to be addressed to increase credibility of governance.

A particular issue of concern was the interpretation of the 'precautionary principle,' an approach applied in decision making and considered a main issue for delaying approvals of permits. This finding resulted in investigating different approaches to risk assessments.

9.3 APPROACHES TO RISK ASSESSMENTS

A broader view on assessment approaches was taken by including risk/safety assessment of food and environmental risks. Firstly, approaches were considered that were applicable to the safety/risk assessment of food/feed and environmental risk assessments (Chapter 4). Secondly, a specific case for safety/risk assessment of cassava is described in Chapter 5. Thirdly, the precautionary approach (or principle) was regarded as a possible cause for delays when applied at the stage of decision making (risk management) in the Chapter 6.

9.3.1 Risk assessment approaches

The delay in the approval of a permit for contained trial research for sorghum as a food/feed crop was used as a case study in Chapter 4 to illustrate problems that could arise when environmental risk assessment does not follow a focused approach. A distinction was made between ways of gathering data with and without a focused

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method of assessment, the 'bucket' versus the 'searchlight' approaches. The focusing steps in the approach to problem formulation were described with reference to an analysis of the assessment of pollen gene flow in sorghum species. Challenges in applying this approach are a) defining 'harm', which should be an agreement between role players, and b) consensus on the 'analysis plan' and 'endpoints' required in the problem formulation, which would require expertise in various disciplines, including crop biology. A further matter would be to amend shortcomings in GMO legislation, specifically ambiguity in the description of 'risk'. An account of the application of the focused approach to food/feed safety assessment is included in Chapter 4.

The general conclusion was that policies and approaches should be developed in advance as a frame within which assessments are conducted. Such framing needs to be an agreement among role players. Scientific inputs would be essential and, because of the complexity of the cases, as illustrated by the sorghum case study, a wider group than the members of the AC could be considered. Such requirements would include knowledge of the environmental risk assessment approach and comprehension of risk hypotheses. This leads further to active participation at international fora, and training of trainers. Establishment of agricultural science platforms seems to be essential, whereby scientists specialised in the application of risk assessment principles and approaches to assessment of agricultural products could build capacity and provide the necessary scientific input at the level of the proposed framing step. The broad scope of different agricultural products, agronomic and plant breeding practices, and food compositional analysis demands great capacity that may be insufficient in South Africa. Of prime importance is a platform striving for centre of excellence status from which national and international scientists could benefit. A critical discipline would be specialisation in risk assessment methodologies and approaches, as scientists need training and experience in these approaches.

9.3.2 Food safety and the importance of compositional analysis

The safety/risk assessment of cassava illustrates an exceptional application of the comparative approach to compositional analysis (Chapter 5). Cassava contains toxicants, cyanogenic glycoside, and therefore does not qualify for a comparator crop plant 'with a history of safe use'. In this case, comparison should be between a crop with improved safety, as well as nutritional quality, and the 'unsafe' comparator. A guideline standard for the toxicant needs to be in place before any safety assessment. A comparative assessment should be augmented by adapted toxicology studies with laboratory animal species.

The requirements for regulatory assessment of crops with increased levels of toxicants should be addressed and policies developed to give direction to research. Cassava with improved levels of starch for industrial use poses a challenge because of the regulatory requirement for assessing the modified crop plant as for food and feed. Such discussion in framing for the assessment is critical. The requirements for such analysis would be to frame the approach for assessment. Knowledge of risk assessments, toxicology, and compositional analysis and a

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thorough knowledge of risk assessment approaches would be required. The conclusion is that capacity building in identifying new approaches to risk assessment and in conducting such assessment is important before research is embarked on.

9.3.3 Precautionary principle

The complexity and importance of policy development upfront on contentious issues in decision making is illustrated when considering possible 'unintended effects on the presence of endogenous allergens' in maize as a specific case. This was investigated in Chapter 6. The precautionary principle is a norm principle with obligations to anticipate harm and moral responsibilities in judging the adequacy of prevailing knowledge. A regulatory authority would find it difficult to reach consensus should no clear guidelines be in place, guidelines based on policies and considered and accepted by all role players The case could be passed on to the courts for a decision or the onus for resolution could even be placed on politicians. Precaution received prominence in the Cartagena Protocol on Biosafety that focuses on transboundary movement of LMOs (living modified organisms). It can be regarded as a principle only when entrenched in legal requirements. A precautionary approach is a reaction by managers to uncertainty, which is present in all risk assessment. Several authors commented that mathematical modelling for decision making has shortcomings because it is based on axioms and assumptions that are not always valid in practice. The conclusion of a number of authors is that the development and interpretation of the precautionary principle is a complex picture of interaction between science, policy and law. It would be important to take the benefit of the crop into consideration in decision making in controversial cases of unintended effects from genetic modification.

New plant breeding methods and new methodologies such as 'omics' are being developed and applied that need prior discussion and policies to determine their place in risk assessment.

It is concluded that prior consideration, as an element in the framing step, should be given to matters that need policy decisions. A broad range of expertise needs to be engaged. National strategies such as food sustainability should be included in framing. Precautionary steps in general may need advance socio-economic and ethical considerations. Stakeholder participation in the contentious issue of precaution is debatable because there is no valid described 'substance' for this principle where societies differ in their perceptions of risk and have different ethical values. Much more research in participation is needed.

9.4 A RISK GOVERNANCE MODEL FOR GENETICALLY MODIFIED ORGANISMS

The results from this research showed that an improved model for risk governance of GMOs needs to be investigated. A model is proposed in Chapter 7.

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National law normally captures the internal arrangements for a risk governance approach. Several models in a continuum of development were applied as reference for an assessment of the South African governance of risk regarding GMOs. The evaluation of the current South African risk governance model reflects the description of the decisionist model, with strong elements of the technocratic model, which indicates a need for improvement, with the most advanced model, the transparent model, in mind. The analysis of the responses from scientists with knowledge of the system showed that the criteria according to the requirements of a transparent model were important to improve credibility. A proposal for an improved governance model is based on the requirements identified by respondents to the questionnaires and the assessment of the implementation of the GMO Act.

The proposed new risk governance for a South African model has as critical requisite a national policy for modern biotechnology (genetically modified organism). The current strategic plan needs be revisited, as do all strategic plans to capture new developments on all governance environments (socio-economic, technical and political). The National Biosafety Strategy for South Africa deals with the application of biotechnology, food security, human health and industrial processes, and not with prescribing risk assessment approaches. Without strong leadership in the development of national policy and a revised strategy to coordinate and reach consensus among government departments implicated in GMO legislation, a ripple effect would be possible to all levels of decision making and stall the progress in application of GMOs permits.

The current status of a national approach and policy on biosafety assessment of GMOs is regarded as outdated and inadequate. The GMO Act 15 of 1997 in its preamble mentions ‘common measure for evaluation and reduction of potential risks’. The amended GMO Act of 2006 contains a variation of the 1997 preamble, with the insertion of ‘socio-economic considerations’, while in its addition of a definition of biosafety it states that it means ‘to avoid potential risk’. The latter is at variance with both the old and amended preambles, and with common scientific principles that state zero risk is impossible. The guideline document for use by the GMO Advisory Committee when considering applications for GMO activities and the guideline for working with GMOs are both outdated and do not refer to a national policy on the approach to GMO risk assessment.

The proposed new model should have two additional steps (phases). The first step, a framing step, is for preparation for risk assessment as interface between risk management and risk assessment. A framing step should have the benefit of policies on various risk assessment matters developed in advance of the commencement of a risk assessment, as well as a risk assessment policy as guidance for each assessment to bridge possible disagreement in judgement of uncertainties. A second step for evaluation (socio-economic; risk-benefit; cost-benefit) is argued in the case study with endogenous allergens. The deliberations should be initiated before the commencement of a risk assessment and followed through to evaluation of all options. This is of critical importance to South African decision making, as many of the rejections for permits were influenced on socio-economic and trade concerns.

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Criteria for good governance should be a permanent structure for the proposed two steps, reflected in independent policy development, openness, transparency and accountability by the various role players, namely decision makers, risk assessors and other relevant stakeholders. The role description should highlight independency for different roles. Decision makers, for example, are not required to conduct risk assessments, as is currently the case. An independent facilitator/chairperson should be considered to direct the meetings. The two additional steps could merge and identify training needs and international exposure to strengthen excellence in scientific performance.

Excellence as a characteristic of good governance implies development of expertise. The three case studies have identified a scope for increased interactivity with research institutes. National research bodies have two reserved places on the GMO Advisory Committee and therefore open doors to strengthening interaction and practical experience both ways as contributors to risk assessments and to link with research platforms. This could be an important source for gathering 'institutional memory', as consistency in membership is valued.

9.5 TOXICOLOGICAL ASSESSMENTS OF NEW PESTICIDE MOLECULES

A proposal is made for improved governance of the toxicological assessment of new pesticides in Chapter 8. The proposal is based on assessment of the practices over almost hundred years of documented experience as well as recommendations from stakeholders obtained by means of a questionnaire. A profile of the history of toxicological assessments is presented according with the continuum of governance models. It is concluded that toxicological assessments have developed from a technocratic to a decisionist model. During the last years of toxicological governance, a structure for peer reviewing existed that is recommendable. The toxicology reports were prepared by supporting toxicologists and then peer reviewed by veterinarians and toxicologists. Proposals are made for addressing the shortage of toxicologists. A number of stakeholders were approached for their views on a credible system. Strong recommendations were made for functional separation between role players, peer reviewing and improved communication. Consequently, a model for toxicological assessment of new pesticide molecules is put forward. The model is based on the projected model for GMO risk governance. Inclusion of a toxicological assessment body and a policy framing body is suggested. An additional advisory body, analogous to the Argentinean advisory platform, which consists of a number of stakeholders, should also be considered. Confidentiality of information should be a matter for policy decisions as such classified information has to be agreed upon by regulatory authorities and applicants.

9.6 APPRAISAL OF THE MODELS

The proposed models will have characteristics that should improve credibility of governance. Independency would be more pronounced by defining roles. Peer reviewing would be considerably improved by inclusion of

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additional expertise and opportunities for prior policy development, training and international exposure. Improved communication would be possible by stakeholder participation, transparency and openness. Accountability would be improved because of greater transparency and defined roles

In both proposed GMO and pesticide governance models, additional steps may increase the time taken to reach a decision. However, there are advantages. The projected system would result in fewer disappointments to applicants because of improved communication upfront. The serious consequences experienced by scientists from national research institutes and academia from the refusal of permits could be prevented by timely communication, policies and training. There may initially be a great need to build capacity, especially for pesticide assessments, but as proposed, alternative measures such as international expertise could be considered.

9.7 IMPLEMENTATION

It is suggested that the models should be implemented incrementally. In particular, implementation of participation at a science-technical level could be contentious because of emotive positions and possible endless debating that would stall the processes. This should be left until researched by international scientists specialised in sociology, psychology and matters related to good governance.

9.8 RECOMMENDATIONS

9.8.1 Genetically modified organism with reference to crop plants

- That a national policy on modern biotechnology be developed, whereupon a national strategy should be planned to give direction to and coordination of departmental policies and strategies.
- That South African GMO legislation be amended to include the proposed model for risk governance of GMOs to improve credibility of risk governance.
- That an additional step in the iterative risk analysis process, according to the proposed mode, be approved for risk assessment framing that reflects ‘independency’ as a criterion for good governance, for structured communication among all role players (risk assessors, risk managers, identified scientists) and identified stakeholders that would guide risk assessments according to agreed policies and that would facilitate and structured capacity building in approved risk assessment approaches. As a result, improved decision making by the GMO Executive Council could be achieved.
- That the additional step provides for policy and guidance on socio-economic and benefit considerations that would direct the risk assessments and also the evaluations of the risk by the Executive Council.
- That additional research be conducted on details of the risk assessment framing step.

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- That South African GMO legislation be improved by corrections to definitions and terminology to reflect the intention and comprehension of risk analysis and that specific reference to 'ecologist' be changed to 'environmental risk assessor'.
- That risk assessors receive training in risk assessment according to the proposed targeted (searchlight) approach.
- That scientists from academic and public research institutes be included in important functions of the proposed risk assessment framing body.
- That improvement in risk communication in all facets of communication be researched and satisfactorily implemented.
- That communication with the applicant be improved in structured participation in the framing step.
- That national research institutes receive a prominent role in advising and policy development as members of the advisory committee and the risk assessment framing body as initiation of a risk assessment platform.
- That stakeholder participation should be researched as a future option in a democratic society.
- That the new model be incrementally implemented.

9.8.2 Governance of toxicological assessment of new pesticide molecules

- That the proposed model for governance of toxicological assessment of new pesticides molecules be considered for adoption in proposed new legislation for pesticides.
- The incremental implementation of the model be considered.
- That the role of relevant public and academic research institutes be seriously considered for capacity building with respect to participating in reviewing of new documentation as members of a proposed review committee, and for accommodating regulatory scientists involved in the reviewing in the milieu of toxicology.
- That a scientific study be conducted to determine a proposed number of toxicologists for sustainability in the regulatory process.
- That a science platform be developed for toxicological expertise.
- That the most appropriate profession of veterinary toxicologists for membership of the proposed bodies be considered.
- That an in-depth research into the merits and membership of the proposed risk assessment framing and reporting body be conducted.
- That an in-depth research into the merits and membership of the proposed toxicological assessment body be conducted.
- That policies and strategies be developed for risk communication.

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9.8.3 Future research

- This study commenced with searching for an answer to 'credibility' in risk governance. The results from the study, some preliminary, other more obviously confirmed, could be the initiative for a much richer investigation into credibility. Credibility or trust in governance encompasses an immersive broad field that could include social, economic, political, and technological sciences. This is indeed a field that could occupy many dedicated scientists for many years. It would be worthwhile to start working towards identifying core issues, of which my research is only one, to improve credibility. However, it would be a long way to go, because of such controversial cases as GMOs and pesticides.

- Growing interest in phytomedicines and phytopesticides is of great future importance. The governance of risk assessment of botanicals may have similar challenges as chemical pesticides and perhaps GMOs but may also have many new challenges. This is an area of governance that needs urgent attention in order to pave the way for a great explosion of information that could benefit mankind. Research on risk governance should be matter of priority to consider.

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