STRATEGY OF THE MAIZE FORUM AND MAIZE TRUST FOR MYCOTOXIN RESEARCH IN SOUTH AFRICA

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1. Background to mycotoxins

The supply of high quality, healthy maize is a national priority since maize represents the staple food of many South Africans. However, maize remains prone to contamination by several toxigenic fungi during the pre-harvest (production), post-harvest (storage) and processing stages. These fungi have the propensity to produce on maize some hazardous toxins such as the aflatoxins, zearalenone, fumonisins, ochratoxins, trichothecenes (deoxy-nevalenol and nivalenol) and diplodiatoxins. Fortunately the aflatoxins, the most notorious group of highly potent hepatocarcinogens occur extremely rarely on South African maize. The isolation and characterization of the toxin(s) produced by a specific toxigenic fungus is a prerequisite for analysing the mycotoxin in agricultural commodities and foods in order to study the impact of the relevant toxin on human and animal health. *Diplodia maydis* is an important contaminant of South African maize, causing ear rot. However, the toxin(s) produced by this fungus still remain a great scientific challenge. The brief background to mycotoxins is presented (see below) to establish the enormity of the problems faced by the grain and cereal industries in South Africa.

Mycotoxins comprise a structurally diverse group of mostly small-molecular-weight toxic compounds, derived from the secondary metabolism of filamentous fungi. These toxic secondary metabolites are produced by a number of fungi, including members of the genera *Aspergillus*, *Penicillium*, *Fusarium*, *Claviceps* and *Alternaria.* Several of the mycotoxins are important environmental and carcinogenic agents and are ubiquitous in a broad range of commodities, causing toxic responses when ingested by mammals (such as man and higher animals), poultry and fish. During 2005 the Council for Agricultural Science and Technology (CAST) internationally considered aflatoxins, trichothecenes, fumonisins, zearalenone, ochratoxin A (OTA) and ergot alkaloids as most relevant for human health. The same toxins, in fact, are also very relevant to animal health.

Mycotoxins pose an enormous threat to the international trade in foods and feeds because of the worldwide distribution of toxigenic fungi in agricultural products. Post-harvest losses in the developing world, in particular, are severe because of inadequate storage facilities and the consequent poor quality of the produce. It is claimed that approximately 60% of Africa's grain supplies are at risk owing to fungal contamination and mycotoxin formation.

In nature, most cereal grains, oil seeds, tree nuts, fruits and dehydrated fruits are susceptible to contamination by mycotoxin-producing fungi. In addition, mycotoxins may occur in beer and wine; worldwide OTA is a frequent contaminant of wines. Not all fungal growth on plants and plant products, however, results in mycotoxin production. Therefore, the occurrence of fungi,

even toxigenic ones, on foods and feeds does not necessarily imply the presence of mycotoxins.

Several environmental factors such as temperature, humidity and soil or storage conditions influence the production of mycotoxins in agricultural commodities. There can be significant year-to-year fluctuations in the levels of mycotoxins in foods and feeds due to many factors such as adverse climatic conditions that favour fungal invasion, growth and mycotoxin formation.

Some of the toxins are important environmental and carcinogenic agents and are ubiquitous in a broad range of commodities, causing toxic responses when ingested by mammals (such as man and higher animals), poultry and fish. Initially mycotoxin production was only linked to the so-called storage fungi growing saprophytically (post-harvest) on stored grains and nuts. Today, however, it is well recognized that some fungi growing parasitically on plants before harvest also have the propensity to produce mycotoxins. Several explanations may be given for their production, such as the likelihood that mycotoxins might play a role in facilitating competition with other micro-organisms for nutrients and space, and the generation of favourable germination conditions for fungal spores

More than 300 mycotoxins are currently known. Most of them are thermally stable and cannot be eliminated during food processing. These toxins induce powerful and dissimilar biological effects in humans and animals. Some are carcinogenic (aflatoxins, ochratoxins and fumonisins), mutagenic (aflatoxins and sterigmatocystin), teratogenic (ochratoxins), oestrogenic (zearalenone), haemorrhagic (trichothecenes), immunotoxic (aflatoxins and ochratoxins), nephrotoxic (ochratoxins), hepatotoxic (aflatoxins, ochratoxins and phomopsins), dermatoxic (trichothecenes) and neurotoxic (ergotoxins, penitrems, lolitrems and paxilline), whereas others display antitumour, cytotoxic and antimicrobial properties. The human ingestion of mycotoxins is due to the consumption of the mycotoxins in plant-based foods such as grains like maize, barley and rice, coffee, nuts and their residues, and metabolites in animal-derived foods, for example aflatoxin M1 (AFM1) in milk and meat products. In addition they have a tremendous economic impact on the animal and food/feed industry.

The global health threat to mankind is based on well-documented human mycotoxicoses such as ergotism (St Anthony's fire), which occurred frequently during the Middle Ages in Europe, alimentary toxic aleukia (ATA) in Russia, acute aflatoxicoses in South and East Asia, and human PLC in Africa and South East Asia. OTA is suspected of playing a role in Balkan endemic nephropathy (BEN) amongst the population living in the former Yugoslavia, and chronic interstitial nephropathy (CIN) in North Africa. The fumonisins are implicated in the aetiology of the high incidence of oesophageal cancer among the inhabitants of the former Transkei region of South Africa. Although the role of mycotoxins in diseases among domestic animals is better established, diagnosis of the mycotoxicosis is extremely difficult owing to the numerous pharmacological effects of the causative toxins, for example aflatoxins (Turkey-X disease), fumonisins (leukoencephalomalacia in horses

and pulmonary oedema in swine), ochratoxins [nephropathy in swine (Danish porcine nephropathy) (DPN)], phomopsin A (lupinosis in sheep) sporidesmin A(facial eczema in sheep) and zearalenone (hyperoestrogenism, vulvovaginitis and abortion in swine). Outbreaks of diplodiosis amongst farm animals are linked to feeds contaminated with *Diplodia maydis*.

Since the discovery of aflatoxins during the 1960s, an increasing number of countries have legislated maximum tolerated levels (MTLs) for an increasing number of mycotoxins with the aim of protecting both human and animal populations from the harmful effects of mycotoxin exposure. The most recent international effort to collate these regulations was undertaken under a Food and Agriculture Organization (FAO) project during 2002 and 2003. A comprehensive compilation has been published as an FAO Food and Nutrition paper (Food and Agriculture Organization, 2004).

Aflatoxin remains the most widely legislated mycotoxin. At least 99 countries have regulatory limits for AFB_1 or the sum of AFB_1, AFB_2, AFG_1 and AFG_2 in food and/or feed.

In South Africa, world-class mycotoxin research has been done over many years at the CSIR and the MRC. The multidisciplinary research undertaken at the two institutions was complementary and managed by an inter-institutional steering committee. The research at the CSIR focussed on the isolation, structural elucidation, synthesis, biosynthesis and analysis of mycotoxins. The structure elucidation involved mass spectroscopy, ^{1}H and ^{13}C N M R spectroscopy and Single-Crystal X-Ray Crystallography, whereas the biosynthetic studies utilized stable isotopes of C, H and O. The research team at PROMEC of the MRC undertook sterling studies on the taxonomy of toxigenic fungi, the effects of fungal–infected cereals (as well as pure mycotoxins) on experimental animals, as well as the *in vivo* and *in vitro* mechanism of action of mycotoxins, the metabolism of mycotoxins, development of mycotoxin analytical methodology and the analysis of mycotoxins in foods and feeds. The research on toxigenic *Fusarium* species and on the fumonisins brought much credit to the PROMEC research team. In the past, the research at both the CSIR and MRC was mainly sponsored by the two statutory councils themselves. The results of these research efforts constituted the base of hundreds of top-class research publications that appeared in international journals with high impact factors. Furthermore, the mycotoxin research earned much international acclaim for South African science and scientists and enabled substantial networking and mutually beneficial, multinational collaboration.

2. Introduction to the Strategy

The Strategy for Mycotoxin Research of the Maize Forum (endorsed by the Maize Trust) comprises an inspiring Vision, Mission, Goal, Objectives and Ancillary Objectives. Mutually beneficial collaboration and networking among researchers from government departments, the ARC, CSIR, MRC and universities in South Africa are fundamentals to the success of this strategy.

The Maize Forum envisages that the effective implementation of the Strategy will lead to the creation of a virtual Centre of Excellence on Mycotoxin Research in Maize (and other cereals) in South Africa by 2012.

3. Elements of the strategy

3.1 Vision for mycotoxin research at the Maize Forum

To enable leading mycotoxin research for the maize industry in South Africa.

3.2 Mission for mycotoxin research at the Maize Forum

It is the mission of the Maize Forum to have world-class mycotoxin research undertaken at South African universities and research institutions, in order to ensure that safe maize is supplied to the food and animal feed industries, and consumers, and export markets.

3.3 Goal for mycotoxin research at the Maize Forum

Sufficient and sustainable production, storage and processing of healthy and high quality maize for the food and feed industries, consumers in South Africa, and for export markets.

3.4 Objectives for mycotoxin research at the Maize Forum

3.4.1 Main objectives

- To support the development and maintenance of a proper database concerning mycotoxin research results on maize (both national and international research findings).
- To support the establishment of the magnitude of mycotoxin contamination of maize during the stages of its production, storage, and processing in South Africa. This objective is to be completed within a three year period
- To support the regular monitoring of the occurrence of the fumonisins, aflatoxins, zearalenone, and trichothecenes (DON and NIV) in locally produced and imported maize.
- To support the determination of the factors which contribute to mycotoxin contamination during the production (pre-harvest), storage (post-harvest) and processing of maize**.**
- To support the development of practical, affordable and environmentally sound methods to manage toxigenic fungi in maize, with particular emphasis on the introduction of resistance in local maize cultivars

3.4.2 Ancillary objectives

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- To support relevant research at internationally accredited laboratories for the analysis of mycotoxins in maize and maize products.
- To develop and introduce statistically sound methods for collecting samples of maize and of maize products for mycotoxin analysis.
- To study the diversity, ecology, and genomics of toxigenic fungi on South African maize and maize products.
- To support mycotoxin research involving *Fusarium verticillioides*, the main producer of fumonisin in maize, and other relevant mycotoxigenic fungi.
- To study the isolation and structural elucidation of important newly discovered mycotoxins.
- To create human capacity relevant to the future needs of the South African cereal and grain industries by training selected post-graduate students in mycotoxin research projects, also in collaboration with international institutions.
- To promote the publication of research findings in high quality peer-reviewed journals.
- To liaise with the Departments of Health in setting regulations for establishing the Maximum Tolerated Levels (MTLs) of mycotoxins in maize and maize products.
- To be a leading source of unbiased research-based information on the levels of mycotoxins in maize and maize products.
- To establish a peer-review working group to evaluate research proposals and progress reports for the Maize Forum.
- To support national and international collaboration in establishing a world-class mycotoxin research programme in South Africa