

Mycotoxins in grain and grain products in South Africa and proposals for their regulation

By

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PREFACE

The National Association of Maize Millers (NAMM) and the National Chamber of Milling (NCM) in South Africa commissioned this study in September 2000. It was a sincere effort on their part to discover the realities surrounding the occurrence of mycotoxins in cereal grain staples and their products in South Africa, the threat these may pose to the health of consumers and practical ways to deal with the situation. The driver for their action was the substantial confusion that arose when a lobby of scientists pushed for adoption of maximum tolerable levels (MTLs) for fumonisins previously recommended for consideration by Gelderblom *et al* (1996) and Marasas (1997). These recommendations were based on classical risk assessment methods, including an exposure assessment and a hazard assessment. Based on toxicological data for rats, with a 1000-fold safety factor, these assessments arrived at recommended maximum levels of 100 – 200 ng/g in food. Little epidemiological data were included and socio-economic practicalities were not taken into consideration in these assessments.

Significantly, Prof Marasas and his team of scientists at the Medical Research Council (MRC), including Dr Gelderblom, were not involved in the initiative to push for statutory adoption of these recommendations. Adoption of these levels would have caused a revolution in the grains industry, as is demonstrated within the pages of this thesis. This thesis attempts to consider in a balanced way the relevant scientific information, as well as stakeholder interests, particularly those of consumers from a national health as well as an economic perspective. It offers a pragmatic approach to the setting of MTLs for substances that are potentially harmful to the health of consumers, based on sound scientific evidence. New MTLs for three mycotoxins have been formulated as well as proposals for their practical implementation.

The National Maize Trust has subsequently reimbursed NAMM and NCM for the costs of this study and it stands to its credit that, through this gesture, the maize industry has accepted the outcomes of the study.

Summary

Mycotoxins in grain and grain products in South Africa and proposals for their regulation

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The purpose of the study was to:

- Report on the occurrence of mycotoxins in grain and grain products in South Africa;
- Compare with other countries;
- Weigh the evidence regarding effects on health of test animals, and human and animal consumers;
- Determine the need for statutory measures to regulate mycotoxins in food; and
- Propose practical measures for controlling mycotoxins in grain and grain products in South Africa.

Good mycotoxin data for maize were obtained from the author's surveys. Data on other local grains is lacking. In domestic maize, fumonisins and deoxynivalenol occur regularly, at levels as low or lower than in Argentina and the USA. Other mycotoxins occur rarely, or at very low levels. Deoxynivalenol is likely to occur regularly in domestic wheat. Aflatoxins were virtually absent in domestic maize, but often occur at concerning levels in imported Argentinean and USA maize. The literature show that aflatoxins are acutely and chronically toxic to humans and animals and most countries maintain regulatory Maximum Tolerable Levels (MTLs) for aflatoxins in grain and grain products. Several countries also maintain regulatory MTLs for deoxynivalenol,

based on lesser scientific evidence. The mycotoxin that occurs most frequently in South African maize, is the fumonisin B group of analogues, with fumonisin B₁ the most abundant. Fumonisin B₁ is produced by *Fusarium verticillioides* (previously known as *Fusarium moniliforme*) and occur in maize worldwide. Fumonisin B₁ cause leukoencephalomalacia in horses, pulmonary oedema in pigs, liver cancer in rats and liver and kidney damage in other animals. A statistical relationship between the occurrence of *F. verticillioides* and fumonisin B₁ in maize and oesophageal cancer in humans has been demonstrated in Transkei and in China. The 'toxins derived from *F. moniliforme*' and fumonisin B₁ have been evaluated as Group 2B carcinogens i.e. possibly carcinogenic to humans, by the International Agency for Research on Cancer of the World Health Organisation.

Based on a review of epidemiological and toxicological evidence of the effects of fumonisin B₁ on humans and animals, their occurrence in maize and maize products, previously proposed MTLs, and the practical implications of MTLs set for maize and maize products, we propose the following MTLs for total fumonisin B₁ in maize and maize products for human consumption:

- 4 µg/g in whole, uncleaned maize;
- 2 µg/g in dry-milled maize products with fat content of ≥ 3.0 %, dry weight basis (e.g., sifted and unsifted maize meal); and
- 1 µg/g in dry-milled maize products with fat content of < 3.0 %, dry weight basis (e.g., flaking grits, brewers grits, samp, maize rice, super and special maize meal)

These MTLs are too high to address a possible link of fumonisin B₁ with neural tube defects in neonates. This potential problem remains to be addressed, possibly by fortification of maize products with folic acid.

We propose MTLs for deoxynivalenol of 2 µg/g in cereal grains for food use, and 1 µg/g in cereal grain food products. Finally, we propose that the current regulatory MTLs for aflatoxins be raised from 10 ng/g (total aflatoxins in unprocessed maize) to 20 ng/g.

Ekserp

Mikotoksiene in graan en graanprodukte in Suid-Afrika en voorstelle vir die regulering daarvan

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Die doel met die studie was om:

- Verslag te lewer van die voorkoms van mikotoksiene in graan en graanprodukte in Suid-Afrika;
- Met ander lande te vergelyk;
- Beskikbare data oor die effek op die gesondheid van toetsdiere en menslike en dierlike verbruikers te bestudeer;
- Te bepaal of daar behoefte na statutêre maatreëls is om mikotoksiene in voedsel te reguleer; en
- Praktiese maatreëls aan die hand te doen om mikotoksiene in graan en graanprodukte in Suid-Afrika te reguleer.

Vir mielies is goeie mikotoksiendata beskikbaar vanuit die skrywer se eie opnames. Daar is egter 'n tekort aan data tov ander grane. Fumonisiene en deoksinivalenol kom dikwels voor in plaaslike mielies teen vlakke soortgelyk of laer as in Argentinië en die VSA. Ander mikotoksiene kom selde voor, of teen baie lae vlakke. Deoksinivalenol kom waarskynlik ook dikwels in plaaslike koring voor. Plaaslike mielies is feitlik totaal vry van aflatoksiene, maar aflatoksiene kom dikwels teen besorgenswaardige vlakke voor in ingevoerde VSA en Argentynse mielies. Uit die literatuur is dit duidelik

dat aflatoksiene akute sowel as chronies giftig is vir mens en dier en die meeste lande handhaaf regulatoriese Maksimum Aanvaarbare Vlakke (MAVe) vir aflatoksiene in graan en graanprodukte. In verskeie lande is regulatoriese MAVE vir deoksinivalenol ook van krag, maar minder wetenskaplike data is beskikbaar as die basis daarvan. Die mees algemene mikotoksien in Suid-Afrikaanse mielies is die fumonisien B-groep van analoë, waarvan fumonisien B₁ die meeste voorkom. Fumonisiene word deur *Fusarium verticillioides* (voorheen bekend as *Fusarium moniliforme*) geproduseer en word wêreldwyd in mielies aangetref. Fumonisiene veroorsaak leukoencephalomalasia in perde, pulmonêre edeem in varke en nier- en lewerskade in ander diere. 'n Statistiese verwantskap tussen die voorkoms van *F. verticillioides* en fumonisiene in mielies en slukdermkanker by mense is in Transkei en China aangetoon. Die Internasionale Agentskap vir Kankernavorsing van die Wêreld Gesondheidsorganisasie het die 'toxins derived from *F. moniliforme*' en fumonisien B₁ as Groep 2 B karsinogene geëvalueer - d.i. moontlik karsinogenies vir mense.

Gebaseer op 'n oorsig van epidemiologiese en toksikologiese gegewens met betrekking tot die effek van fumonisiene op mens en dier, die voorkoms van fumonisiene in mielies en mielieprodukte, MAVE wat voorheen aan die hand gedoen is, en die praktiese implikasies wat MAVE vir die mieliebedryf inhou, word die volgende nuwe MAVE vir fumonisiene (totaal) in mielies en mielieprodukte vir menslike verbruik aan die hand gedoen:

- 4 µg/g in heel, onskoongemaakte mielies;
- 2 µg/g in mielieprodukte van die droëmaalbedryf, met 'n vetinhoud ≥ 3.0 %, droëmassabasis (bv. gesifte en ongesifte meliemeel); en
- 1 µg/g in mielieprodukte van die droëmaalbedryf, met 'n vetinhoud < 3.0 %, droëmassabasis (bv. meliegruis, brouersgruis, stampmielies, melierys, super and spesiale meliemeel)

Hierdie vlakke is egter onvoldoende om 'n moontlike verband tussen fumonisiene en neuraalbuisdefekte by pasgeborenes aan te spreek. 'n Oplossing vir dié probleem moet elders gevind word, moontlik deur fortifisering van mielieprodukte met foliensuur.

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Ten opsigte van deoksinivalenol word 'n MAV van 2 $\mu\text{g/g}$ vir graan bestem as voedsel aan die hand gedoen, en 1 $\mu\text{g/g}$ vir graanprodukte. Laastens word aan die hand gedoen dat die huidige regulatoriese MAV vir aflatoksiene van 10 ng/g (totale aflatoksiene in onverwerkte mielies) na 20 ng/g verhoog word.

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GLOSSARY AND ABBREVIATIONS USED

AFMA – Animal Feed Manufacturers Association in South Africa

AFB₁, AFB₂, AFG₁, AFG₂, AFM₁, AFM₂ - Aflatoxin B₁, B₂, G₁, G₂, M₁ & M₂ respectively

AFLA - aflatoxins

AME - Alternariol monomethyl ether

ARG maize – yellow maize imported from Argentina

ASIR – age standardised incidence rate

BGYF - bright green yellow fluorescence

Carcinogen – a substance that causes cancer in animals and/or humans

CFSAN – Center for Food Safety and Nutrition of the FDA

CIT - citrinin

CVM – Center for Veterinary Medicine of the FDA

DAS - Diacetoxyscirpenol

DON - Deoxynivalenol

E-OFS – Eastern Orange Free State

E-Tvl – Eastern Transvaal

ENSO – El Nino Southern Oscillation

FAO – Food and Agriculture Organization of the United Nations

FBs – Two or more of fumonisin B₁, B₂, B₃, B₄

FB₁, FB₂, FB₃, B₄ – fumonisin B₁, B₂, B₃ and B₄ respectively

FDA – Food and Drug Administration in the USA

Feed – products intended for animal consumption

Feed components – products intended for mixing with other products in predetermined ratios to produce a balanced ration for animal use

FGIS - Federal Grain Inspection Service in the USA

Food – products intended for human consumption

Fungi – a diverse group of plants that lack chlorophyll and which obtain their food as saprophytes from dead organic matter, and/or as parasites from other living organisms

GLC – Gas liquid chromatography

HBV – hepatitis B virus

HCV – hepatitis C virus

HFB – hydrolysed fumonisins through alkali treatment

HPLC – High Pressure Liquid Chromatography

HT-2 – HT-2 toxin

IACs - Immunoaffinity columns; ELISA or antibody test kits

kt – kiloton, or thousand metric tons

LEM - leucoencephalomalacia, a condition caused by FBs in horses, where cavities develop in the white matter of the brain

MBN - methylbenzyl nitrosamine

Mixed feed – a balanced ration consisting of a mixture of feed components, intended for animal consumption

MON - Moniliformin

MRC – The Medical Research Council in Tygerberg, South Africa

Mt – Megaton, or million metric tons

MTL – maximum tolerable level

Mycotoxicooses - diseases in animals and humans resulting from the consumption of mycotoxins

Mycotoxins – secondary metabolites produced by fungi, some of which are toxic to plants animals and humans, and some are toxic and carcinogenic to animals and humans

N-OFS – northern Orange Free State

N-MBN – *N*- methylbenzyl nitrosamine

NIV - Nivalenol

NOAEL – no observed adverse effect level

NS – statistically not significant

OA – ochratoxin A

OC – oesophageal cancer

PAT - patulin

PDI – probable daily intake

ppb – parts per billion, or ng/g, or µg/kg, or mg/metric tonne

ppm – parts per million, or µg/g, or mg/kg, or g/metric tonne.

PWV – Pretoria, Witwatersrand, Vereeniging area

RSA maize – locally produced South African white or yellow maize

Squamous cells or squamous epithelium – tile-like cells on the surface layers of a body tissue

t – metric ton

T-2 - T-2 toxin

TDI – Tolerable daily intake: the daily intake of a toxin that should be harmless

TLC – Thin layer chromatography

USA maize – yellow maize imported from the United States of America

W-Tvl – western Transvaal

WHO – World Health Organization of the United Nations

ZEA – Zearalenone