AGENCE FRANÇAISE DE SÉCURITÉ SANITAIRE DES ALIMENTS

French Food Safety Agency

Risk assessment for mycotoxins in human and animal food chains

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Summary report

December 2006

Abbreviations

JECFA : Joint FAO/WHO Expert Committee on Food Additives
SCF : Scientific Committee of Food (Comité scientifique européen de l'alimentation humaine)
AESA/EFSA : Autorité Européenne de Sécurité des Aliments/European Food Safety Authority
AFSSA : Agence Française de Sécurité Sanitaire des Aliments/French Food Safety Agency
EC : European Commission

PTWI : Provisional Tolerable Weekly Intake
ADI : Acceptable Daily Intake
MTD : Maximum TolerableDose
LOAEL : Lowest observed adverse effect level
NOAEL : No observed adverse effect level
NOEL : No observed effect level
LD50 : Lethal Dose 50 : dose of a substance which results in the death of 50 % of the animals

IARC : International Agency for Research on Cancer
Classification produced by the IARC (Preambule of the IARC monographs– 19 January 1999)

- Group **1** : The agent (the mixture) is carcinogenic to human beings. The exposure circumstances result in exposure which is carcinogenic for human beings.
- Group **2A** : The agent (mixture) is probably carcinogenic to human beings. The exposure circumstances result in exposure which is probably carcinogenic to human beings.
- Group **2B** : The agent (the mixture) may be carcinogenic to human beings. The exposure circumstances result in exposure which may be carcinogenic to human beings.
- Group **3** : The agent (the mixture, circumstances of exposure) cannot be classified in terms of their carcinogenicity to human beings (the studies cannot be interpreted in terms of the presence or absence of carcinogenic effect because of major qualitative or quantitative limits, or because no experimental carcinogenicity data are available).
- Group **4** : The agent (the mixture) is probably not carcinogenic to human beings.

A_w : water activity
g : gram
ng : nanogram
µg : microgram
b.w. : body weight
l.w. : live weight

BEN : Balkan Endemic Neuropathy

ELISA : Enzyme Linked ImmunoSorbent Assay
RIA : Radio Immuno Assay
GPC or GC : Gas (phase) chromatography
MS : Mass spectrometry
UV : ultra-violet
ECD : Electron capture detection
TLC : Thin layer chromatography
HPLC or LC : High performance liquid chromatography or Liquid chromatography

LOQ : limit of quantification
LOD : limit of detection

DNA : deoxyribonucleic acid
tRNA: transfer ribonucleic acid

Introduction

Mycotoxins are secondary metabolic products from moulds which can grow on the plant either in the field or during storage and are potentially toxic for human beings and animals. More than 300 secondary metabolites have been identified although only around 30 have true toxic properties which raise concerns. These toxins are found as natural contaminants in many foodstuffs of plant origin, particularly cereals but also fruits, hazelnuts, almonds, seeds, fodder and foods consisting of or manufactured from these products and intended for human or animal consumption.

Mycotoxins are produced by moulds belonging in particular to the *Aspergillus, Penicillium* and *Fusarium* genera (table 1).

Table 1: Mycotoxins and the associated moulds which produce them found in human and/or animal foodstuffs

	Mycotoxins	Principal producing moulds
Regulated mycotoxins or those in the course of being regulated	Aflatoxins B1, B2, G1, G2	*Aspergillus flavus, A. parasiticus, A. nomius*
	Ochratoxin A	*Penicillium verrucosum, Aspergillus ochraceus, Aspergillus carbonarius*
	Patulin	*Penicillium expansum, Aspergillus clavatus Byssochlamys nivea*
	Fumonisins B1, B2, B3	*Fusarium verticillioides, F. proliferatum*
	Trichothecenes (DON)	*Fusarium graminearum, F. culmorum F. crookwellense, F. sporotrichioides F. poae, F. tricinctum, F. acuminatum*
	Zearalenone	*Fusarium graminearum, F. culmorum F. crookwellense.*
	Ergot Alkaloids	*Claviceps purpurea, C. paspali, C. africana*
Other mycotoxins	Citrinine	*Aspergillus terreus, A. carneus, A. niveus Penicillium verrucosum*, *P. citrinum, P. expansum*
	Alternaria toxins (alternariol, alternariol methyl ether…)	*Alternaria alternata, Alternaria solani*
	Cyclopiazonic acid	*Aspergillus flavus, A. versicolor, A. tamarii Penicillium dont P. camemberti*
	Sterigmatocystin	*Aspergillus nidulans, A. versicolor, A. flavus*
	Sporidesmins	*Pithomyces chartarum*
	Stachybotryotoxins	*Strachybotrys chartarum*
	Endophyte toxins (ergovaline, lolitreme B)	*Neotyphodium coenophialum, N. lolii*
	Phomopsins	*Phomopsis leptostromiformis*
	Tremorgenic toxins	*Penicillium roquefortii, P. crustosum, P. puberrelum Aspergillus clavatus, A. fumigatus*

Toxinogenic moulds
Two groups of toxinogenic (mycotoxin producing) fungi (or moulds) can be distinguished. The first consists of fungi which invade their substrate and produce mycotoxin on old or stressed plants: this is the area of field toxins. The other group contains those which produce toxins after harvesting: these are described as storage toxins. Fungi from the ground or plant debris may disseminate their spores onto the plant or seeds and then proliferate during storage if conditions allow.

Toxinogenic moulds may develop in all climates on any solid or liquid supports as soon as nutritional substances and moisture (water activity A_w over 0.6) are present, hence the wide variety of contaminated foodstuff substrates. The foods contaminated with mycotoxins may be classified into two major groups: foods and substances of plant origin and those of animal origin. Of the substances and foods of plant origin, cereals and their derivatives carry the greatest risk in view of their frequency of contamination and extensive consumption in Europe regardless of type of diet. Other plant products are dried fruit and vegetables (Oil-bearing seeds, beans, raisins), spices, coffee, cocoa and fermented juices and products (apple juice, grape juice, beer, wine and cider). Amongst the products and foods of animal origin, milk, eggs, meat, offal and all products derived from them merit attention.

Some moulds are used in the production of condiments or foods such as cheeses and cured meats and fish meats and because of this must meet strict safety criteria. Several species of fungi have been used for centuries to prepare foods in the East and Far East. New uses of micromycetes are hindered by fears about the presence of mycotoxins. In the past they were selected based on lack of observed toxicity although they are now screened by toxicogenomic methods in order to detect toxicogenesis genes.

Mycotoxins
Mycotoxins may be classified into polycetoacids, terpenes, cyclopeptides and nitrogenous metabolites, depending on their biological origin and structure. They can also be more simply classified according to their major toxic effects. Amongst the groups of mycotoxins considered to be important from a processed-foods and health perspective are the aflatoxins, the ochratoxins and ochratoxin A in particular, patulin, fumonisins, zearalenone and the trichothecenes, specifically deoxynivalenol. It should be noted that toxicity may vary considerably within a structural group and that the danger may not always be due to the toxin itself but to its metabolites and possible synergistic effects in cases of multiple contamination.

Mycotoxins and consumer risk
The toxicity of these natural contaminants may be direct, or indirect through organisms which consume the contaminated food products.

Some mycotoxins cause very acute toxicity (single exposure to a high dose), although it is very rare in Europe to be exposed to toxic doses by ingesting a contaminated food on only one occasion.

Historically, the longest known mycotoxicoses is ergotism. This disease is also called "St-Anthony's fire", "sacred fire" or "fire sickness" . It is caused by *Claviceps* toxins produced by rye ergot and presents as delirium, prostration, violent pain, abscesses and gangrene of the extremities leading to serious incurable incapacity. Epidemics occurred in the 8th to 16th century because of poor population dietary conditions particularly the consumption of flours contaminated by ergots from these fungi. The last episode in France occurred in 1951 at Pont Saint-Esprit, in the Gard.

Chronic effects (repeated exposure to low or even very low doses) are the most worrying because of eating habits and the lasting effect of the toxins.

Toxicity is variable (table 2). Some toxins have heptatotoxic effects (aflatoxins), others are oestrogenic (zearalenone), immuno/haematotoxic (patulin, trichothecenes, fumonisins), dermonecrotic (trichothecenes), nephrotoxic (ochratoxin A) or neurotoxic (tremorgenic toxins). Some mycotoxins are recognised or suspected to be carcinogenic. These include aflatoxin B1 and ochratoxin A. In addition, several mycotoxins may be present in the same product or same serving of food.

Table 2 : Identified or suspected effects of the major mycotoxins and cellular and molecular mechanisms of action identified experimentally

Toxin	Effects	Cellular and molecular mechanisms of action
Aflatoxin B1 + M1	Hepatotoxicity Genotoxicity Oncogenicity Immunomodulation	Formation of DNA adducts Lipid peroxidation Bioactivation by cytochromes P450 Conjugation to GS-transferases
Ochratoxin A	Nephrotoxicity Genotoxicity Immunomodulation	Effect on protein synthesis. Inhibition of ATP production Detoxification by peptidases
Patulin	Neurotoxicity *In vitro* mutagenesis	Indirect enzyme Inhibition
Trichothecenes (Toxin T-2, DON, …)	Hematotoxicity Immunomodulation Skin toxicity	Induction of apoptosis in haemopoietic progenitor cells and immune cells. Effect on protein synthesis Abnormal changes to immunoglobulins
Zearalenone	Fertility and Reproduction	Binding to oestrogen receptors Bioactivation by reductases Conjugation to glucuronyltransferases
Fumonisin B1	Central nervous system damage Hepatotoxicity Genotoxicity Immunomodulation	Inhibition of ceramide synthesis Adverse effect on the sphinganin/sphingosin ratio Adverse effects on the cell cycle.

There is another, indirect, risk to human consumers through the possible presence of residues in production from commercially reared animals exposed to food contaminated by mycotoxins.

These residues consist of the toxin itself and/or its bioformed metabolites retaining the toxic properties of the parent compound. Species of farmed animals therefore represent a vector for these toxins or their metabolites in products such as meat, milk or eggs. This applies particularly to aflatoxin B1, the aflatoxin M1 metabolite of which is found in milk from mammals which have eaten feed contaminated by aflatoxin B1. The mycotoxins are generally heat stable and are not destroyed by usual cooking and sterilisation procedures. Their ability to bind to plasma proteins and their lipophilic nature allow toxins to persist in the body following repeated exposure at close intervals.

Mycotoxins and risk to animals

Monogastric farm animals, poultry and pork are particularly at risk of the mycotoxicoses because of the large part cereals play in their diet and the lack of a ruminal reservoir containing micro-organisms which can degrade the toxins before they are absorbed in the intestine. The susceptibility of poultry to aflatoxins led to their discovery following a sudden outbreak of fatal hepatotoxicity which occurred in 1960 in turkey farms in Great Britain. This led to the identification of the relationship between moulds-toxins-diseases and the development of modern mycotoxicology. Similarly, many cases of nephropathy in pigs reported a few years later in Denmark led to the discovery of the natural contaminating effects of ochratoxin A in barley and a description of its toxic effects.

In France, apart from sporadic cases of acute events which are seen in different species of animals, most of the problems relate to chronic contamination by fusariotoxins (trichothecenes, zearalenone, fumonisins) in foods produced in France or imported. Intermittent problems due to importation of contaminated starting materials justify monitoring and control procedures. In addition, the development of moist farm storage techniques (silage, tied bales) and the use of moist foods as brewers grain draff and beet pulps can also be a risk for developing moulds and for mycotoxins being present[1].

Assessment of mycotoxic risk

The mycotoxins, which are generally recognised to originate from plant contamination, are a very topical food quality and safety problem. Regulations have already been introduced for aflatoxins and ergot in human and animal foods, for ochratoxin A, patulin, DON, zearalenone and fumonisins in human foods, and they are being prepared for ochratoxin A, DON, zearalenone and fumonisins in animal feed.

Assessing mycotoxic risk is difficult. The risk is mostly a natural one as human beings cannot control its development (which is due particularly to climatic conditions) and varies as fungal contamination is difficult to control. Multiple contamination may also occur because of the ability of the same yeast to produce different mycotoxins. Several toxins from the same structural family or of different structures may be found in the same food product and particularly in a serving containing different food ingredients. This natural situation raises problems as few studies have been conducted on toxic interactions and those that have are poorly informative.

In view of this, it would be appropriate to set up preventive measures including agronomic strategies (good agricultural practice, including choice of varieties, growing practices and plant protection treatments etc) and improving the harvesting, storage and monitoring conditions throughout the food chain. Organic production restricts the use of fungicidal treatments but places emphasis on techniques which are unfavourable to contamination with mycotoxins such as crop rotation, working the earth and crop history. Although limited data are available on contamination of organic products by mycotoxins, variable contamination rates have been reported although it has not been possible to establish major differences from the contamination rates in products obtained from conventional farming[2].

Finally, continued research is required to further improve knowledge about the toxicity of these substances and in particular about associations of mycotoxins, between mycotoxins and infectious pathogens or between mycotoxins and other contaminants.

Aim of this document

This document presents a review of the knowledge available about mycotoxins which carry a risk to human and/or animal health.

Each section handles a mycotoxin or family of mycotoxins, its physico-chemical and toxicological properties, development factors for the toxinogenic mould(s), analytical methods, effects on human and/or animal health through epidemiological data where these are available, data about the contamination of foodstuff products and an estimate of the dietary exposure of the French mainland population and a review of the regulations.

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1 Good practice for manufacture of silage for improved management of health risks. Afssa Report 2004. www.afssa.fr

2 Nutritional and health assessment of foods obtained from organic farming. Afssa Report 2003. www.afssa.fr

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Conclusions and recommendations

In 1998, the French High Council for Public Hygiene[1] produced a report reviewing knowledge on mycotoxins. The impact of mycotoxins on animal nutrition and health was not examined in this document. Since then, many publications and contamination data obtained from monitoring have improved knowledge about certain mycotoxins and their impact on human and animal health and have allowed estimates of dietary exposure levels to be made.

The French Food Safety Agency decided to undertake a review of knowledge available on mycotoxins which impact on human and/or animal health, to assess the risks from mycotoxins entering the human and animal food chain and to produce certain recommendations.

The specialist expert committees “Residues and chemical and physical contaminants" and "Animal nutrition", issues the following recommendations.

MYCOTOXINS

Mycotoxins are secondary metabolic products from yeasts which can grow on the plant in the field or during storage and which have potentially toxic effects on human beings and animals. These toxins are found as natural contaminants in many plant products, cereals and also fruits, animal feeds and processed foods and products obtained from these foodstuffs intended for human and animal consumption. Animal products such as milk, eggs, meat or offal can also be contaminated through the animal diet. Mycotoxins are generally heat stable and are not destroyed by usual cooking and sterilisation procedures.

The groups of mycotoxins considered to be important from a food processing and health perspective are the aflatoxins, ochratoxin A, the trichothecenes, particularly deoxynivalenol, the fumonisins, zearalenone and patulin. Other mycotoxins which have been less well studied in terms of their toxic effects but which may have health effects in human beings and/or animals have also been taken into account in this study.

In general terms, the mycotoxins described in this document are food contaminants which carry a danger to human and/or animal health. The nature of the danger is based on toxicological data, most of which are incomplete. Contamination data are frequently very variable because of sampling difficulties in view of the heterogenic nature and very variable growth of toxicogenic moulds, and difficulties in measurement.

Risk characterisation must be refined using new data on toxic effects obtained from studies conducted in accordance with internationally recognised guidelines and on contamination levels obtained from monitoring and control plans conducted over several years, considering the two methods of production – organic and conventional – and using validated quantitative analytical methods.

Although some mycotoxins have been better studied than others in terms of their toxicological properties and their effects on human and animal health, and average consumer exposure is generally low particularly because of the measures taken to reduce contamination of foods, it would be appropriate to formulate a number of recommendations to improve knowledge and management of the risks to human beings and animals from these mycotoxins occurring in foods. It should be noted that the toxicological data available principally concern toxins consumed individually and not the effects resulting from associations of mycotoxins which may be present simultaneously in the same foodstuff or in the same serving of food.

Mycotoxins are often distributed very heterogeneously in plant products. Sampling quality has a key impact on the analytical result. Afssa recommends that validated sampling plans be created using a final sample which is as representative as possible of the overall salubrity of a foodstuff.

[1] Conseil Supérieur d’Hygiène Publique de France

The next section of this opinion states the conclusions and recommendations for each mycotoxin or group of mycotoxins.

AFLATOXINS

The aflatoxin group and its major representative aflatoxin B1 (both in terms of content and prevalence in at risk foods and of its toxic effects) is the best studied and most regulated group of mycotoxins. They can be found in many regions of the world, mostly in nuts, dried fruits, oil bearing seeds or spices but also in cereals. Aflatoxin B1 has also been found to be present in milk in the form of its M1 metabolite.

It is the only group of mycotoxins identified to be clearly carcinogenic in human beings. The European and international bodies have not set an acceptable daily dose (ADI) for aflatoxins. These substances have genotoxic carcinogenic effects, with no threshold, and the only realistic approach is to reduce exposure to as low a level as possible following the ALARA (As Low As Reasonably Achievable) principle.

Animals are more or less sensitive to the toxic effects of aflatoxins, depending on the species. Long term exposure to low doses of aflatoxins present in animal foods (corn feed and maize seeds, cotton, nuts and in corn silage for ruminants) may cause effects ranging from hepatic changes to liver tumours. Transfer of aflatoxin B1 into poultry, eggs and meat has been described in animals exposed to high levels in their diet. In addition, 1 to 6% of the amount of aflatoxin B1 absorbed by a dairy cow are excreted in the milk in the form of AFM1.

Climatic conditions in Europe were usually considered not to permit the development of aflatoxin contamination in foods. The alerts in the summer of 2003 in Italy suggest an emergent risk of contamination in South European countries

Current regulatory measures in the European Union relate to dietary foodstuffs and animal food. The monitoring and control activities maintain risk at a very low level.

Afssa recommends:

- in scientific terms: that metabolism and transfer studies be conducted in poultry, eggs and meat and in the milk of young ruminants exposed to low amounts of aflatoxins. In addition, further studies should confirm the level of transfer into the milk of high-yielding cows, which until now has only been established from only one study;

- in regulatory terms: control plans intended to confirm the application of legislative measures taken in the European Union should be continued. A control plan based on repeated monitoring for corn production over several successive years in the warmest French regions should allow aflatoxin levels to be measured depending on climatic conditions;

- in preventive terms: the regulatory measures may be restrictive for some professionals particularly those in countries which cover a large proportion of the "aflatoxin – at risk" areas. Because of this, these measures should be accompanied by good practice guides to be used in production and processing. This type of initiative, which is currently adopted by some international bodies responsible for management of food risks, must therefore be encouraged.

OCHRATOXIN A

OTA is a mycotoxin produced during the storage of many foodstuffs (cereals, coffee, cocoa, dried fruit, spices, etc) and occasionally in the field on grapes. It is also liable to be present in the offal (particularly blood and kidneys) of animals which have eaten contaminated foods.

Nephrotoxic effects have been clearly identified in animals and are suspected in human beings. The ADI was revised by EFSA in 2006 to 120 ng/kg b.w./week. This revision was based particularly on the demonstration that OTA had no direct genotoxic effects.

Afssa recommends:

- in scientific terms: we still do not know the origin and toxicological significance of the presence of low amounts of OTA in human blood and in breast milk and no relationship with dietary exposure has been established. Epidemiological studies which are required to inform this area and provide a better estimate of the risk for human beings are recommended;

- in analytical terms: because of the large amount of data showing OTA contamination of foodstuff products below the limit of detection and calculation method, exposure is probably over-estimated. More sensitive analytical techniques should be developed in order to refine exposure estimates to better characterise the risks to the consumer;

- in terms of knowledge of contamination levels: rye and buckwheat appear from the monitoring and control plans to be the most highly contaminated: it would therefore be appropriate to increase measurements of OTA in these products.

TRICHOTHECENES

The Trichothecenes are mycotoxins produced by many species of *Fusarium*. More than 160 trichothecenes have been identified and are classified into 4 groups depending on their chemical structure. The major compounds are toxins T-2 and HT-2 (group A) and nivalenol (NIV) and deoxynivalenol (DON) (group B). The last one of these mycotoxins is the most common and most abundant. The trichothecenes which contaminate human and animal foods are mostly found in cereals and their derivatives. Human exposure from ingestion of products from animals coming from exposed farms is low.

Group A trichothecenes may produce changes in the blood count and in immune function in chronic poisoning. Questions need to be asked about the effects of exposure to low doses of these microtoxins. Group B trichothecenes cause a fall in dietary consumption and a resultant reduction in zootechnical performance, mostly in pigs.

Afssa recommends:

- in scientific terms: in order to support the acceptable daily intake set in 2001 and 2002, it is recommended that toxicological studies be conducted following the internationally recognised guidance notes. These should allow the differential toxicity of the different trichothecenes to be established. Studies should also be conducted to improve toxicological knowledge about associations of fusarium toxins, particularly group B trichothecenes with zearalenone;

- in analytical terms: the European Commission has set maximum limits for DON in starting materials and foodstuffs intended for human consumption. The development of rapid multi-detection methods compatible with the regulatory limits to be used for in-house controls is recommended;

- in terms of knowledge about contamination and exposure levels: the levels of toxins T-2 and HT-2 in cereal products should be tested in the monitoring and control plans, with analytical limits permitting exposure to be estimated.

ZERALENONE

Zearalenone is produced by several species of *Fusarium* which grow on field cereals and also during storage and malting (wheat). Corn semolina and flour are the most commonly contaminated foods.

The most worrying toxic effect of zearalenone is its endocrine interfering action due to its oestrogenic activity. The effect on human being is not established. Conversely pigs, particularly young females, are sensitive to zearalenone. Zearalenone is bio-activated into α-zearalenol which has greater oestrogenic activity than that of the parent compound.

The PTDI of 0.2 µg/kg b.w./d set by the SCF in 2000 has been adopted to characterise consumer risk. Human dietary exposure is below the acceptable daily dose apart from the vegetarian/macrobiotic population which exceeds the toxicological reference limits by 185%. Farm animals can be exposed to high levels of zearalenone contaminating cereals and cereal co-products, which may carry risks of oestrogenic effects, particularly in pig.

Afssa recommends:

- in scientific terms:
  - that toxicological studies be conducted following the internationally recognised guidelines in order to review the acceptable daily intake which was set in 1999 by JECFA and in 2000 by SCF which used studies that are now considered to be inadequate;
  - that the interactions between zearalenone and other endocrine interfering substances be studied;
  - that studies be conducted to improve toxicological knowledge about associations of fusarium toxins, particularly zearalenone with the trichothecenes;
  - that further studies be conducted on the presence of zearalenone and its metabolites, particularly α-zearalenol, in animal products, in order to assess their transfer into food products of animal origin;
- in terms of monitoring of contamination: the plans should be supported by including wheat-based cereal products for human and animal consumption.

FUMONISINS

The fumonisins B1, B2, B3 and B4, produced by different species of *Fusarium*, form a structurally related group of mycotoxins. Contamination of corn by fumonisins, particularly in Southern European cultivation farming appears to vary from year to year depending on meteorological conditions.

Of the different fumonisins, the effects of fumonisin B1 are the best described: this causes adverse changes in sphingolipid metabolism, not all of the toxicological consequences of which are known. Knowledge about the toxicity of the other fumonisins is extremely limited and the differential toxicity between fumonisins is unknown.

Afssa recommends:

- in scientific terms: that studies be undertaken to better characterise the danger of the fumonisins, particularly their immunotoxic and carcinogenic effects;

- the terms of monitoring of contamination: the French population has low exposure to fumonisins because of its limited consumption of corn and the low levels of transfer of these toxins into animal products. Levels measured in cereal based products intended for young children in the monitoring and control plans show that controls should be tightened in these products

- in regulatory terms: the animal population has greater exposure as corn may form a large part of its diet. In terms of animal health, equine leucoencephalomalacia is the main disease seen. Corn products used in animal feeds particularly for horses therefore carry a particular risk. In general, the maximum contents recommended by the Commission appear to be too lax both in terms of protecting animal health and the levels seen in starting materials.

PATULIN

Patulin a natural contaminant of fruits, particularly apples. It is also found in silages intended for ruminant feeds. Dietary exposure to patulin is much lower than the provisional maximum acceptable daily dose in all population categories.

Patulin is regulated for many foods, particularly for fruit juice and purées intended for children. In light of the observed levels of exposure this appears to protect the consumer.

Afssa recommends:

- in scientific terms:
  - few toxicological studies are available and those which are are relatively old. Uncertainty remains about the fate of this mycotoxin which is difficult to monitor analytically in biological matrices. Toxicology studies conducted according to the internationally recognised guidance notes are required;

  - In 2004, a study, in the rat exposed to patulin reported disturbances of circulating steroid hormones which correlated with testicular and thyroid abnormalities. This information should be confirmed by additional studies in view of toxicologists' current concerns to recognise the endocrine interferring effects of any food contaminant;

- in terms of monitoring of contamination of animal foods: it is likely that farmed ruminants are exposed from consumption of silage or commercially rejected apples. The actual danger in animals is still poorly known in view of the lack of knowledge about the toxicity and fate of this toxin. It would be desirable to set up a monitoring plan for acid stored foods (fodder or seed silage, tied fodder bales) liable to favour the development of toxigenic fungi;

- in analytical terms: assay methods should be developed to monitor the fate of patulin in animal biological matrices.

OTHER MYCOTOXINS WHICH MAY BE FOUND IN HUMAN FOOD OR ANIMAL FEED

Claviceps purpurea
Claviceps purpurea toxins no longer appear to represent a major health risk to human beings under current dietary conditions. Although the transfer of alkaloids into animal products is poorly understood, the current European legislation appears to guarantee the health of farmed animals and that animal products are safe.

Afssa recommends:

- in terms of contamination: that the level of cereal contamination be monitored according to changes in farming techniques and varieties cultivated and in imported cereals (rye);

- in analytical terms: that analytical methods be available for the major *Claviceps* toxins.

CITRININ

It is unlikely that citrinin carries a risk to human beings. The risk of poisoning comes above all from consuming contaminated cereals used for animal foods and particularly in foods for pigs and poultry.

ALTERNARIA TOXINS

Whist continued awareness must be given to characterising natural contamination from and the toxic properties of *Alternaria* toxins there are currently no objective reasons to prioritise this risk in terms of the safety of foods intended for human beings or farmed animals.

CYCLOPIAZONIC ACID

It is unlikely that cyclopiazonic acid carries a major health risk to human beings. The risk of exposure comes most from eating contaminated cereals. Its presence as a co-contaminant with aflatoxin B1 in North America is not thought to have any adverse consequences as it is believed to reduce the danger of aflatoxins by contributing towards their metabolic inhibition.

TREMORGENIC TOXINS

It is essential to characterise natural contamination from tremorgenic toxins in order to assess their risk in human foods. The known high toxicity of verruculogen and penitrem in animals raises questions about the risk which they represent and therefore about their prevalence in foods intended for farmed animals.

OTHER MYCOTOXINS MOSTLY FOUND IN ANIMAL FOODS

SPORIDESMINS

The presence of sporidesmins is a real health problem in certain areas of animal farming particularly for sheep. The health risk to human beings is poorly understood and limited information is available about its transfer into animal products. It is therefore important to establish the fate of sporidesmins in animals and to set up research on transfer into milk.

STACHYBOTRYOTOXINS

Stachybotryotoxicoses are equine disorders, the prevalence of which is difficult to measure. Whilst these diseases are well known in human being following inhalation or contact exposure, they raise few concerns in terms of human dietary exposure.

ENDOPHYTE TOXINS

The risk of poisoning comes from ruminants, particularly cattle, eating contaminated green fodder. These toxins can be responsible for production losses in affected animals. It is unlikely that endophyte toxins carry a risk to human beings.

PHOMOPSINS

The risk of poisoning comes particularly from eating contaminated lupin seeds used in animal feeds. No cases have been reported in France although awareness must be maintained because of the increasing proportion of imported seeds. It is unlikely that phomopsins carry a risk to human beings. However, transfer studies into animal products should be conducted, because of the toxicological profile of these toxins.