Annex B TOX/2020/34

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)

Potential risks from aggregated dietary exposure to mycotoxins

Overview of mycotoxin families and their associated mycotoxins

As described in paragraph 88 of the main discussion paper, tables have been compiled to provide a detailed yet succinct overview of all mycotoxin families previously covered in the scope of TOX/2017/30[1], their associated mycotoxins, the species of fungus that produces them, as well as their recommended health-based guidance values as set by authoritative bodies such as the European Food Safety Authority (EFSA), Joint FAO/WHO Expert Committee on Food Additives (JECFA), Scientific Committee on Food (SCF), World Health Organisation (WHO), National Institute for Public Health and the Environment (RIVM), Federal Institute for Risk Assessment (BfR), Committee for Medicinal Products for Veterinary Use (CVMP), and French Food Safety Agency (AFSSA).

It is hoped that the gathered data could assist in the grouping of mycotoxins based on their toxic endpoints.

[1] TOX/2017/30 scoping paper available on the COT website.

Table 1 Provides an overview of the *Aflatoxins* family and its associated mycotoxins; aflatoxin B_1, aflatoxin B_2, aflatoxin G_1, aflatoxin G_2 and their respective limits in cereal based food commodities; in accordance to Regulation (EC) 1881/2006 (and its amendments). These mycotoxins are produced by *Aspergillus flavus*, *nomius* and *parasiticus*. They do not have an associated health-based guidance value(s) since the mycotoxins in this family are genotoxic and carcinogenic.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative report	Endpoint	Key Study
AFB_1	Cereals and processed cereal products	4	SCF (1996)	Hepatotoxicity – leading to liver carcinogenicity.	Various, refer to report link.
			JECFA (1998)	Hepatotoxicity – leading to liver carcinogenicity.	
AFB_2	Cereal-based processed food for infants and young children	0.1	JECFA (2002) AFM_1	Hepatotoxicity – leading to liver carcinogenicity, a NOEL was determined at 0.1 mg total intake over 21 months (male Fischer rat study).	Cullen *et al*., (1987)
AFG_1	Dietary foods for special medical purposes (intended specifically for infants)	4	JECFA (2007)	Hepatocarcinogenic.	Wogan *et al*., (1974)
	Corn and rice (unprocessed)	10	EFSA (2007) AFB_1	Hepatotoxicity – leading to liver carcinogenicity, a $BMDL_{10}$ of 0.17 µg/kg bw/day was utilised for Margin of Exposure calculations (male Fischer rat study).	
AFG_2			JECFA (2016)	Similar conclusions to 2007 evaluation. Hepatocarcinogenic.	

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: AFB_1 = Aflatoxin B_1; AFB_2 = Aflatoxin B_2; AFG_1 = Aflatoxin G_1; AFG_2 = Aflatoxin G_2; HBGV = Health-based guidance value; NOEL = No observed effect level, BMDL10 = Benchmark dose level, 10%.

Table 2 Provides an overview of Ochratoxin A and its respective limits in cereal based food commodities; in accordance to Regulation (EC) 1881/2006 (and its amendments). These mycotoxins are produced by the *Penicillium* spp. and *Aspergillus* spp. families. Its recommended health-based guidance values are also provided based on various authoritative reviews.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (ng/kg)	Endpoint	Key Study
OTA	Unprocessed cereals	5	SCF (1996)	TDI; 0.2-16 ng/kg bw/day, provisionally supports the lower range (*i.e.* 0.2-5).	Potential genotoxicity on the lower range, whilst the highest is nephrotoxicity.	Refer to report, range is based on other estimates of TDIs by other authoritative bodies.
			SCF (1998)	TDI; 1.2-14 ng/kg bw/day but preferably below 5 ng/kg bw/day.		
			JECFA (2001)	PTWI; 100 ng/kg bw.	Nephrotoxicity; LOEL 8 µg/kg bw/day representing an early marker of renal toxicity in female pigs.	Cumulative studies by Krogh & Elling groups (1977-1988), where effects on enzymes and kidney function were not examined in the 2-year study; however, from these studies the LOEL of 8 µg/kg for effects on the kidneys was established by JECFA in their 2001 evaluation.
	Products derived from unprocessed cereals intended for direct consumption	3	JECFA (2007)	The PTWI of 100 ng/kg bw was retained.	Nephrotoxicity; LOEL 8 µg/kg bw/day representing an early marker of renal toxicity in female pigs.	
	Cereal-based food for infants and young children	0.5	EFSA (2006)	Initially a TDI of 18 ng/kg bw, however, considering the long half-life of OTA in humans a TWI of 120 ng/kg bw was considered to be more appropriate.	Nephrotoxicity; LOEL 8 µg/kg bw/day representing an early marker of renal toxicity in female pigs (total uncertainty factor applied was 450).	
	Dietary foods for special medical purposes (intended specifically for infants)	0.5	EFSA (2010)	The PTWI of 120 ng/kg by was retained.	Nephrotoxicity; LOEL 8 µg/kg bw/day representing an early marker of renal toxicity in female pigs (total uncertainty factor applied was 450).	

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments. Abbreviations: OTA = Ochratoxin A; HBGV = Health-based guidance value; TDI = Tolerable daily intake; PTWI = Provisional tolerable daily intake; LOEL = Lowest observed effect level.

Table 3 Provides an overview of Patulin and its respective limits in fruit juices, apple products and cereal based food commodities; in accordance to Regulation (EC) 1881/2006 (and its amendments). Patulin is produced by *Aspergillus* spp. and *Penicillium* spp families including; *A. clavatus*, *P. expansum*, *P. patulum*, *P. aspergillus*, *P. byssochlamys*, and *P. expansum.* Its recommended health-based guidance values are also provided based on various authoritative reviews.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
PAT	Fruit juices, concentrate	50	JECFA (1990)	PTWI; 7 µg/kg bw	Combined reprotoxicity, long-term toxicity/carcinogenicity study. NOEL; 0.1 mg/kg bw/day in Wistar rats.	Becci *et al*., (1981)
	Spirit drinks	50	SCF (1994)			
	Solid apple products	25				
	Apple juice and solid apple products	10	JECFA (1995)	PMTDI; 0.4 µg/kg bw	Combined reproductive toxicity, long-term toxicity/carcinogenicity study in Wistar rats. NOEL; 0.1 mg/kg bw (administered 3 times weekly; equivalent to 43 µg/kg bw/day), with an application of UF of 100.	
	Baby foods other than processed cereal-based foods for infants and young children	10	SCF (2000)			

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: PAT = Patulin; HBGV = Health-based guidance value; PTWI = Provisional tolerable daily intake; PMTDI = Provisional maximum tolerable daily intake; NOEL = No observed effect level.

Table 4(a) Provides an overview of the Type A trichothecene family and its associated mycotoxins; T-2 and HT-2 toxins. These mycotoxins are produced by *Fusarium* spp. including; *F. sporotrichoides*, *F. poae*, *F. equiseti*, *F. acumninatum*, or *Cephalosporium, Verticimonosporum, Trichoderma, Trichothecium* and *Stachybotrys* which are other crop invasive species. These mycotoxins do not currently have a regulatory limit as set in Regulation (EC) 1881/2006 (and its amendments), however, the recommended health-based guidance values based on various authoritative reviews are listed below.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
T-2	Unprocessed cereals and cereal products	N/A	SCF (2001)	Combined t-TDI; 0.06 µg/kg bw	Sub-acute (3 weeks) (leukopenia/reduced antibody production) LOEL; 0.029mg/kg bw/day in pigs. Applied UF of 500.	Rafai *et al*., (1995)
			SCF (2002)			
HT-2			JECFA (2001)	PMTDI; 0.06 µg/kg bw		
			EFSA (2017)	ARfD; 0.3 µg T2 or HT2/kg bw	Acute (emesis); $BMDL_{10}$ of 2.97 µg/kg bw/day calculated for emetic effects in mink for both T2 and HT2 toxins. UF of 10 was applied.	Wu *et al*., (2016)

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: T-2 = T-2 toxin; HT-2 = HT-2 toxin; HBGV = Health-based guidance value; t-TDI = Temporary tolerable daily intake; PMTDI = Provisional maximum tolerable daily intake; ARfD = Acute reference dose; LOEL = Lowest observed effect level; $BMDL_{10}$ = Benchmark dose level, 10%; UF = Uncertainty factor.

Table 5(b) Provides an overview of the Type A trichothecene family and its associated mycotoxin; 4,15-diacetoxyscirpenol. This mycotoxin is produced by species from the *Fusarium* spp. family. It does not currently have a regulatory limit as set in Regulation (EC) 1881/2006 (and its amendments), however, its recommended health-based guidance values based on various authoritative reviews are listed below.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
4,15-DAS	No regulatory limit	N/A	JECFA (2017)	PMTDI; 60 ng/kg bw per day for 4,15-DAS, T-2 and HT-2 toxins, alone or in combination.	4,15-DAS and T-2/HT-2 toxins are structurally similar, and there is evidence that they cause similar effects at the biochemical and cellular levels, have similarities in toxic effects in vivo and have an additive dose effect when co-exposure occurs.	Refer to JECFA report.
			EFSA (2018)	ARfD; 3.2 µg/kg bw.	Emesis. NOAEL 32 µg/kg bw (equivalent to 1.2 mg/m² (i.v. administration of phase I clinical trials of Anguidine).	Murphy *et al*., (1978)
				TDI; 0.65 µg/kg bw.	NOAEL of 65 µg/kg bw for haematotoxicity and myelotoxicity based on Phase I clinical trials of Anguidine (cytostatic anticancer drug). Reported health effects at doses from 3-5 mg/m² from Phase II clinical trials (equivalent to 81-135 µg/kg bw.	
			COT (2018)	The COT agreed that it was appropriate to use the human studies with DAS (anguidine) administered i.v. as a cytostatic anticancer drug in the hazard characterisation. The COT agreed with the EFSA establishment of an ARfD for DAS.		

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: 4,15-DAS =4,15-diacetoxyscirpenol; HBGV = Health-based guidance value; PMTDI = Provisional maximum tolerable daily intake; ARfD = Acute reference dose; TDI = Temporary tolerable daily intake; NOAEL = No observed adverse effect level; i.v = intravenous.

Table 6(a) Provides an overview of the Type B trichothecene family and its associated mycotoxin; Deoxynivalenol (and its acetylated metabolites). This mycotoxin is produced by species from the *Fusarium* spp. family. Its recommended health-based guidance values are also provided based on various authoritative reviews.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
DON (15-Ac DON and 3-Ac DON naturally occurring metabolites)	Durum wheat, oats and corn (unprocessed)	1,750	SCF (1999)	t-TDI; 1 µg/kg bw	Chronic (growth retardation) NOAEL; 0.1 mg/kg bw day in mice and an uncertainty factor of 100.	Iverson *et al*., 1995
	Other cereals (unprocessed)	1,250	SCF (2002)	TDI: 1 µg/kg bw		
	Cereal flours used as raw material in food products	750	JECFA (2001)	PMTDI; 1 µg/kg bw for DON and acetylated forms.		
	Cereal products as consumed and other cereal-based products as retail stage (*e.g.* bread, pastries, biscuits, cereal snacks and breakfast cereals)	500	JECFA (2011)	ARfD; 8 µg/kg bw for DON and acetylated, however, limited data from human case reports indicate that dietary exposures of up to 50 µg/kg bw/day are not likely to induce emesis.	Acute (emesis); $BMDL_{10}$ of 0.21 mg/kg bw/day calculated for emetic effects in pigs for both DON and its acetylated derivatives.	Young *et al*., (1983); Pollman *et al*., (1985)
	Cereal-based processed food for infants and young children	200	EFSA (2017)	TDI; 1 µg/kg bw	Chronic (growth retardation) NOAEL; 0.1 mg/kg bw day in mice and an uncertainty factor of 100.	Iverson *et al*., (1995) with the support of Bondy *et al*., (2016)
				ARfD; 8 µg/kg bw for DON and acetylated forms.	Epidemiological data from mycotoxicoses NOAEL of 26 µg DON/kg bw per eating occasion for vomiting (default uncertainty factor of 3.16 for toxicokinetic differences in the human population was needed).	Luo *et al*., (1987)

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: DON = Deoxynivalenol; 15-AcDON = 15-acetyldeoxynivalenol; 3-AcDON = 3-acetyldeoxynivalenol; HBGV = Health-based guidance value; -t-TDI = Temporary tolerable daily intake; TDI= Tolerable daily intake; PMTDI = Provisional maximum tolerable daily intake; ARfD = Acute reference dose; NOAEL = No observed adverse effect level; $BMDL_{10}$ = Benchmark dose level, 10%.

Table 7(b) Provides an overview of the Type B trichothecene family and its associated mycotoxin; Nivalenol and Fusarenon-X. Nivalenol is produced by *Fusarium* spp species including; *F. crookwellense*, *F. poae*, *F. culmorum* and *F. graminearum*, whilst Fusarenon-X in addition can also be produced by *F. nivale and F. equiseti*. Neither have regulatory limits as set in Regulation (EC) 1881/2006 (and its amendments), however, its recommended health-based guidance values based on various authoritative reviews are listed below.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
NIV	No regulatory limit	N/A	SCF (2000)	t-TDI; 0.7 µg/kg bw	Chronic (growth retardation) LOAEL; 0.7 mg/kg bw/day in mouse studies 1 and 2 years.	Ohtsubo *et al*., (1989); Ryu *et al*., (1988)
			RIVM (2002)			
			VKM (2013)			
			EFSA (2013)	TDI; 1.2 µg/kg bw	Immunological differences (decrease in WBC) $BMDL_{05}$; 0.35 mg NIV/kg bw/day for haematological disturbances in WBC in rats. Application of 300 as an uncertainty factor.	Takahashi *et al*., (2008)
FUS-X	No regulatory limit	N/A	RIVM (2002)	Unable to establish a temporary TDI due to data insufficiencies.	Acutely toxic (oral); LD_{50} 4.4 mg kg/bw in rats and 4.5 mg/kg bw in mice. Fus-x ribotoxic, actively targets organs that contain actively proliferating cells (*e.g.* thymus, spleen, small intestine, testes and bone marrow).	Ueno *et al*., (1983); Ueno *et al*., (1984)
			COT (2019)	Comparison with the HBGV for DON (ARfD; 8 µg/kg bw) was considered appropriate since the oral emetic potency of Fus-X relative to DON is 1.04. Comparative toxicity data suggests that it is more toxic than other type B trichothecenes (DON and acetylated forms and NIV) when administered orally, however, had lower emetic potency than Type A.	Acute (emesis); $BMDL_{10}$ of 0.21 mg/kg bw/day calculated for emetic effects in pigs for both DON and its acetylated derivatives.	Young *et al*., (1983); Pollman *et al*., (1985)
					Epidemiological data from mycotoxicoses NOAEL of 26 µg DON/kg bw per eating occasion for vomiting (default uncertainty factor of 3.16 for toxicokinetic differences in the human population was needed).	Luo *et al*., (1987)

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments. Abbreviations: NIV = Nivalenol; FUS-X = Fusarenon=X; HBGV = Health-based guidance value; -t-TDI = Temporary tolerable daily intake; TDI= Tolerable daily intake; LOAEL = Lowest observed adverse effect level; WBC = White blood cells; $BMDL_{05}$ = Benchmark dose level, 5%; LD_{50} = Lethal dose, 50%; $BMDL_{10}$ = Benchmark dose, 10%.

Table 8 Provides an overview of Zearalenone, its respective limits in cereal based food commodities; in accordance to Regulation (EC) 1881/2006 (and its amendments). Zearalenone is produced my species of the Fusarium spp. family including; *F. graminearum, F. culmorum, F. equiseti* and *F. verticillioides*. Its recommended health-based guidance values are also provided based on various authoritative reviews.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
ZEN	Unprocessed cereals other than maize	100	JECFA (1998)	ADI; 0-0.5 µg/kg bw (Note: this is for the metabolite α-zearalenone).	Level causing no hormonal effect in monkeys (ovariectomised female cynomolgus monkeys); 0.5 mg/kg bw/day.	Singh *et al.*, (1984); CIC, (1985)
	Unprocessed maize	350				
	Cereal flours other than corn flours	75	JECFA (2000)	PMTDI; 0.5 µg/kg bw	No hormonal effects in pigs (15 days study in pigs), most sensitive species. NOEL 40 µg/kg bw/day.	Edwards *et al.*, (1987)
	Corn flours	200				
	Products derived from unprocessed cereals intended for direct consumption	50	SCF (2000)	t-TDI; 0.2 µg/kg bw	No hormonal effects in pigs (15 days study in pigs), most sensitive species. NOEL 40 µg/kg bw/day, safety factor of 200.	Bauer *et al.*, (1987)
	Corn intended for direct consumption, corn-based snacks and breakfast cereals	100	EFSA (2011)	Group TDI; 0.25 µg/kg bw/day	EDC (pituitary adenomas) in male B6C3F1 mice. $BMDL_{10}$ of 6.39 mg/kg bw/day. NOEL 10.4 µg/kg bw/day.	NTP (1982); Dölll *et al.*, (2003)
	Cereal-based foods (including corn-based foods) for infants and young children	20	EFSA (2016)			

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: ZEN = Zearalenone; HBGV = Health-based guidance value; ADI = Acceptable daily intake; PMTDI = Provisional maximum daily intake; t-TDI = Temporary tolerable daily intake; TDI = Tolerable daily intake; NOEL = No observed effect level; EDC = Endocrine; $BMDL_{10}$ = Benchmark dose level, 10%; CIC = Coulston International Corp; NTP = National Toxicology Program.

Table 9 Provides an overview of the *Fumonisins* family and its associated mycotoxins; fumonisin B_1, fumonisin B_2, and their respective limits in cereal based food commodities; in accordance to Regulation (EC) 1881/2006 (and its amendments). These mycotoxins are produced by Fusarium spp species including; *F. verticillioides*, *F. proliferatum*, *F. fujikuroi*, *F. anthophilum*, *F. dlamini*, *F. napiforme* and *F. thapsinum*. Its recommended health-based guidance values are also provided based on various authoritative reviews.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key study
FB_1	Unprocessed corn	4,000	JECFA (2001)	PMTDI; 2 µg/kg bw for FB_1, FB_2 and FB_3, alone or in combination.	Nephrotoxicity (for FB1); NOEL for renal toxicity in Fischer 344N rats as 0.2 mg/kg bw/day with a safety factor of 100.	Howard *et al*., (2001) for chronic rat study; Hard *et al*., (2001) for re-evaluation of renal tumours.
	Corn grits, meal and flour	1,000	JECFA (2012)		Hepatotoxicity; $BMDL_{10}$ of 0.165 mg/kg bw/day calculated for megalocytic hepatocytes in mice (uncertainty factor 100).	Bondy et al., (2012)
FB_2	Corn-based breakfast cereals and snacks	800	JECFA (2017)			
	Corn-based food for infants and young children	200	EFSA (2018)	TDI: 1 µg/kg bw; group TDI with all subtypes (FB_{1-4}) based on assessment for structural similarity.	Hepatoxocixity; $BMDL_{10}$ of 0.1 mg/kg bw/day calculated for megalocytic hepatocytes in mice (uncertainty factor 100).	

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: FB_1 = Fumonisin B_1; FB_2 = Fumonisin B_2; HBGV = Health-based guidance value; PMTDI = Provisional maximum tolerable intake; TDI = Tolerable daily intake, NOEL = No observed effect level; $BMDL_{10}$ = Benchmark dose level, 10%;

Table 10 Provides an overview of Citrinin and its respective limits in food supplements based on rice fermented with red yeast (*Monascus purpureus*); in accordance to Regulation (EC) 1881/2006 (and its amendments). This mycotoxin is produced by species of *Aspergillus* spp., *Penicillium* spp. and *Monascus* spp. It does not have a recommended health-based guidance value, however a level of no concern based on nephrotoxicity was established based on the European Food Standards Authority (EFSA) review.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
CIT	Food supplements based on rice fermented with red yeast (*Monascus purpureus*)	2,000	EFSA (2012)	No HBGV was set, although, a level of no concern for nephrotoxicity of 0.2 µg/kg bw/day was established.	Nephrotoxicity; NOAEL 20 µg/kg bw/day in rats (sub-chronic; 90-day), UF of 100.	Lee *et al*., (2010)

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: CIT = Citrinin; HBGV = Health-based guidance value; NOAEL = No observed adverse effect level; UF = Uncertainty factor.

Table 11 Provides an overview of the Ergot alkaloid family and its 12 associated mycotoxins and their respective limits in cereal based food commodities; in accordance to Regulation (EC) 1881/2006 (and its amendments). These mycotoxins are produced by species from the *Claviceps* spp. family including; *C. Purpurea*, *C. fusiformis*. Its recommended health-based guidance values are also provided based on various authoritative reviews.

Mycotoxin	Commodities	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
Ergots considered as a sum of all twelve mycotoxins): Ergocristine, Ergotamine, Ergocryptine (α and β forms), Ergometrine, Ergosine, Ergocornine and their respective -inine forms. Note: -inine forms are described to be biologically inactive on the neuroreceptor sites, however, interconversion can take place in alkaline or acidic conditions.	Milling products of barley, wheat, spelt, oats grains (with ash content <900 mg/100 g)	100 until July 2022 where it lowers to 50†	WHO (1990)	None set. It was concluded that human exposure to low levels of ergolines appears to be widespread. Outbreak data in Ethiopia and India indicate that *C. purpurea* alkaloids (*i.e.* ergotamine group) produced more severe effects. Highlighted that only low levels of ergolines remain in prepared foods as cleaning and milling processes remove the sclerotia; additionally, heat processing denatures/destroys most alkaloids of the ergotamine group.		N/A
			CVMP (1999)	In human medicine usual oral doses are 500 µg; 3 times a daily or up to (1.8 mg daily ~0.03 mg/kg bw).	N/A	N/A
	Milling products of barley, wheat, spelt, oats grains (with ash content >900 mg/100 g)	150†	BfR (2004)	Report in German: Advises for pregnant and breastfeeding women to avoid consumption of rye bread which contains ~2,000-3,000 µg/kg. Other adult age groups not expected to observe adverse/fatal effects till 5-10 g fresh intake of ergot.		N/A
	Barley, wheat, spelt and oats placed on the market for the final consumer	150†	AFSSA (2009)	Report in French: Doesn't seem to include any hard limits. Just sets out as it is in the regulation.		N/A
	Rye milling products and rye placed on the market for the final consumer	500 until July 2022 where it lowers to 250†	EFSA (2012)	Group ARfD; 1 µg/kg bw for the sum of ergot alkaloids.	Tail muscular atrophy (13-week rat feeding study of ergotamine). $BMDL_{10}$ 0.33 mg/kg bw/day, uncertainty factor of 3.	Spieijers *et al.*, (1993)
	Cereal-based food for infants and young children	20		TDI; 0.6 µg/kg bw for the sum of ergot alkaloids.	Tail muscular atrophy (13-week rat feeding study of ergotamine). $BMDL_{10}$ 0.33 mg/kg bw/day, uncertainty factor of 600.	

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments. †According to developing policies (links to FSA website).
Abbreviations: HBGV = Health-based guidance value; ARfD = Acute reference dose; TDI = Tolerable daily intake; $BMDL_{10}$ = Benchmark dose limit; 10%.

Table 12 Provides an overview of Cyclopiazonic acid. It does not currently have a regulatory limit as set in Regulation (EC) 1881/2006 (and its amendments), nor does it have a recommended health-based guidance value. Cyclopiazonic acid is produced by species from the *Aspergillus* spp. and *Penicillium* spp. families. The Committee of Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) have reviewed the compound in 2019 and concluded that it does not pose a health concern for infants aged 0 to 12 months and children aged 1 to 5 years.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV	Endpoint	Key Study
CPA	No regulatory limit	N/A	COT (2019)	No risk assessments or evaluations of CPA by European or other international authoritative bodies. COT MOEs ranged from 4,500-100,000.	NOAEL of 0.1 mg/kg bw/day (sub-acute; 90 days) study in dogs (unknown provenance).	Nuehring *et al*., (1985)

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: CPA = cyclopiazonic acid; HBGV = Health-based guidance values; MOE = Margin of Exposure; NOAEL = No observed adverse effect level.

Table 13 Provides an overview of Moniliformin. It does not currently have a regulatory limit as set in Regulation (EC) 1881/2006 (and its amendments), nor does it have a recommended health-based guidance value. This mycotoxin can be produced by species from the *Fusarium* spp. and *Penicillium melanoconidium*. It has been reviewed by the European Food Safety Authoritative reports (EFSA) and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT).

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV	Endpoint	Key Study
MON	No regulatory limit	N/A	EFSA (2018)	Unable to establish a HBGV due to the limitations in the available data.	Acute (cardiotoxicity): NOAEL 6 mg/kg bw sub-acute study in rats.	Johnsson *et al*., (2013)
					Chronic (haematoxicity): 28-day study in barrow pigs. $BMDL_{05}$ 0.20 mg/kg bw from the dose-response data on the decrease in haematocrit and haemoglobin = POD for MOE.	Jonsson *et al*., (2015)
			COT (2018)	The COT agreed with the MOE approach taken by EFSA for assessing the human health risk of MON.		
			COT (2019)			

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: MON = Moniliformin; HBGV = Health-based guidance value; NOAEL = No observed adverse effect level; $BMDL_{05}$ = Benchmark dose level, 5%; POD = Point of Departure; MOE = Margin of Exposure.

Table 14 Provides an overview of Neosolaniol (metabolite of T-2 toxin; Type A trichothecene). It does not currently have a regulatory limit as set in Regulation (EC) 1881/2006 (and its amendments), and its recommended health-based guidance values based on various reviews of authoritative bodies.

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	HBGV (µg/kg)	Endpoint	Key Study
NEO	No regulatory limit	N/A	SCF (2002)	PMTDI for T2- and HT-2 (only); 0.06 µg/kg bw	Subacute (3 weeks) (leukopenia/reduced antibody production) LOEL; 0.029mg/kg bw/day in pigs. Applied UF of 500.	Rafai *et al*., 1995
			JECFA (2001)	PMTDI for T2- and HT-2 (only); 60 ng/kg bw/day, alone or in combination.	LOEL of 0.029 mg/kg bw per day for changes in white and red blood cell counts identified in the 3-week dietary study in pigs.	
			EFSA (2011)	Group TDI; 1µg/kg bw (T2; x1, HT-2; x1, NEO; x0.3)	Immunological differences (reduction in antibody response to a specific antigen in pigs). LOAEL; 29 µg/kg bw/day NOAEL = $BMDL_{05}$ 10 µg/kg bw/day derived for T2 (uncertainty factor of 100).	
			EFSA (2017)	Group ARfD; 0.3 µg/kg bw	Acute (emetic effects in mink): $BMDL_{10}$-$BMDU_{10}$ of 2.97-49.8 µg/kg bw T2 or HT-2.	Wu *et al*., (2016)
				Group TDI; 0.02 µg/kg bw (T2; x1, HT-2; x1, NEO; x0.3)	$BMDL_{10}$; 3.33 T2 µg/kg bw/day for reduction in the number of peripheral leucocytes in sub-chronic study in rats, uncertainty factor 200.	Rafai *et al*., (1995) (total leucocyte count); Rahman *et al*., (2014) (total leucocyte, thrombocyte, haem counts and body weight effects).
			COT (2018)	Exposure assessment; exceed EFSA TDI from 145 – 315% for infants and young children, however, unlikely that they are regularly exposed to these levels. Therefore, unlikely that dietary exposure levels of T2, HT-2 and NEO would be of any toxicological concern.		

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: NEO = Neosolaniol; HBGV = Health-based guidance value; PMTDI = Provisional maximum tolerable daily intake; TDI = Tolerable daily intake; ARfD = Acute reference dose; LOEL = Lowest observed effect level; LOAEL = lowest observed adverse effect level; NOAEL = No observed adverse effect level; $BMDL_{05}$ = Benchmark dose level, 5%; $BMDL_{10}$ = Benchmark dose level, 10%; $BMDU_{10}$ = Benchmark dose upper, 10%,

Table 15 Provides an overview of Sterigmatocystin (STC). It does not currently have a regulatory limit as set in Regulation (EC) 1881/2006 (and its amendments), nor does it have a recommended health-based guidance value. It is produced by species from the *Aspergillus* spp. family including; *A. flavus*, *A. parasiticus*, *A. versicolor* and *A. Nidulans*. *A. versicolor* is the most common producer. STC also shares the same biosynthetic pathway with aflatoxins (STC is a pre-cursor; in aflatoxin samples it is possible to have traces of STC). It has been reviewed by the European Food Safety Authoritative reports (EFSA), The Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT).

Mycotoxin	Commodity	Limit (µg/kg)*	Authoritative reports	Endpoint	Key Study
STC	No regulatory limit		EFSA (2013)	$BMDL_{10}$; 0.16 m/kg bw/day based on the incidence of haemangiosarcomas in rats (based on limited tumorgenicity data).	Maekawa *et al*., (1979)
			JECFA (2017)		
			COT (2019)	Mean and 97.5th percentile MOEs for UK infants and young children, based on the $BMDL_{10}$ of 0.16 mg/g bw per day, are all > 10,000. Therefore, the exposures are unlikely to be of toxicological concern.	

*Limit in accordance with Regulation No. (EC) 1881/2006 (µg/kg) and its amendments.
Abbreviations: STC = Sterigmatocystin; HBGV = Health-based guidance value; $BMDL_{10}$ = Benchmark dose level; MOE = Margin of Exposure.

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