Joint International Symposium
Global Past, Present and Future Challenges in Risk Assessment –
Strengthening Consumer Health Protection

Risk Assessment of Aflatoxins

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Chun, Hyang Sook

Chung-Ang University,

Dept. of Food Science & Technology, Food Toxicology Lab.

MINISTRY OF FOOD AND DRUG SAFETY
National Institute
of Food and Drug Safety Evaluation

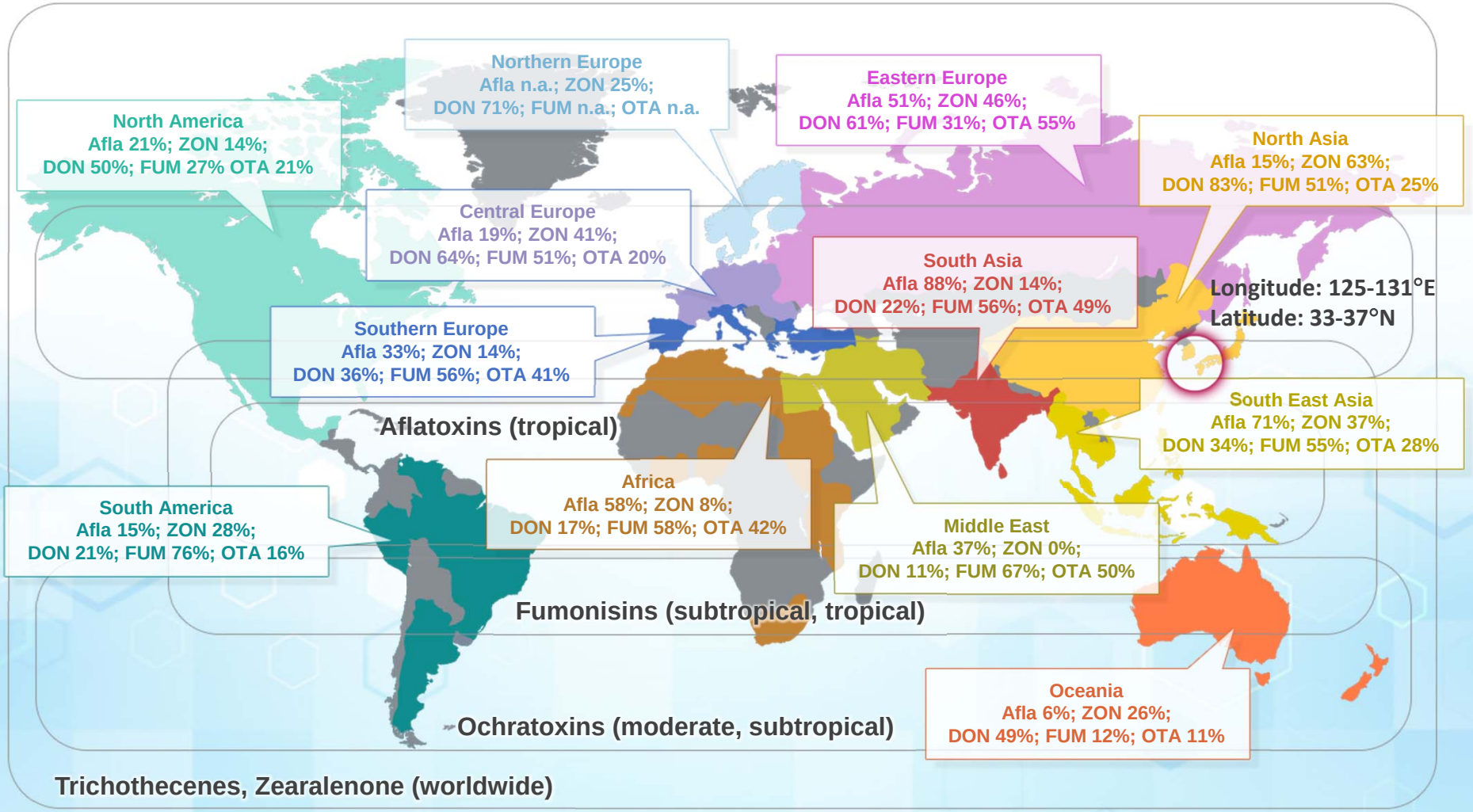
Outline of Presentation

Contents

Aflatoxins in food: an unavoidable problem

Aflatoxins

Geography and Mycotoxins: South Korea



Aflatoxins?

- Difuranocoumarin derivatives produced by the fungi *Aspergillus flavus* and *Aspergillus parasiticus*
  - Aflatoxins are secondary fungal metabolites.
  - Aflatoxin types include B1, B2, G1, G2.
  - B1 is most prevalent and toxic aflatoxin.

- Aflatoxin has received considerable attention due to their significance in agricultural loss and human health.

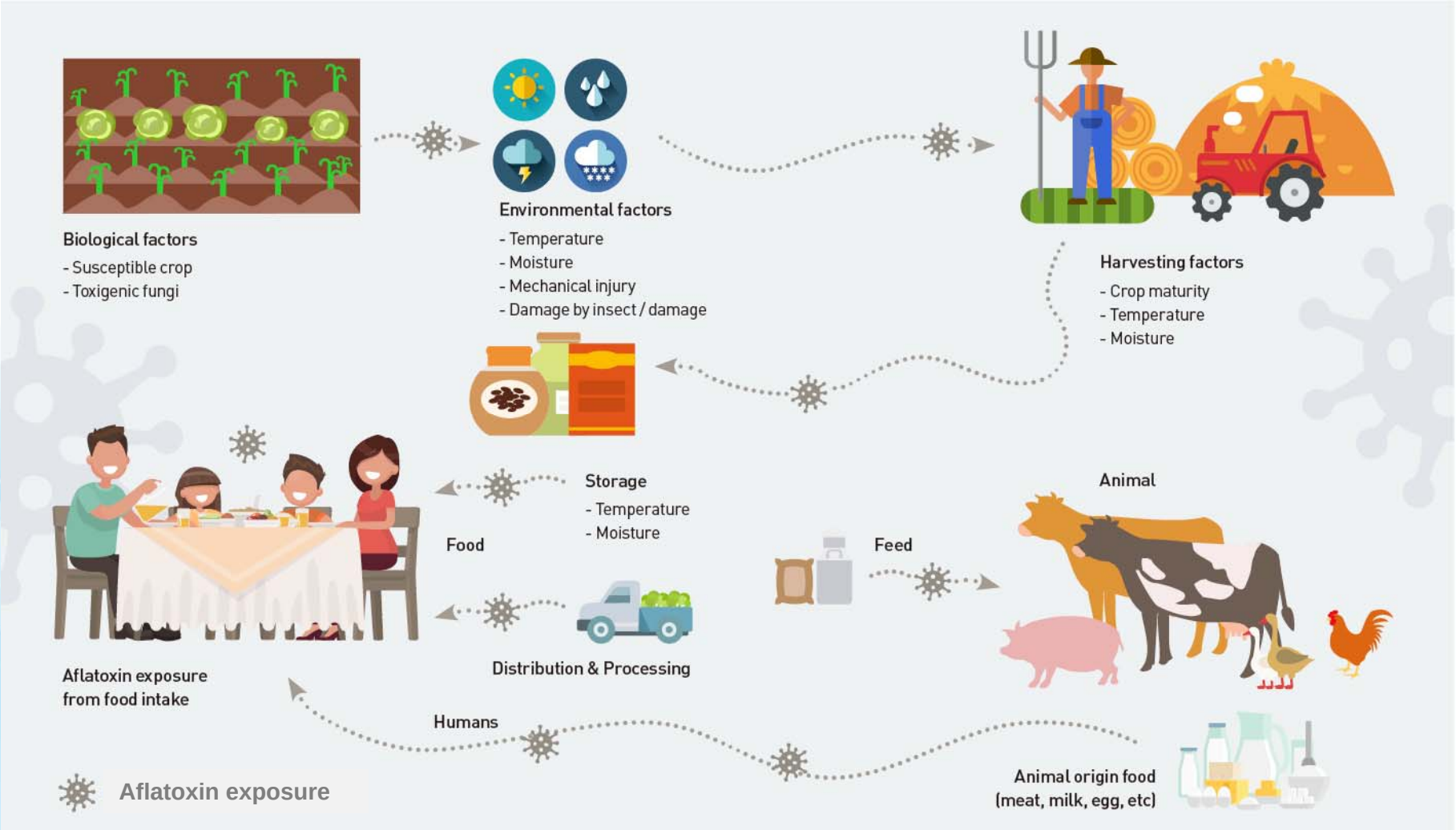
- Aflatoxin is epidemiologically implicated as carcinogen in humans and an environmental contaminant which is widespread in nature, therefore chronic toxicity is of greater concern than acute toxicity.

- Major source of exposure: cereals, peanuts/nuts, spices etc.

- How to control aflatoxins?

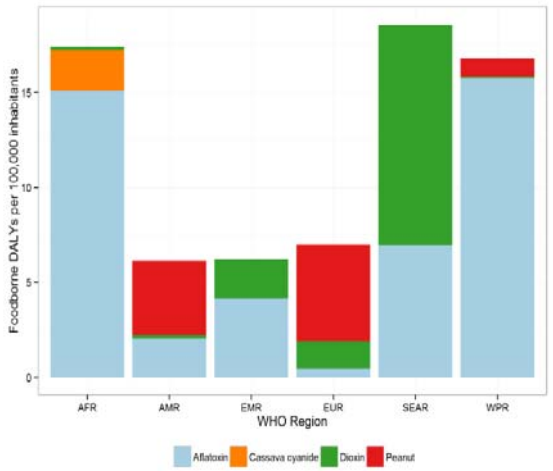
Aflatoxins?

Aflatoxin exposure throughout the food chain



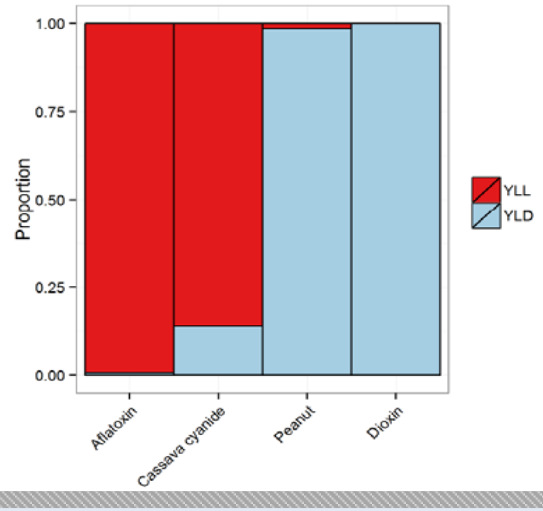
How important is aflatoxins?

Relative contribution to the DALY incidence



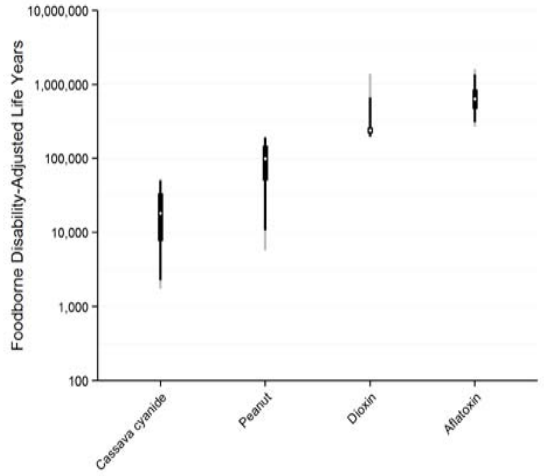
- Deaths and disability adjusted life years (DALYs)
- African Region (AFR)
- Southeast Asia Region (SEAR)
- Western Pacific Region (WPR)
- Eastern Mediterranean Region (EMR)
- Europe (EUR)
- Americas Region (AMR)

Relative contributions from YLLs and YLDs



- Years lived with disability (YLD),
- Years of life lost (YLL)

DALY of four chemicals From contaminated food



- DALY for each of four chemicals from contaminated food ranked from lowest to highest with 95% UI (The dot in the middle of each box represents the median, the box the 50% UI, the dark bar the 95% UI, and the light bar the 95% UI).

WHO report on global burden of foodborne diseases, aflatoxin is one of the main issues.

Gibb et. al. (2016).

Regulatory limits for aflatoxins-1

- Permitted maximum levels of aflatoxins vary greatly, depending on whether the country imports or exports the affected commodities.
- Very strict regulation can be costly.

Target food	Classification	Comparison target country or organization (μg/kg)				
		Korea	Codex	EU	USA	Japan
Cereals, legumes, peanuts, nuts and their simple processed products (grinding, cutting, etc.)	B1+B2+G1+G2	15.0	15(Groundnuts, almonds, hazelnuts, Brazil nuts and pistachio)	4.0 (All cereals and all products derived from cereals) 10.0 (Maize and rice) 15.0 (Groundnuts),) 15.0 (Almonds, pistachios and apricot kernels) 15.0 (Hazelnuts and Brazil nuts) 10.0 (Other tree nuts)	20 (All food)[c)] 15 (Brazil nuts, groundnuts and processed products,, pistachio)c)	10 (All food)[c)]
	B1	10.0	-	2.0 (All cereals and all products derived from cereals) 5.0 (Maize and rice) 8.0 (Groundnuts)a), 12.0 (Almonds, pistachios and apricot kernels) 8.0 (Hazelnuts and Brazil nuts) 5.0 (Other tree nuts)		
Cereal products and legume products	B1+B2+G1+G2	15.0	-	4 (All cereals and all products derived from cereals, including processed cereal products)		
	B1	10.0	-	2 (All cereals and all products derived from cereals, including processed cereal products)		
Groundnuts (peanuts) and other oilseeds and processed products	B1+B2+G1+G2	15.0	-	4 (Groundnuts and processed products)b)		
	B1	10.0	-	2 (Groundnuts and processed products) b)		

Regulatory limits for aflatoxins-2

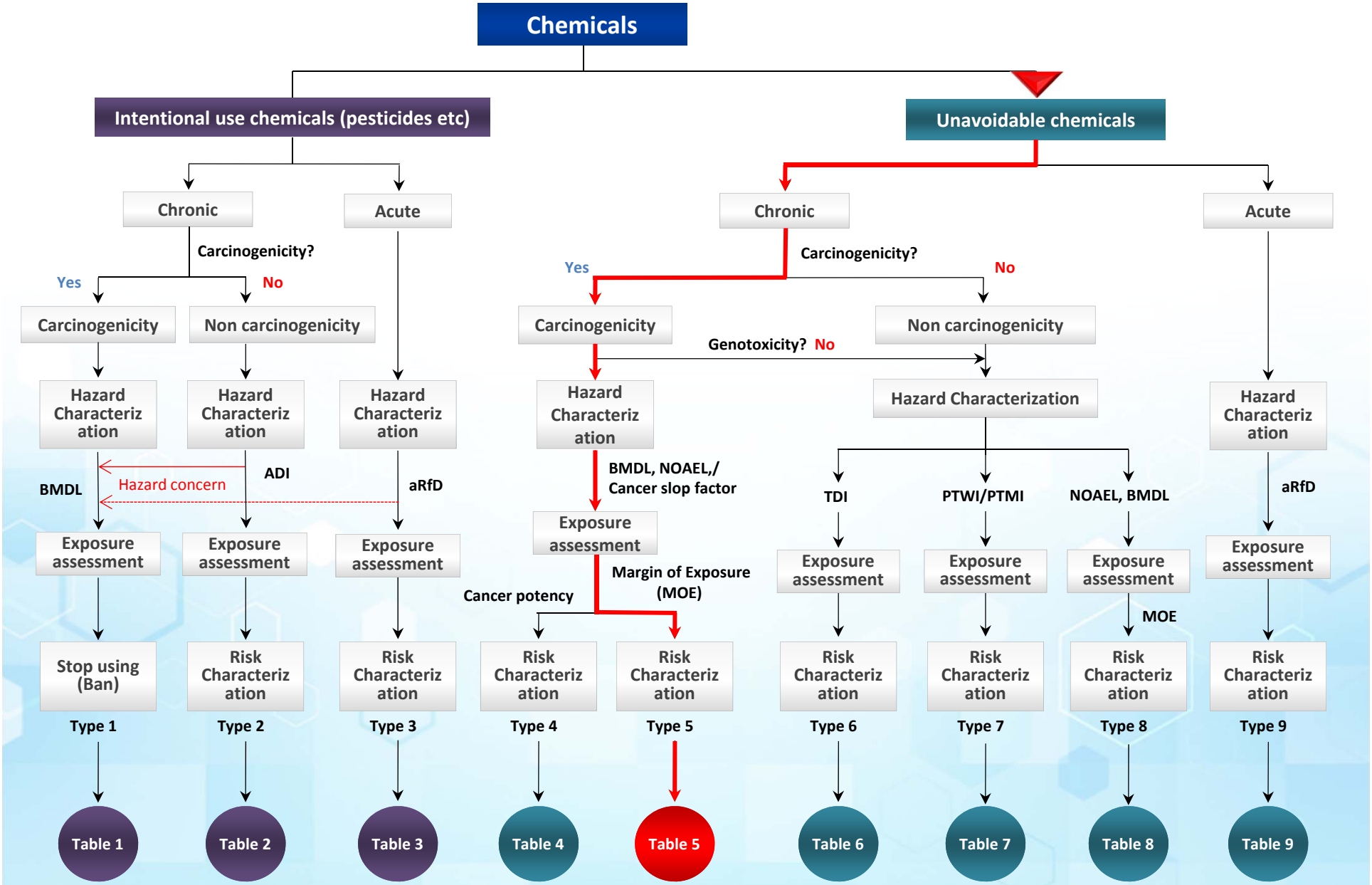
Target food	Classification	Comparison target country or organization (μg/kg)				
		Korea	Codex	EU	USA	Japan
Soy sauces/pastes, red pepper powder and curry powder	B1+B2+G1+G2	15	-	-	20 (All food)[c] 15 (Brazil nuts, groundnuts and processed products,, pistachio)[c]	10 (All food)[c]
	B1	10	-	-		
Nutmeg, turmeric, dried pepper, dried paprika and natural species	B1+B2+G1+G2	15	-	10.0 (Capsicum spp., Piper spp, nutmeg, ginger, turmeric)		
containing these	B1	10	-	5.0 (Capsicum spp., Piper spp, nutmeg, ginger, turmeric)		
Wheat flour	B1+B2+G1+G2	15		-		
	B1	10		-		
Dried fruits	B1+B2+G1+G2	15	-	10		
				4.0 (Products intended for direct human consumption)		
	B1	10	-	5		
				2.0 (Products intended for direct human consumption)		
Infant foods, follow-up foods, cereal foods for infants and young children, other foods for infants and young children	B1	0.1	-	0.10 (Including Dietary foods for special medical purposes intended specifically for infants)		

[a] Exception of Ground nuts(peanuts) and other oilseeds for crushing for refined vegetable oil production
[b] Exception of Crude vegetable oils destined for refining and refined vegetable oils
[c] Sum of B_1, B_2, G_1 and G_2

Risk Assessment

Establishing Standards	appropriate protection level (food contaminants et al.)
Priority setting	Implementing policies and providing management plans.
Reducing risk	perception differences through risk communication

Flowchart of Risk Assessment in NiFDS



Hazard Identification

One of most potent mutagenic and carcinogenic substances known

Liver cancer in most species

Some evidence humans are at lower risk than other species

B1 (AFB1) most common, most studied, most toxic

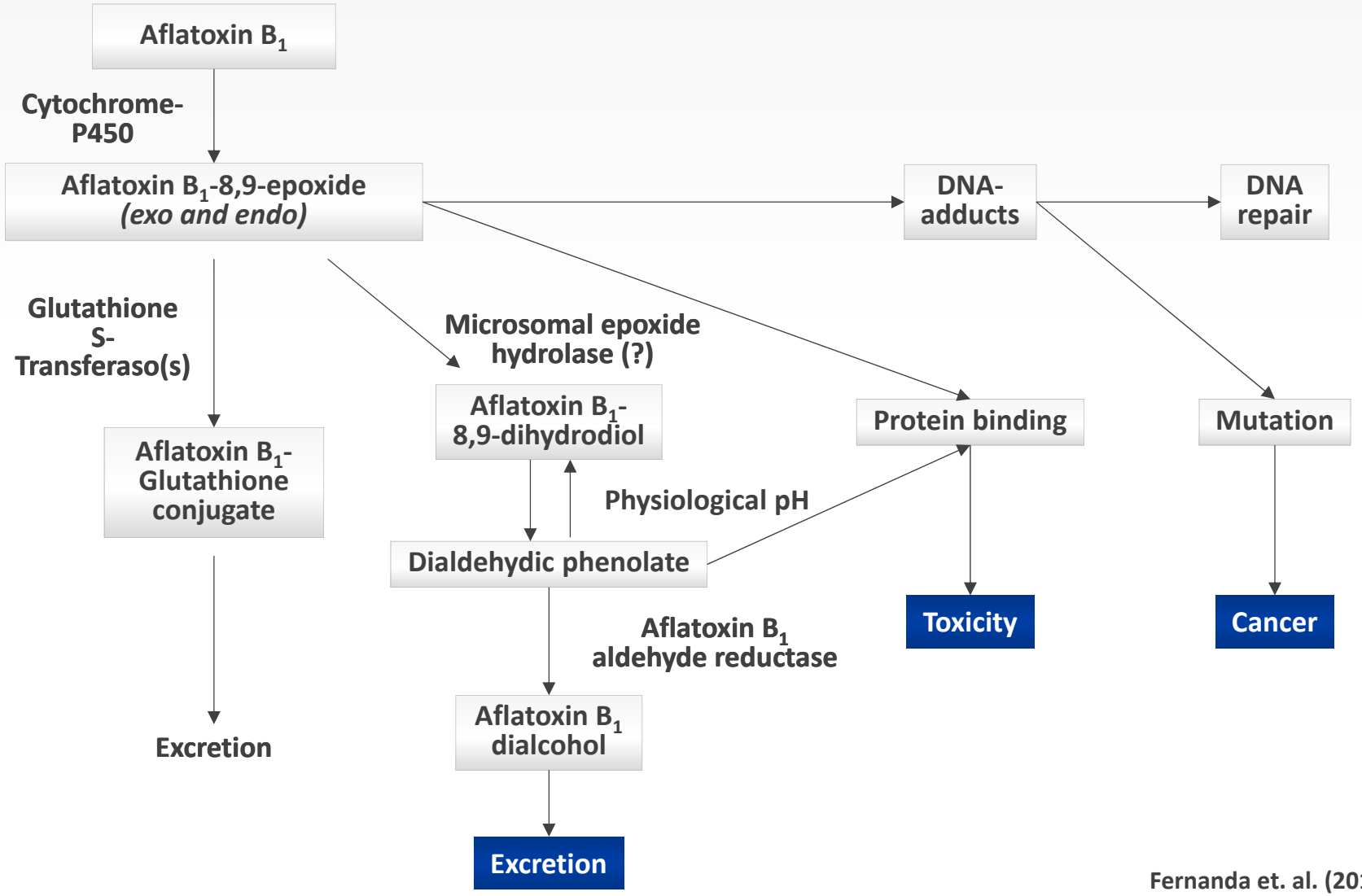
Toxicity varies by species

- LD50 0.5 mg/kg for duckling
- LD50 60 mg/kg for mouse
- Binds to nucleic acids in some species
- Difficult to assess for humans

Death usually from liver damage

Hazard Identification

Major metabolic processes of aflatoxin B_1



Fernanda et. al. (2016).

Hazard Identification

Epidemiological studies for aflatoxin B1 and liver cancer

Country	Region	AFB1 intake (ng/kg b.w./day)	Liver cancer rate/year[a]	Liver cancer rate/60 years[a]
Kenya[b]	Highland	4.2	14	840
	Midland	6.8	43	2,580
	Lowland	12.4	58	3,480
Swaziland[c]	High veldt	14.3	35	2,100
	Middle veldt	40.0	85	5,100
	Lebombo	32.9	89	5,340
	Low veldt	127.1	184	11,040
Transkei[d]	Four districts	16.5	91	5,460
Mozambiqu[e]	Manhica-Mangud	20.3	121	7,260
	Massinga	38.6	93	5,580
	Inhambane	77.7	218	13,080
	Inharrime	86.9	178	10,680
	Morrumbene	87.7	291	17,460
	Homoine-Maxixe	131.4	479	28,740
	Zavala	183.7	288	17,280
China[e]	Guangxi B	11.7	1,754	105,240
	Guangxi B	90.0	1,822	109,320
	Guangxi C	704.5	2,855	171,300
	Guangxi D	2,027.4	6,135	368,100

[a] Age-adjusted annual incidence of liver cancer for men per one million individuals. The age distributions of the population groups studied did not deviate significantly from each other. In the study from China, the incidence of HBsAg + carriers was 23% of all members of the cohort and in the study from Swaziland and (presumably) Kenya it was 21–.28%, whereas no information was found for Mozambique. The calculation of the lifetime liver cancer rate (last column) assumed a lifespan of 60 years.
[b] Peers et al. (1976) as corrected by Carlborg (1979).
[c] Peers and Linsell (1977).
[d] Van Rensburg et al. (1985).
[e] Yeh et al. (1989).

EFSA Journal (2007).

Hazard Characterization

BMD10 and BMDL10 on the development of liver cancer in rats by exposure to AF B1*

Model	Log (likelihood)	AIC	Accept	BMD10 (μg/kg b.w./day)	BMDL10 (μg/kg b.w./day)
BMDS					
Gamma		75.52	Yes	0.47	0.23
Logistic		73.54	Yes	0.45	0.34
Log-logistic		75.52	Yes	0.48	0.26
Log-probit		75.50	Yes	0.48	0.28
Multistage		75.61	Yes	0.44	0.17
Multistage-Cancer		73.64	Yes	0.42	0.17
Probit		73.52	Yes	0.41	0.31
Weibull		75.56	Yes	0.46	0.21
Quantal-Linear		78.24	No	0.14	0.10
PROAST					
Gamma	-34.76		Yes	0.47	0.23
Logistic	-34.77		Yes	0.45	0.34
Log-logistic	-34.76		Yes	0.48	0.26
Log-probit	-34.75		Yes	0.48	0.28
Two-stage	-34.82		Yes	0.42	0.34
Weibull	-34.78		Yes	0.46	0.21
LVM: E2	-34.76		Yes	0.41	0.31
LVM: H2	-37.04		No	0.20	-

* Wogan et al., 1974

Hazard Characterization

Toxicity information for major mycotoxins

Mycotoxin	Units	TDI	TDI***	IARC
Aflatoxin B1	NOT ESTABLISHED		**$BMDL_{10}$ = 170 ng/kg bw/day**	**GROUP 1**
Aflatoxin M1				GROUP 2B
Ochratoxin A	PTWI*	1.0	0.11 µg/kg bw./week	GROUP 2B
Fumonisin	TDI**	2.0	1.65 µg/kg bw/day	GROUP 2B
Patulin		0.4	0.4 µg/kg bw/day	GROUP 3
Deoxynivalenol		1.0	1 µg/kg bw/day	GROUP 3
Zearalenone		0.5	0.4 µg/kg b.w./day	GROUP 3

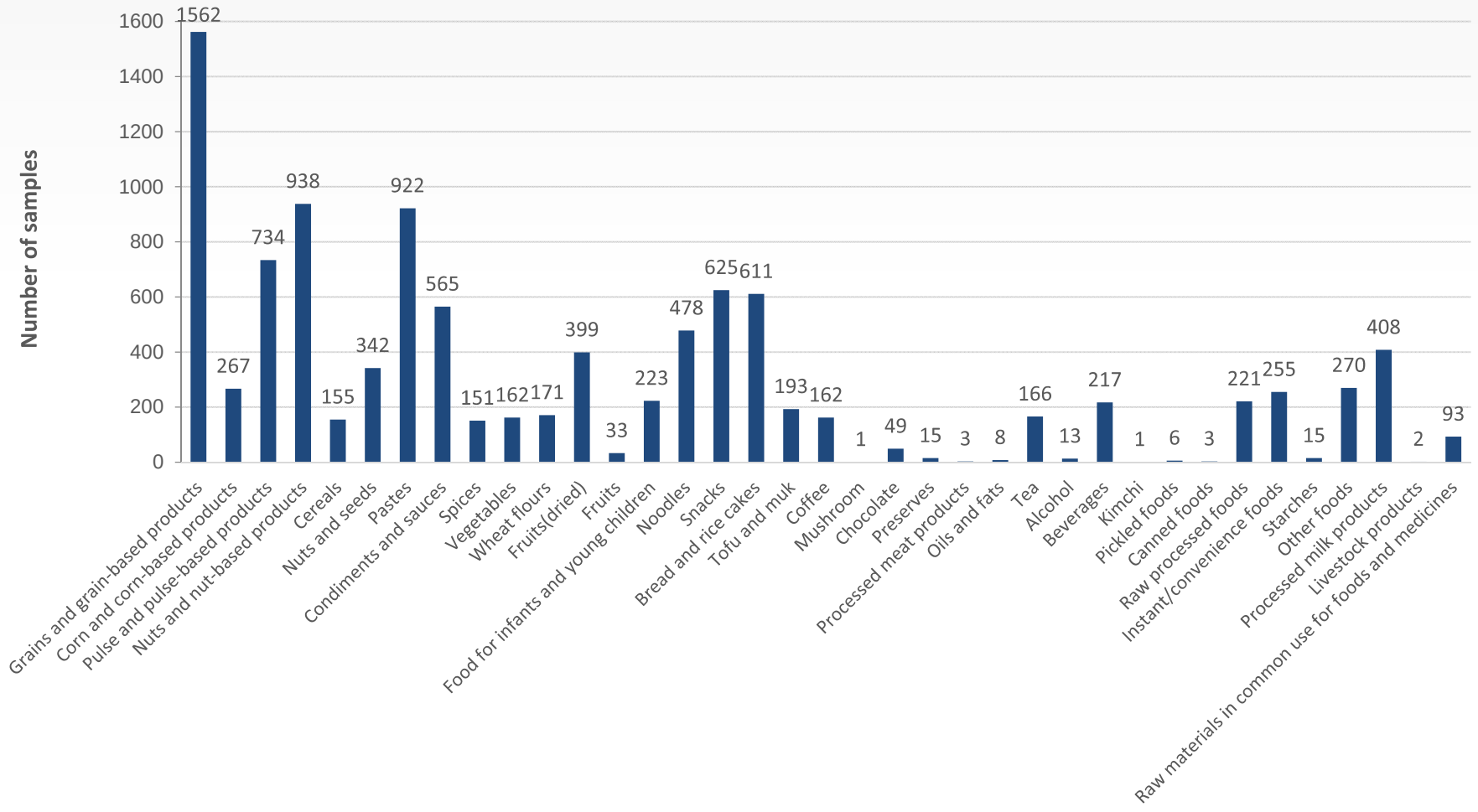
* PTWI: Provisional tolerable weekly intake (ng/kg bw/week)
** TDI: Tolerable daily intake (ng/kg bw/day)
*** As designated by the National Institute of Food Drug Safety Evaluation

Dietary Exposure Assessment

- **Aflatoxin contamination**
  - 10,443 samples from 300 products during 2012-2015
  - analyzed by HPLC and LC-MS/MS
- **Food consumption**
  - the Korea National Health and Nutrition Examination Survey (KNHANES, 2011–13)
  - the mean and extreme intake (P95) by age
- **Body weight**
  - calculated using the MIMS/MAP 3.0 & Oracle 10g programs

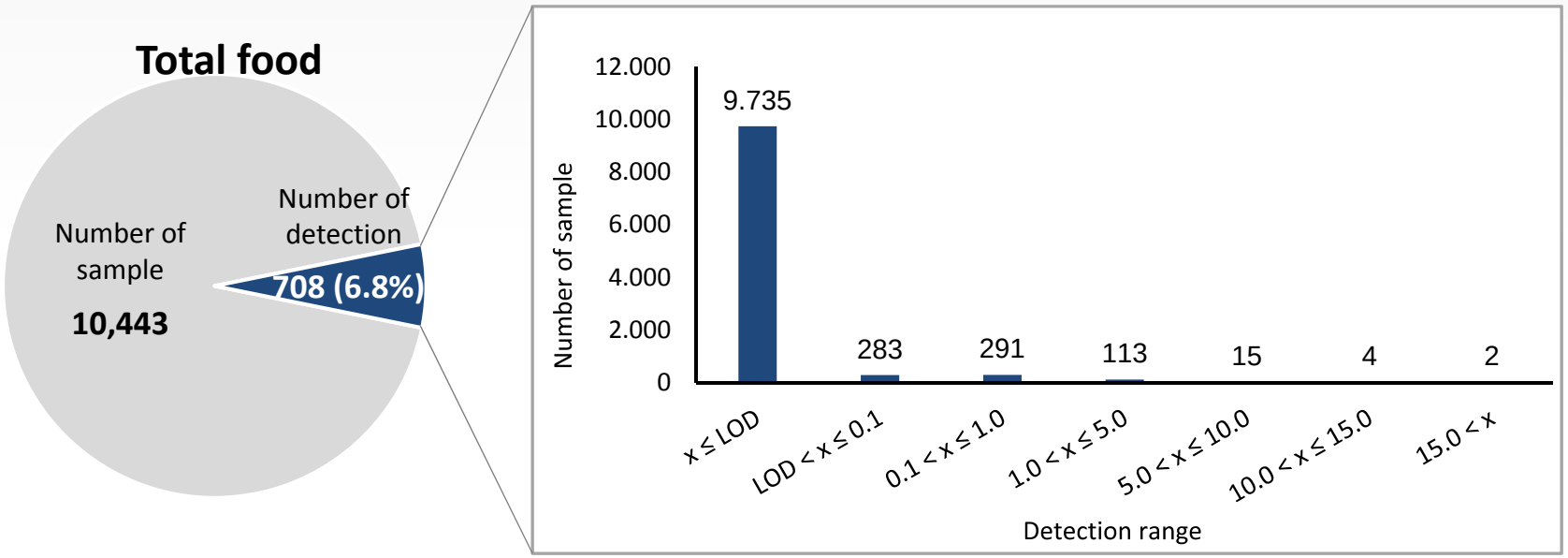
Dietary Exposure Assessment

Number of food samples tested for aflatoxins



Dietary Exposure Assessment

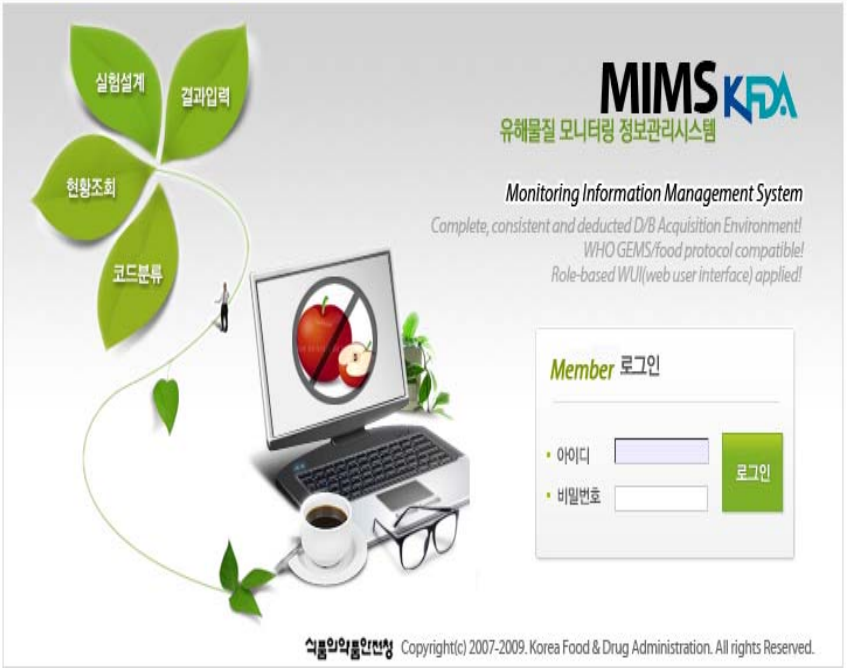
Total aflatoxins detection range in food



Samples were analyzed using high-performance liquid chromatography (HPLC) and mass spectrometry (MS), according to the CODEX HPLC or HPLC/MS/MS method, while “nondetects” were evaluated using ND (0) and ND (limit of detection, LOD).

Dietary Exposure Assessment

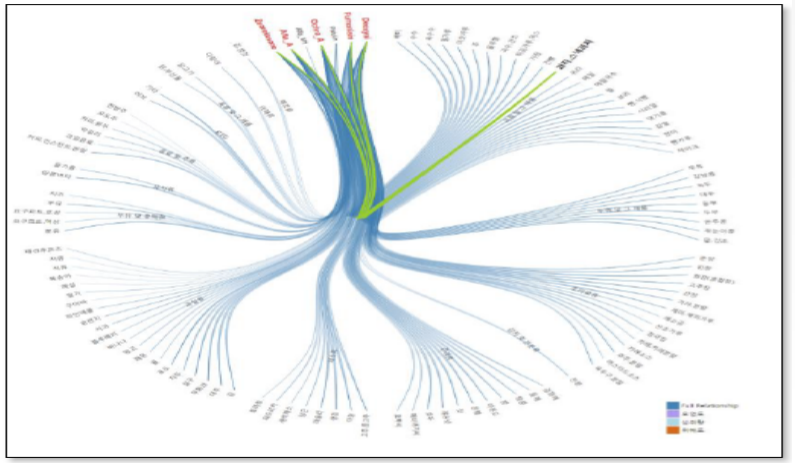
Data Management System in NiFDS



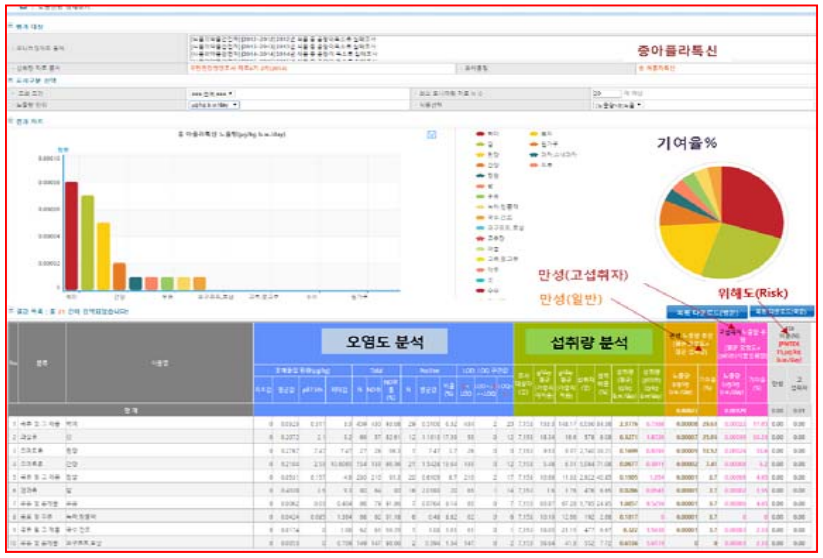
Collection program
of hazardous substances monitoring DB &
(MIMS, Monitoring Information Management System)
(MAP, Monitoring database and Assessment Program)

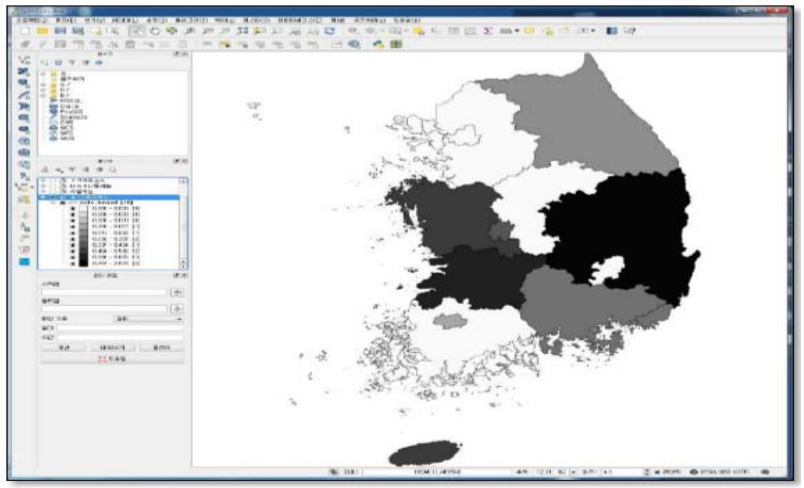
Dietary Exposure Assessment

Data Management System in NiFDS



SNA: Food-Hazard network analysis





GIS: Contamination Map(eg, Total Afl.)

Dietary Exposure Assessment

Concentrations of aflatoxin in food

Category	No. of samples	LC %	Concentration range(LB / UB) (μg/kg)			
			Mean	Median	Minimum	Maximum
Grains and grain-based products	1562	92	0.09 / 0.23	0 / 0.04	0 / 0	74.86 / 74.86
Corn and corn-based products	267	91	0.10 / 0.21	0 / 0.08	0 / 0	4.55 / 4.55
Pulse and pulse-based products	734	96	0.02 / 0.09	0 / 0.02	0 / 0	7.25 / 7.25
Nuts and nut-based products	938	93	0.10 / 0.18	0 / 0.03	0 / 0	12.20 / 12.20
Cereals	155	86	0.03 / 0.22	0 / 0.05	0 / 0	1.26 / 1.26
Nuts and seeds	342	93	0.04 / 0.15	0 / 0.02	0 / 0	6.62 / 6.62
Pastes	922	88	0.10 / 0.23	0 / 0.03	0 / 0	10.61 / 10.61
Condiments and sauces	565	86	0.04 / 0.17	0 / 0.06	0 / 0	6.85 / 6.85
Spices	151	88	0.34 / 0.66	0 / 0.23	0 / 0	9.51 / 9.51
Vegetables	162	98	0.01 / 0.14	0 / 0.07	0 / 0	1.44 / 1.44
Wheat flours	171	96	0.02 / 0.13	0 / 0.02	0 / 0	1.20 / 1.20
Fruits(dried)	399	94	0.02 / 0.18	0 / 0.07	0 / 0	3.20 / 3.20
Fruits	33	100	-(a)	-	-	-
Food for infants and young children	223	98	0 / 0.07	0 / 0.07	0 / 0	0.14 / 0.16
Noodles	478	98	0.01 / 0.13	0 / 0.02	0 / 0	1.08 / 2.18
Snacks	625	97	0.01 / 0.17	0 / 0.04	0 / 0	2.12 / 2.18
Bread and rice cakes	611	98	0 / 0.05	0 / 0.02	0 / 0	2.16 / 2.18
Tofu and muk	193	95	0.05 / 0.10	0 / 0.0	0 / 0	1.16 / 1.16
Coffee	162	96	0.03 / 0.06	0 / 0.03	0 / 0	3.27 / 3.27
Mushroom	1	100	-	-	-	-
Chocolate	49	98	0 / 0.17	0 / 0.02	0 / 0	0.06 / 2.18
Preserves	15	100	-	-	-	-
Processed meat products	3	100	-	-	-	-
Oils and fats	8	100	-	-	-	-
Tea	166	93	0.04 / 0.14	0 / 0.02	0 / 0	1.36 / 2.18
Alcohol	3	100	-	-	-	-
Beverages	217	98	0 / 0.05	0 / 0.02	0 / 0	0.7 / 0.7
Kimchi	1	100	-	-	-	-
Pickled foods	6	100	-	-	-	-
Canned foods	3	100	-	-	-	-
Raw processed foods	221	82	0.02 / 0.07	0 / 0.02	0 / 0	1.67 / 1.67
Instant/convenience foods	255	95	0.01 / 0.10	0 / 0.03	0 / 0	1.46 / 2.18
Starches	15	87	0.06 / 0.21	0 / 0.03	0 / 0	0.68 / 0.96
Other foods	270	87	0.04 / 0.12	0 / 0.04	0 / 0	4.65 / 4.65
Processed milk products	408	98	0 / 0.06	0 / 0.01	0 / 0	0.71 / 0.71
Livestock products	2	100	-	-	-	-
Raw materials in common use for foods and medicines	93	94	1.07 / 1.14	0 / 0.03	0 / 0.01	93.44 / 93.44

LC: left-censored data(values below the limit of detection)

(a): not calculated where all data were left-censored or the number of data was very limit

Dietary Exposure Assessment

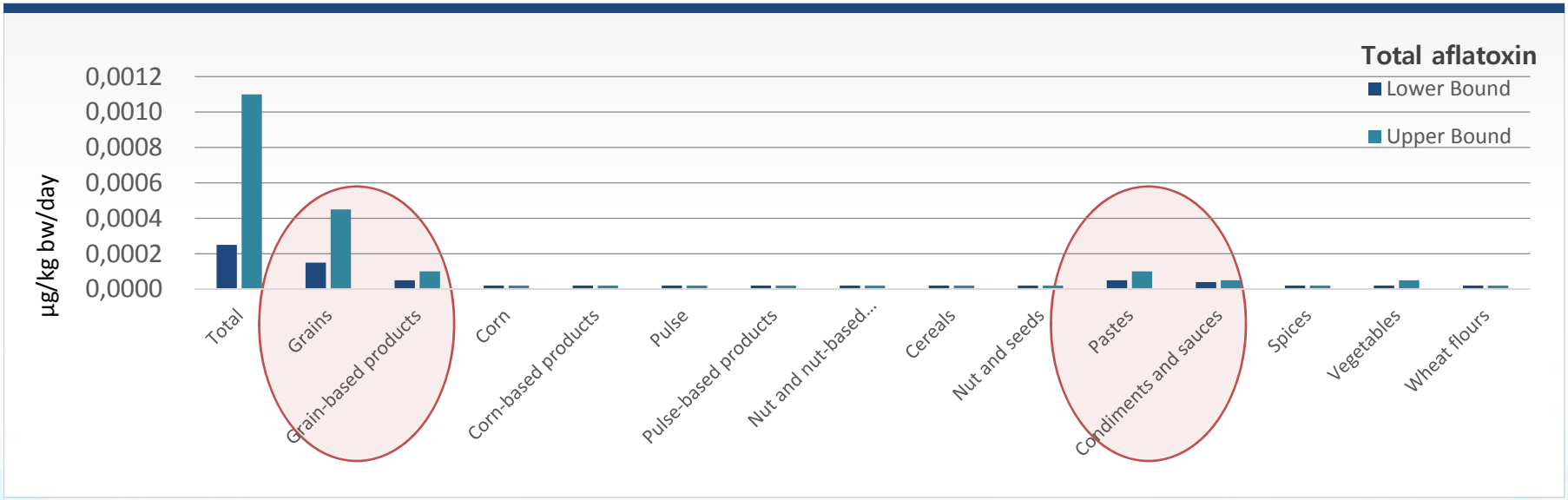
The average and high consumer exposure to aflatoxin by age class

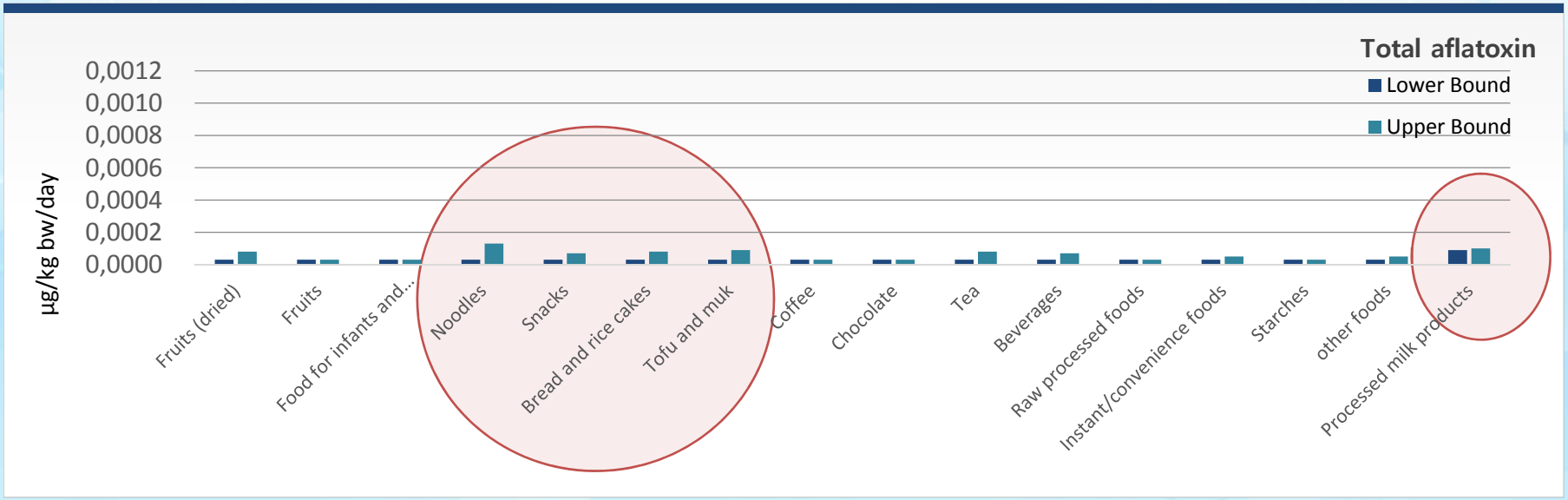
Population groups	Estimates exposure for average consumer [a] (ng/kg b.w./day)		Estimates exposure for high consumer [b] (ng/kg b.w./day)	
	LB	UB	LB	UB
All population	**0.263**	**1.105**	0.777	3.596
Adults[c]	0.255	1.056	0.729	3.347
1~2 years	**0.614**	**3.049**	1.912	10.393
3~6 years	0.537	2.502	1.650	7.636
7~12 years	0.375	1.657	1.181	5.595
13~19 years	0.242	1.060	0.773	3.815
20~64 years	0.252	1.052	0.721	3.335
65 <	0.273	1.085	0.783	3.485

[a] Average intake is based on average occurrence and average consumption.
[b] High consumer is based on average occurrence and 95th percentile consumption.
[c] 20 < group

Dietery Exposure Assessment

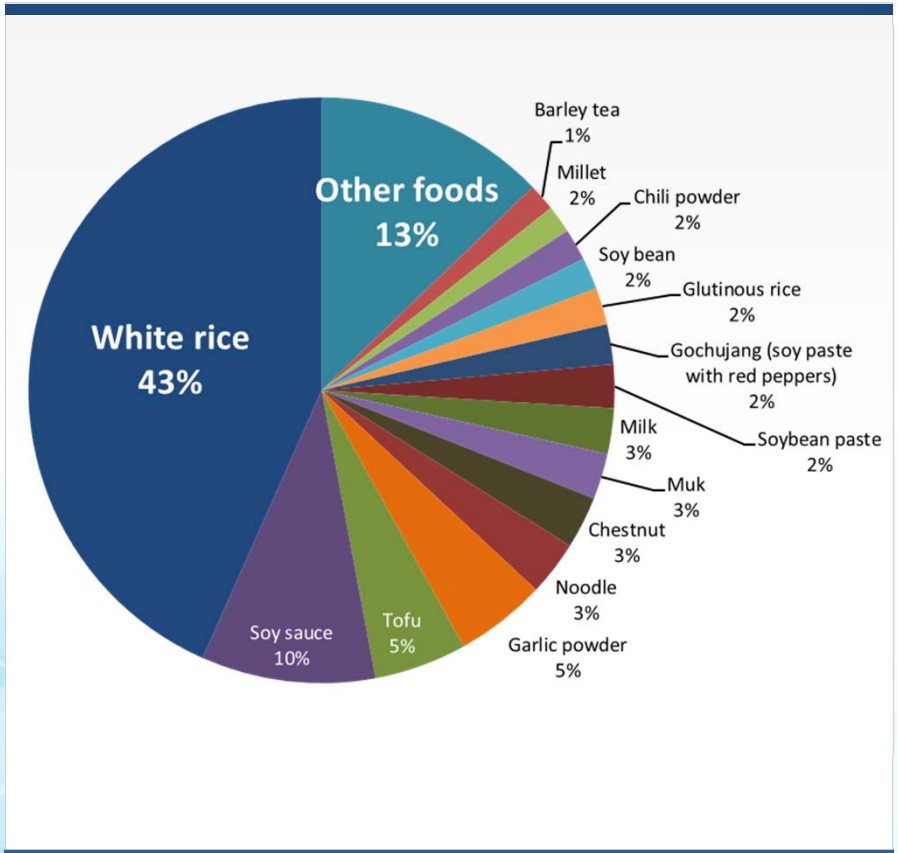
Daily aflatoxin exposure in each food group



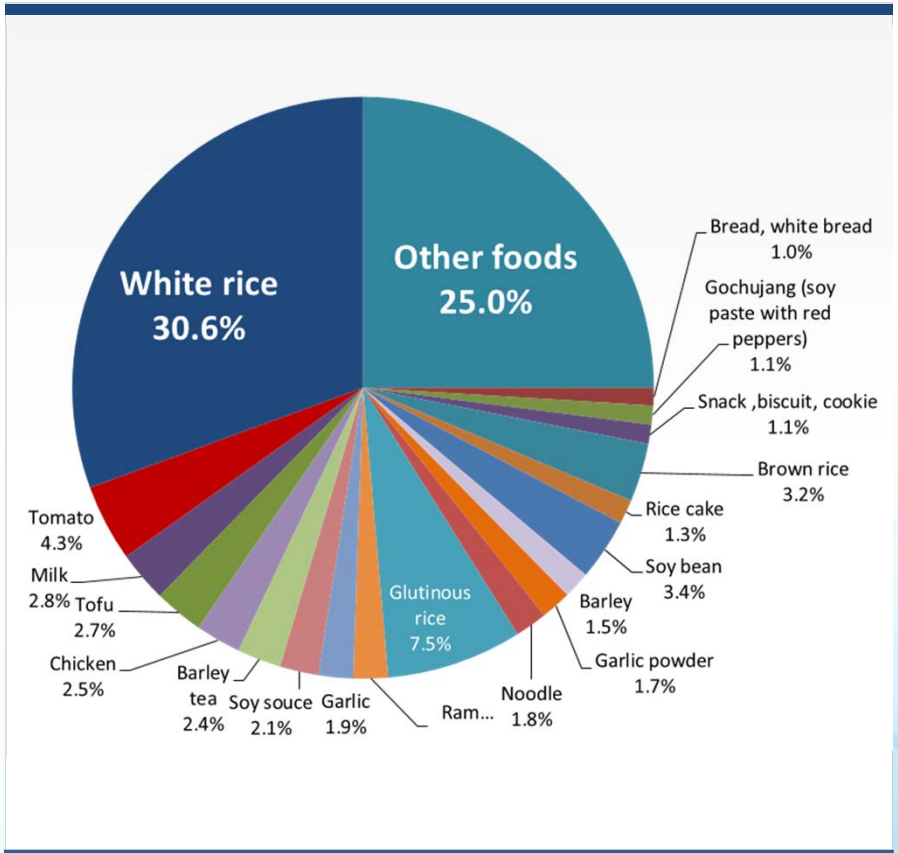


Dietary Exposure Assessment

Contribution of each food to dietary exposure of aflatoxins



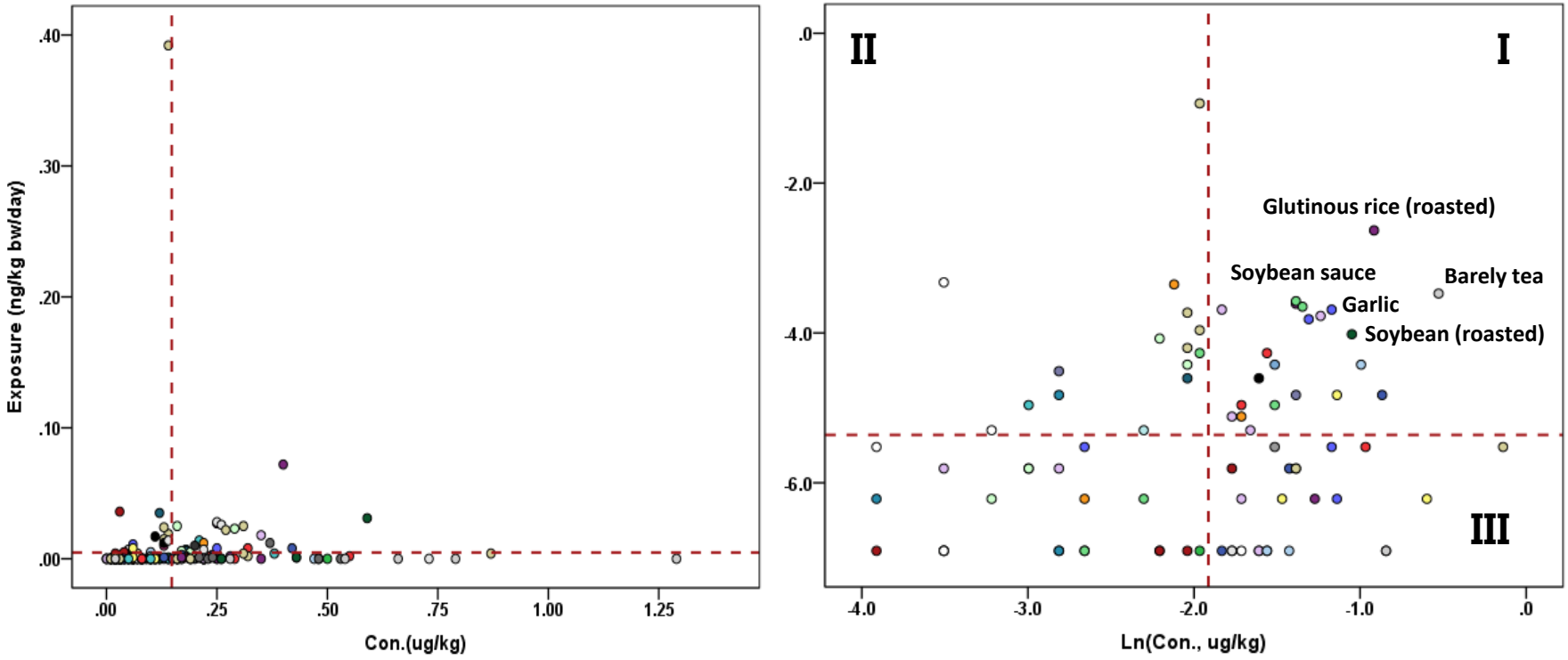
Contribution to aflatoxin exposure using LB concentration in all population

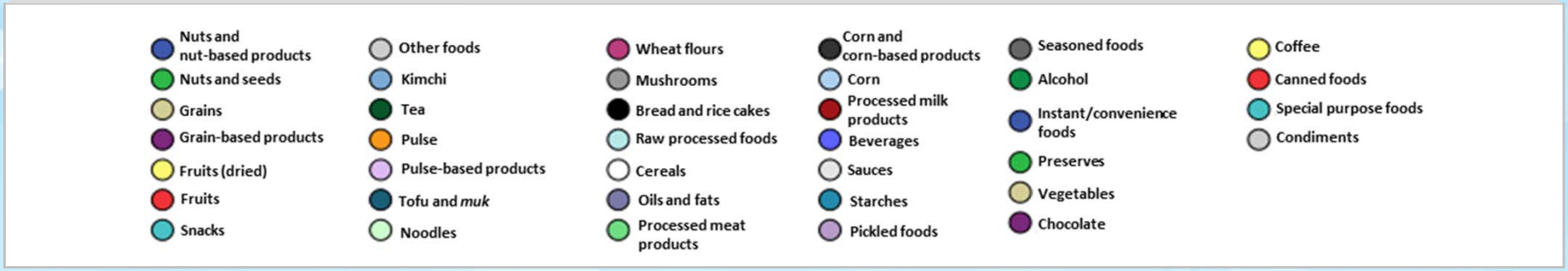


Contribution to aflatoxin exposure using UB concentration in all population

Dietary Exposure Assessment

Foods with high contamination & exposure level (Group I)





Diet Style of Korean

“Korean Diet is different from Western-style Diet”

Grain (Rice etc) consumption = 300g/day

Risk Characterization

Low possibility of hazardous effects related to aflatoxin exposure through food intake

The aflatoxin risk from food intake: the margin of exposure (MOE) method

$$MOE = \frac{BMDL_{10}\ (\mu g/kg\ bw/day)}{Daily\ exposure\ (\mu g/kg\ bw/day)}$$

The mean daily exposure for total aflatoxin: 0.0011 μg/kg bw/day

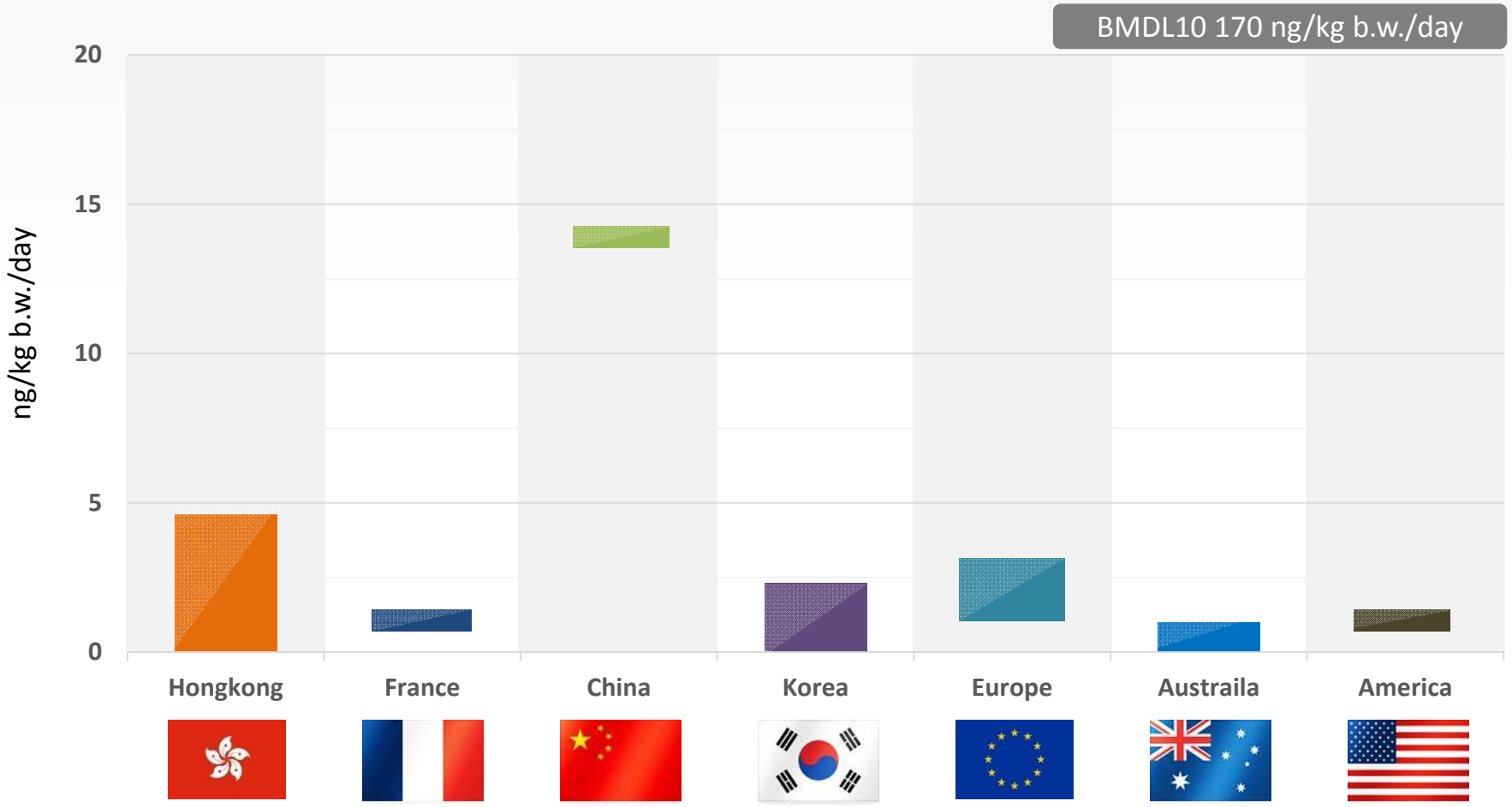
$BMDL_{10}$ for aflatoxin: 0.170 μg/kg bw/day

Koreans maintaining an average diet were assessed to have a low possibility of hazardous effects related to aflatoxin exposure.

Nevertheless, because aflatoxins are carcinogenic and genotoxic, their levels in food should be continuously monitored and minimized following the ALARA principle.

Risk Characterization

Comparison of Exposure Levels with Foreign Countries



Risk Management

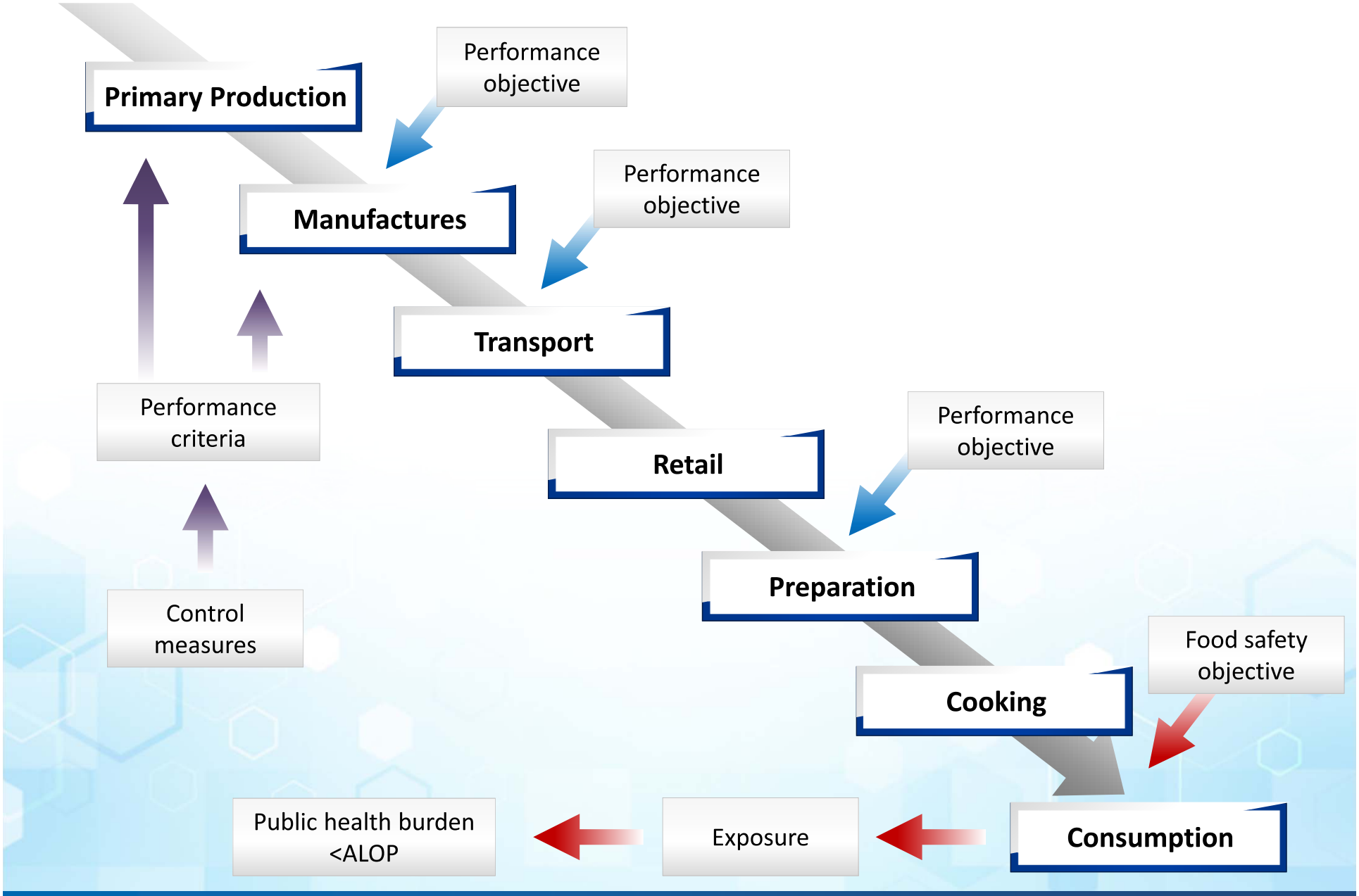
Reduction strategy

Home

- Keep cereals and processed products in cool dark place
- Maintain a balanced diet
- Check the expiration date and discard the moldy food
- Be careful when storing nuts
- Purchase from trusted retailers

Industry

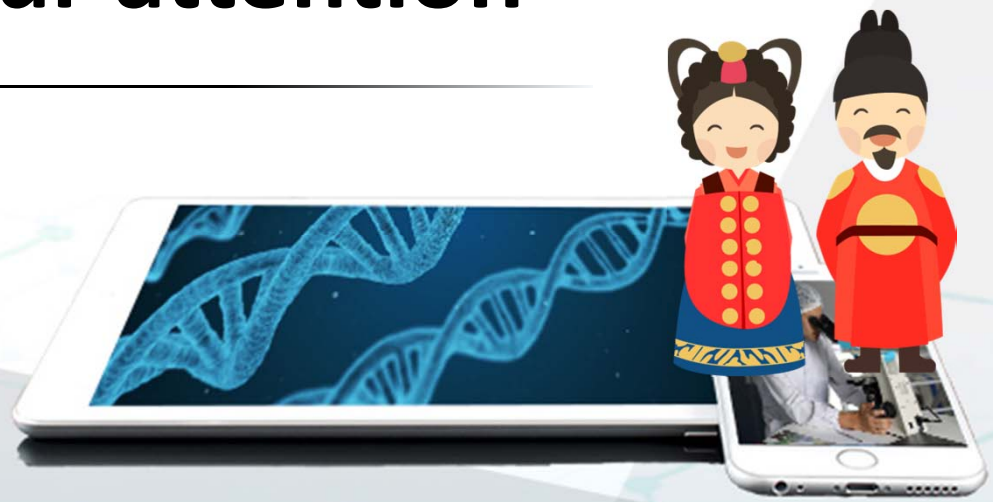
- Apply GAP/GMP/HACCP to minimize mycotoxin contamination
- Select a reliable supplier when purchasing food ingredients
- Preservation conditions (cool, dark place, dry place) based on first-in-first-out
- Maintain raw material supply and demand records



Food safety practices throughout the food chain

MINISTRY OF FOOD AND DRUG SAFETY
National Institute
of Food and Drug Safety Evaluation

Thank you
for your attention



MINISTRY OF FOOD AND DRUG SAFETY
National Institute
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