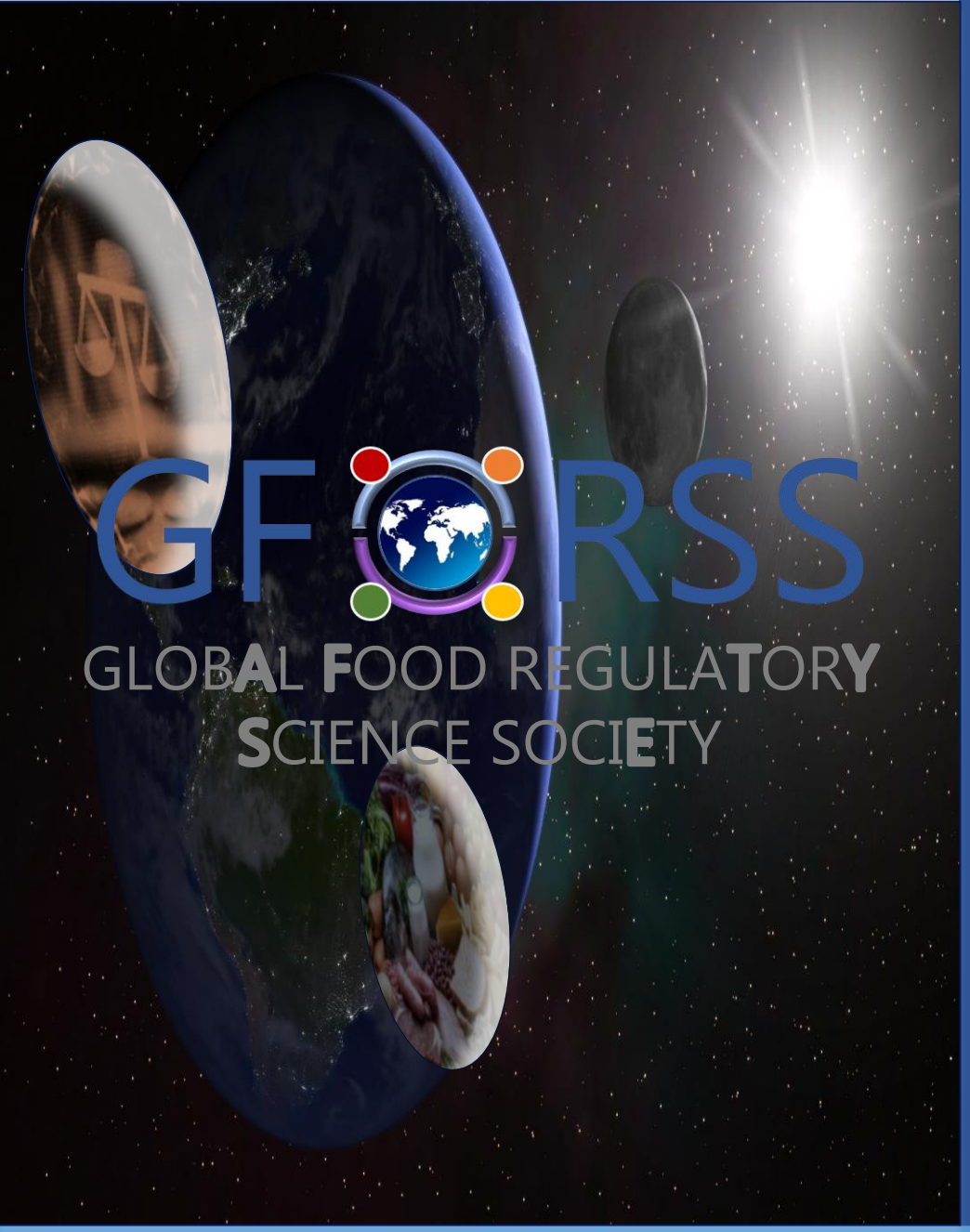


Risk Assessment: Aflatoxins in Food

Day 3 – 28 February, 2023

9:00 – 9:45

Dr. Silvia Dominguez| *Global Food Regulatory Science Society (GFoRSS)*

Risk assessment questions

- ❑ Does the level of aflatoxin X in food Y pose a health risk to Egyptian consumers?
- ❑ Does the existing ML (?) for aflatoxin X in food Y provide adequate protection to Egyptian consumers?
- ❑ Are there any Egyptian population groups that may be more at risk than others to aflatoxin exposure?
  - Consumption patterns, coexisting conditions …

Risk assessment questions (cont.)

- ❑ Are there any specific foods driving the exposure of the Egyptian population to aflatoxin X or to aflatoxins in general?
- ❑ Which aflatoxin poses the highest risk to the Egyptian population?
- ❑ Is the Egyptian population's overall exposure to aflatoxins within "safe" limits?
- ❑ Would the establishment of ML or other standards for specific aflatoxin-food combinations enhance protection of Egyptian population?

Group exercise

1. Formulate a risk assessment question and outline what type of results we would need to answer it
2. Formulate a risk assessment question related to the AFM1 / dairy milk occurrence data we extracted

Development of a formal risk assessment

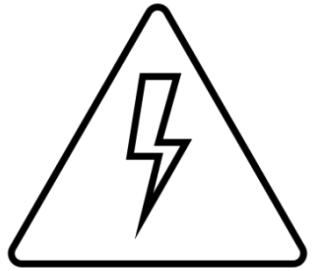
✓Risk assessment question

1. Hazard identification: description of the food safety issue
2. Hazard characterization: description of the hazard andits adverse health effects
3. Exposure assessment: level of hazard the population is exposed to
4. Risk characterization: is this exposure “safe”?

1. Hazard identification

Why is this hazard a food safety concern for this population?

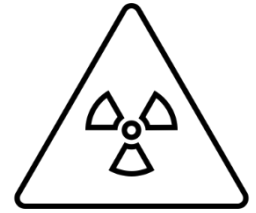
- ❑ Epidemiological data
- ❑ Reports of occurrence of hazard at levels above MTL (?)
- ❑ Reports of export rejects (e.g., RASFF)
- ❑ Country-specific factors that may increase risk:
  - High consumption (e.g., ractopamine / beef liver / Egypt)
  - Food processing / handling / storage practices (e.g., grains storage)
  - Population-specific (e.g., dietary habits, prevalence of hepatitis B/C virus)
  - Weather (?)



2. Hazard characterization

What exactly is the hazard and how toxic is it?

- ❑Hazard description (sources, chemical structure, under which conditions it is produced, in which form it is expected to reach the consumer …)
- ❑What are the possible adverse health effects
- ❑Which doses can produce these adverse health effects
- ❑Domestic legislation / international standards (e.g., MTL for AFB1 in Egypt 2 µg/kg)



3. Exposure assessment

- Level of hazard the population is exposed to (ng/kg bw per day):

$$Estimated\ daily\ intake\ of\ contaminant = \frac{\Sigma(Daily\ food\ intake\ x\ Concentration\ in\ food)}{Body\ weight}$$

- Standard body weight (60 kg), adapted (70 kg Egypt), per age group…
- Sum if considering exposure from different food sources
- Output form: distribution or point values, depending on inputs

4. Risk characterization

Exposure to contaminant from dietary source(s) is compared to reference “safe” value to assess risk

Is the estimated exposure “safe”?

- ❑Margin of exposure (MOE)
- ❑Hazard index (HI) or hazard quotient (HQ)
- ❑Carcinogenic potency

Margin of exposure

- Substances both genotoxic and carcinogenic = no tolerable daily intake
- Compare exposure to an **animal study's** reference point (RFD)

$$MOE = \frac{RFD}{EDI}$$

  - Benchmark dose (BMD): causes low but measurable response
  - BMD lower confidence limit 10% (BMDL10): lowest dose that is 95% certain to cause ≤10% cancer incidence
  - Ex. AFB1: 400 ng/kg bw per day (JECFA, 2001)

- MOE ≥ 10 000 little concern (EFSA, 2005)

Hazard index

- Compare exposure to an **animal study's** reference point (RFD)

$$HI = \frac{EDI}{RFD}$$

- Aflatoxins (no tolerable daily intake)
  - TD50 (daily dose that induces tumours in ½ of laboratory animals) / 50 000 (uncertainty factor)
  - Ex. AFM1 0.2 ng/kg bw per day (Sharafi et al., 2022)

- HI > 1 risk (EFSA, 2020)

Carcinogenic potency in **humans**

- FAO/WHO (2018), EFSA (2020)
- Aflatoxins = hepatocellular carcinoma (HCC)
- Higher potency if HBV+ (ex. AFB1: 0.01 -; 0.3 +)
- Cancer potency (expressed as HCC cases per year per 10^5 individuals per ng/kg bw per day):

$$P\ cancer = (PHBV^{-}\ x\ \%HBV^{-}) + (PHBV^{+}\ x\ \%HBV^{+})$$

- Risk of HCC incidence (expressed as HCC cases per year per 10^5 individuals):

$$HCC\ risk = P\ cancer\ x\ EDI$$

Uncertainty

- There is no perfect model
- Sources: data gaps, assumptions, models…
- How do they affect risk assessment outputs?
  - Over / under estimation

Sources of uncertainty	Direction[a]
Extrapolation of the occurrence data to the whole of Europe for certain food categories	+/–
Potential reduction of the aflatoxin concentration due to processing not considered for some samples	+
Use of analytical data from targeted sampling	+
Large proportion of left-censored data in the data set	+/–
Assumptions from the summing of the individual aflatoxins at the level of sample	+/–
Uncertainty in the exposure assessment in the study by Yeh et al. (1989)	+/–
Estimated cancer potency for hepatitis B surface antigen negative subjects is more uncertain because based on relatively few cases	+/–
Use of upper bound cancer potencies	+
Assumption on the co-infection of HBV and HCV in Europe	+
The HBV and HCV status cannot be taken into account when using animal data for the risk characterisation	+/–
Cancer potency and reference point for aflatoxin B1 applied to 'aflatoxin total'	+

+ : uncertainty with potential to cause overestimation of exposure/risk; –: uncertainty with potential to cause underestimation of exposure/risk.

EFSA (2020)

Monte Carlo: Inputs

- ❑Random sampling from distributions
- ❑Ex. loop using triangular distributions for concentration and consumption, and MOE to characterize risk
- ❑Ex. nunc=10, nvar=100 (usually a lot more)
  - 10 simulations
  - 100 dietary exposures per simulation

```
for (u in 1:nunc)
{
 conc <-rtri(nvar,min,max,mode)
 conso<-rtri(nvar, min_conso, max_conso, mode_conso)
 expo<-(conso*conc)/bw
  mean_expo[u]<-mean(expo)
 MOE<-RFD/expo
  mean_MOE[u]<-mean(MOE)
  risk<-MOE>10000
  riskpernvar[u]<-sum(rbernoulli(nvar,risk))
}
```

- ✓Number of simulations
- ✓Number of exposures per simulation
- ✓Body weight
- ✓Concentration distribution parameters
- ✓Consumption distribution parameters
- ✓RFD

Monte Carlo: Outputs (using made-up inputs)

- **Exposure**: distribution, mean[95% CI]
- **MOE**: distribution, mean[95% CI]
- **Risk**: For each of the 10 simulations, how many of the 100 simulated exposures had MOE > 10 000
  - Mean risk

- Outputs examples based on made-up inputs:

```
> summary(expo)
    Min.  1st Qu.   Median     Mean  3rd Qu.     Max.
0.001644 0.013036 0.024233 0.029873 0.042875 0.094534
> summary(mean_expo)
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.02775 0.02908 0.03004 0.03036 0.03115 0.03336
> summary(MOE)
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
   2631    9265   14523   30404   27172  219710
> summary(mean_MOE)
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  25021   27219   29312   30039   33210   35303
> quantile(mean_MOE,c(0.025,0.975))
    2.5%    97.5%
25411.18 35081.16
> riskpernvar
 [1] 70 67 75 80 72 67 65 73 67 74
```

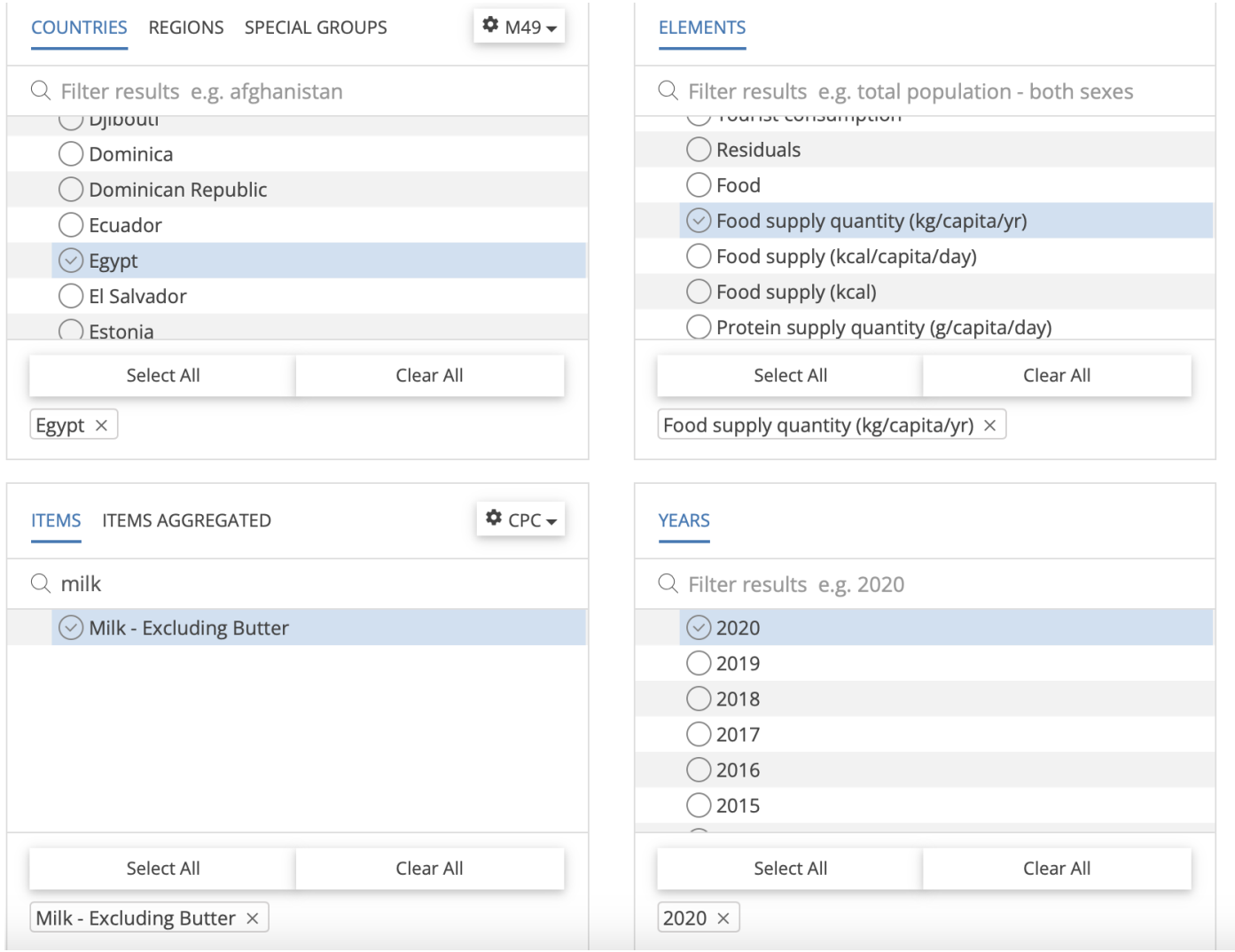
Example: AFM1 and raw milk

- AFM1 MTL Egypt = 0.05 ppb (ug/kg) = 50 ng/kg
  - Raw milk, heat-treated milk and milk for the manufacture of milk-based products
  - Based on EU regulation
  - Risk assessment question: Does the MTL of 50 ng AFM1/kg milk protect Egyptians that consume raw milk?

1. Calculate exposure
   - Milk consumption in Egypt
   - Concentration of AFM1 in milk sold in Egypt
2. Characterize risk

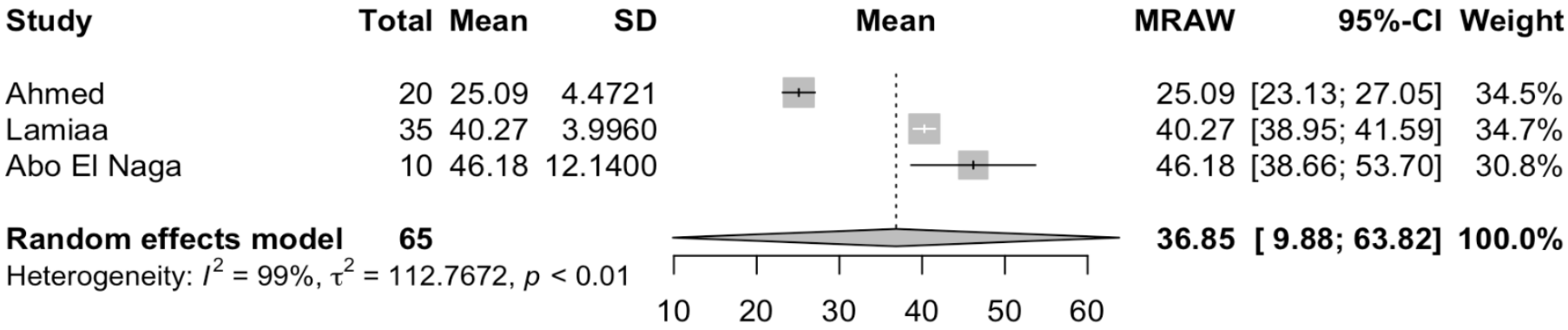
Milk Consumption

- From FAO Food balance sheets: https://www.fao.org/faostat/en/#data/FBS
- 26.91 kg/capita/year
  - Not raw milk specificially
- Considering 365 days:
  - 0.074 kg per day
- Could do it for specific populations (children) if we have consumption data



AFM1 Concentration

- Pooled mean AFM1 concentration in raw milk in Egypt = 36.85 ng/kg



- Could do it also for min and max concentration. Exactly the same procedure.

Exposure to AFM1 from raw milk in Egypt

- Using concentration from published studies:
  - EDI = (36.85 ng/kg * 0.074 kg per person per day) / 70 kg bw
  - $\frac{36.85*0.074}{70}$ = 0.039 *ng/kg bw per day*
- Using MTL = 50 ng/kg as concentration
  - EDI = (50 ng/kg * 0.074 kg per person per day) / 70 kg bw
  - $\frac{50*0.074}{70}$ = 0.053 *ng/kg bw per day*

Characterize risk

- Hazard index = EDI / RFD
  - RFD AFM1 = 0.2 ng/kg bw per day (Sharafi et al., 2022)
  - HI <1 = low concern

- $HI = \frac{0.039}{0.2} = 0.195$ using reported AFM1 concentration
- $HI = \frac{0.053}{0.2} = 0.265$ using AFM1 MTL as concentration

Characterize risk

- MOE = RFD / EDI
  - RFD AFM1 = 570 ng/kg bw per day (Sharafi et al., 2022)
  - MEO> 10000 = low concern

- MOE $= \frac{570}{0.039} = 14615$ using reported AFM1 concentration
- MOE$= \frac{570}{0.053} = 10754$ using AFM1 MTL as concentration

Characterize risk

- Carcinogenic risk

$$P\ cancer = (PHBV^{-}\ x\ \%HBV^{-}) + (PHBV^{+}\ x\ \%HBV^{+})$$

$$HCC\ risk = P\ cancer\ x\ EDI$$

- AFM1 PHBV- = 0.001
- AFM1 PHBV+ = 0.03
- % HBV in Egypt??...

Conclusion

- Risk assessment question: Does the MTL of 50 ng AFM1/kg milk protect Egyptians that consume raw milk?

- Your answer based on risk assessment results: ….
- Explain sources of uncertainty

ngiyabonga
рахмат
danke
謝謝
teşekkür ederim
Баярлалаа
spas
mersi
kia ora
barka
welalin
tack
mahalo
tapadh leat
спасибо
faafetai lava
vinaka
blagodaram
dank je
misaotra
matondo
paldies
grazzi
спасибі
kiitos
dankie
nanni
nandri
dhanyavad
thank you
gracias
хвала
asante
manana
bedankt
bayarlalaa
graçie
hvala
maururu
köszönöm
akun
dankon
aciu
obrigada
murakoze
tenki
enkosi
djiere dieuf
tau
mochchakkeram
dziękuję
дякую
mamnun
chokrane
chnorakaloutioun
gratias ago
gràcies
sulpáy
go raibh maith agat
sobodi
dĕkuji
sagolun
sukriya
kop khun krap
taiku
obrigado
arigatô
takk
dakujem
trugarez
mèsi
didi madloba
najis tuke
ありがとう
tanemirt
grazie
kam sah hamnida
rahmat
terima kasih
rahmet
ευχαριστώ
diolch
dhanyavadagalu
shukriya
mercé
мерси
তোমাকে ধন্যবাদ
감사합니다
xièxie
merci