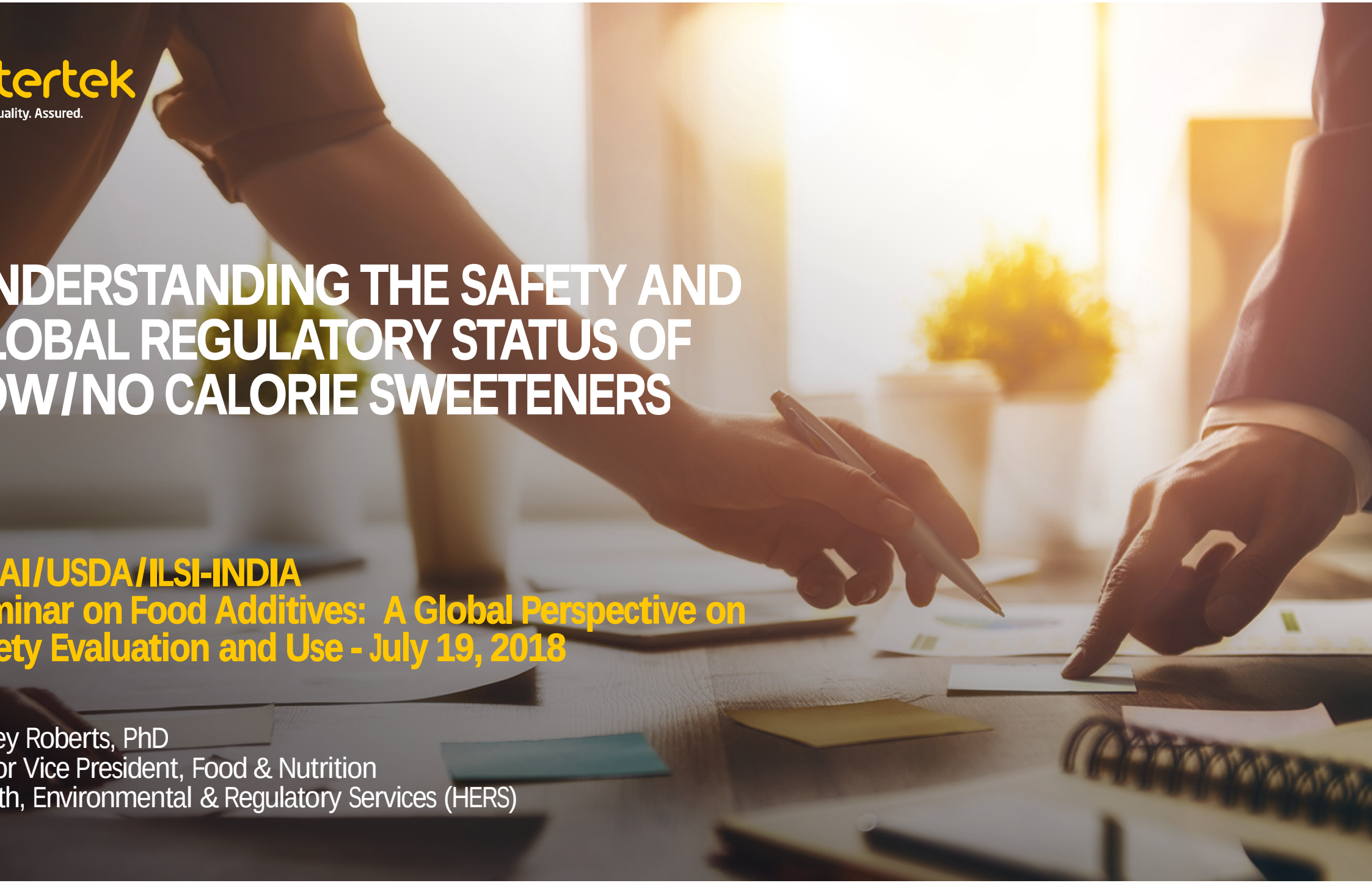
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uality. Assured.
NDERSTANDING THE SAFETY AND
LOBAL REGULATORY STATUS OF
OW/NO CALORIE SWEETENERS
AI/USDA/ILSI-INDIA
minar on Food Additives: A Global Perspective on
ety Evaluation and Use - July 19, 2018
ey Roberts, PhD
or Vice President, Food & Nutrition
th, Environmental & Regulatory Services (HERS)

ECLARATION OF INTERESTS

I hold the position of Senior Vice President, Food & Nutrition in the Health, Environmental & Regulatory Services (HERS) Division at Intertek. The subject of this presentation is within the scope of Intertek's mandate.

Financial Interests (IFAC): My travel and accommodations are being sponsored by the International Food Additives Council. IFAC is a global association representing manufacturers and users of food additives and food ingredients.

Financial Interests (CCC): My travel and accommodations are being sponsored by the Calorie Control Council. CCC is an international association representing manufacturers and users of low-, no- and reduced-calorie ingredients, foods and beverages, including high-intensity sweeteners.

UTLINE

LNCS Safety and the Acceptable Daily Intake

Estimated Dietary Exposures Relative to the ADI

Global Regulatory Landscape

Global Labeling Requirements

NCS SAFETY AND THE CCEPTABLE DAILY INTAKE

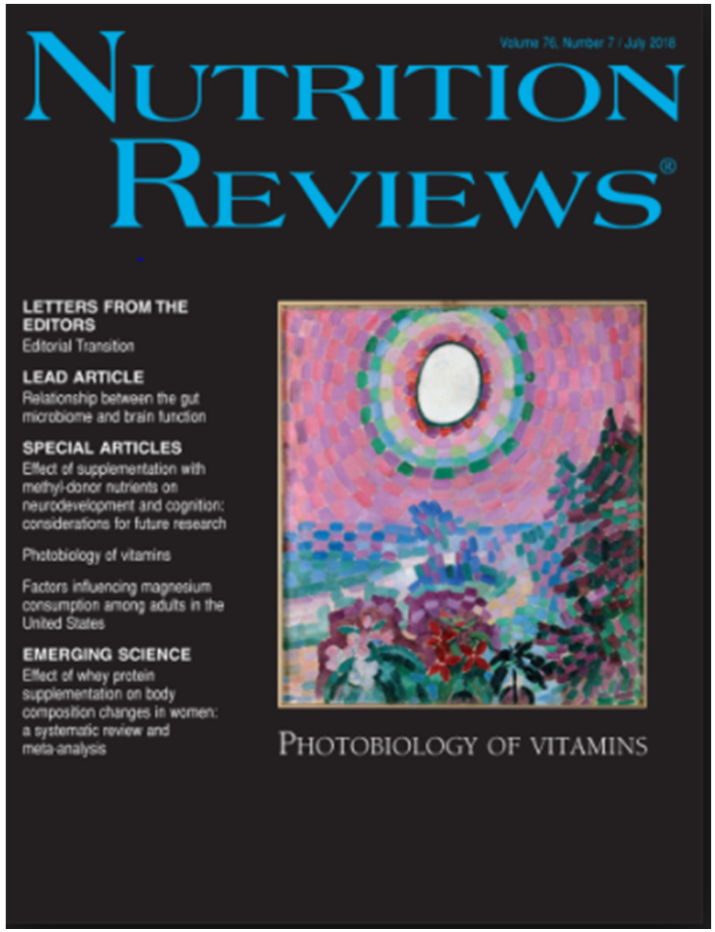
IE SAFETY DATABASE NECESSARY FOR APPROVAL

Prior to approval and authorization a comprehensive database has to be developed by the applicant and presented to the Regulatory Authority for independent evaluation

Technical (manufacturing, specifications, technological function and case for need), toxicological information and exposure analysis provide the core of the data

This information is submitted in the form of a dossier on which the risk assessment is conducted

L LNCS ARE USED IN PRODUCTS AT VERY LOW LEVELS; RAPIDLY IMINATED FROM THE BODY AFTER CONSUMPTION



Biological Fate of Low Calorie Sweeteners; Magnuson et al, 2016
Vol. 74(11):670–689

- Safety review covers aspartame, acesulfame potassium (Ace-K), stevia and sucralose
- Elimination from the body is rapid, with no bioaccumulation of either the LNCS or their metabolites
- The high sweetness intensity of LNCS means very little is actually used in foods and beverages
- Their low levels of use, combined with their efficient metabolic and excretion profiles results in systemic exposure that is short and minimal

OXICOLOGY TESTING IS EXTENSIVE AND HAS RELEVANCE TO HUMANS CROSS ALL AGE GROUPS

Extensive studies conducted in multiple species with direct relevance to humans

Toxicology Studies	Human Concern
Short-term toxicity studies	Will a consumer get sick shortly after drinking the product?
Reproductive and Developmental toxicity studies	Safe for children? What if a consumer is pregnant/nursing?
Cancer studies; genetic toxicity studies	Will any of the ingredients have a potential to cause cancer?
Longer-term toxicity studies	Will small amounts over time lead to sickness?

- ***These tests are required by all international expe***
- ***The results demonstrate the safety for LNCS acro all age groups including pregnant women and children***

ASE STUDY FOR ASPARTAME

Toxicology Studies	Human Concern	Results for Aspartame
Vill a consumer get sick hortly after drinking the product?	Short-term toxicity studies	No evidence of toxicity in multiple species
fe for children? What if a consumer is pregnant/nursing?	Reproductive and Developmental toxicity studies	No evidence of adverse effects in multiple species
ill any of the ingredients ave a potential to cause cancer?	Cancer studies; genetic toxicity studies	Non-genotoxic in in vitro and in vivo tests No evidence for carcinogenicity
Vill small amounts over time lead to sickness?	Longer-term toxicity studies	No evidence for long-term safety risks

Safety Reviews and Approval

- JECFA safety evaluation in 1981
- Approved for use in the US in 198
- Multiple safety reviews in Europe, affirming its safety
  - 1997
  - 2002
  - 2006
  - 2009
  - 2013

UMORS ABOUT ASPARTAME PERSIST BUT ARE CONSISTENTLY REJECTED

Allegation	Basis for the allegation	Flaws in the Study	Regulatory Opinion(s)
partame causes zures	Limited study in children (1994)	• Study used only 10 children • Single aspartame dose (> 1 gram) administered to each child • Dose given was more than 7x higher than the amount US children aged 6-11 consume in foods/beverages	• EFSA reviewed this study; rejecte its finding and affirmed safety of aspartame for all age groups • Health Canada notes clinical stud show there is no link between aspartame consumption and seizures
partame **(and e-K)** is not safe pregnant omen	Danish study involving pregnant women (2011)	• Study authors did not adjust for potential confounders (e.g. caffeine use, medical histories which could contribute to pre-term deliveries etc.)	• EFSA reviewed and dismissed the study. EFSA concluded "there is evidence available to support a causal relationship between the consumption of low-calorie sweetened soft drinks and prete delivery"

AFETY ASSURANCE AND THE ADI

The ADI has been defined by JECFA as

- "An estimate of the amount of a food additive, expressed on a bodyweight basis, that can be ingested over a lifetime without appreciable health risk"

The ADI is usually expressed as a numerical value in mg/kg bw/day

The ADI has been used for the past 50 years to establish safe intakes of food additives including LCS

Toxicological protocols adopted for LCS cover all periods of rapid growth and development maturation and aging and therefore all circumstances of human exposure are covered

Exposure during the juvenile period is taken into account and so the **ADI does apply to children**

ALCULATION OF THE ADI

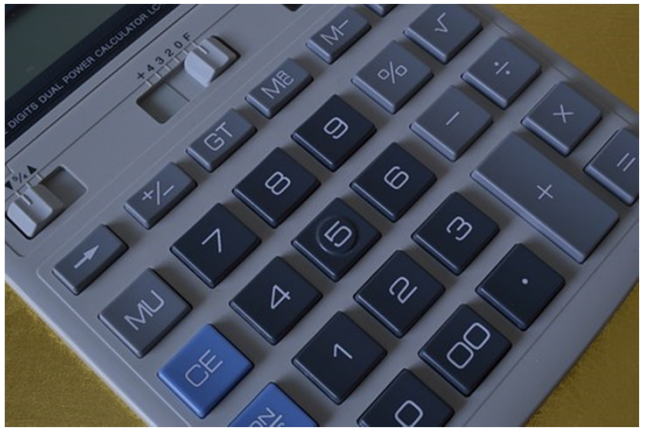
ADI (mg/kg/day) = NOAEL/safety factor

NOAEL = No-Observed-Adverse-Effect Level

- From long-term studies
- For the most sensitive endpoint in the most sensitive species

Apply "safety factor" (usually 100) to account for

- differences between individuals (10 X)
- differences between humans and animals (10 X)



IERE ARE MANY REASONS WHY THE ADI IS UNLIKELY TO BE EXCEEDED IN NY AGE GROUP

Not all categories with approved uses for LNCS actually use them. For example in a published Italian study, out of 100 approved food/beverage categories; only 25 use LNCS

Dietary intake estimates are overly conservative and assume the maximum permitted level is used in all food

Dietary intake estimates assume the sweetener is used alone, not in combination

Dietary intake studies assume a person consumes all food categories containing LNCS each day

Based on these points, and considering the high degree of conservatism in these types of estimates, it is very unlikely for the ADI to be exceeded

STIMATED DIETARY XPOSURES RELATIVE TO HE ADI

ummary of Intake Estimates from Around World

XPOSURE LEVELS ARE VERY LOW DUE TO HIGH SWEETNESS POTENCIES

weetener	Sucrose sweetness equivalence	Examples of brand names containing sweetener	ADI (mg/kg bw/d)	Maximum daily mg intake based on 70kg person
cesulfame K	200 x	Sweet One® Sunett®	15	1050
spartame	200 x	Nutrasweet® Equal® Sugar Twin®	40	2800
accharin	400 x	Sweet and Low® Sweet Twin® Sweet'N Low® Necta Sweet®	5	350
ucralose	600 x	Splenda®	15	1050
teviol Glycosides	~300 x	Truvia® PureVia® Enliten®	4	280

AILY INTAKE OF ASPARTAME IS A SMALL FRACTION OF THE ADI

United States: [1]Aspartame Intakes vs. ADI

Low- and No- Calorie Sweetener Users	Est. Aspartame Intake (mg/kg bw/day)	Percent of ADI (ADI=50 mg/kg bw/day) FDA ADI
All Low-Calorie Sweetener Users		
50th Percentile	4.8	10%
95th Percentile	13.3	27%
Children, 6-11 yrs (subgroup)		
50th Percentile	5.5	11%

Korea: [3]Aspartame Intakes vs. ADI

Low- and No- Calorie Sweetener Users	Est. Aspartame Intake (mg/kg bw/day)	Percent of ADI (ADI=40 mg/kg bw/day)
50th Percentile	0.14	0.35%
90th Percentile	4.6	12%
Children, 6-11 yrs (subgroup)	0.6	1.5%

Australia: [4]Aspartame Intakes vs. ADI

Low- and No- Calorie Sweetener Users	Est. Aspartame Intake (mg/kg bw/day)	Percent of ADI (ADI=40 mg/kg bw/day)
All Low-Calorie Sweetener Users		
50th Percentile	2.56	6%
90th Percentile	5.3	13%

New Zealand: [4]Aspartame Intakes vs. ADI

Low- and No- Calorie Sweetener Users	Est. Aspartame Intake (mg/kg bw/day)	Percent of ADI (ADI=40 mg/kg bw/day)
All Low-Calorie Sweetener Users		
50th Percentile	1.69	4.2%
90th Percentile	3.9	10%

TIMATED ASPARTAME EXPOSURE
SA ESTIMATED ASPARTAME CONSUMPTION IN USERS ONLY

	Toddler	Children	Adolescent	Adults
ean	1.6-16.3	1.8-12.6	0.8-4.0	0.7-8.5
gh level	7.5-36.0	6.3-32.4	2.3-13.2	2.4-27.5

- Reported as mg/kg body weight/day
- Minimum-maximum across all 26 dietary surveys studies conducted in 17 different European countries
- Conservative estimates: Assumed that all processed foods contained aspartame at maximum permitted level or highest reported use level
- Compare to ADI of 40 mg/kg/d to ensure no group exceeding
- Even at the highest levels of consumption, intakes are less than 50% of the ADI

(EFSA Aspartame review 2013)

UCRALOSE DAILY INTAKE IS A SMALL FRACTION OF THE ADI

ed States

w- and No- Calorie eetener Users	Sucralose Intake (mg/kg bw/day)	Percent of ADI (ADI=15 mg/kg bw/day; Europe)
Low-Calorie Sweetener Users		
h Percentile		
rs+ (all ages)	1.6	11%

tralia

w- and No- Calorie eetener Users	Sucralose Intake (mg/kg bw/day)	Percent of ADI (ADI=15 mg/kg bw/day; Europe)
Low-Calorie Sweetener Users		
h Percentile (all ages)	0.45	3%
h Percentile (all ages)	2.44	16%

ea

w- and No- Calorie eetener Users	Sucralose Intake (mg/kg bw/day)	Percent of ADI (ADI=15 mg/kg bw/day; Europe)
ean		
2 years	0.23	0.15%

CE-K DIETARY EXPOSURES ARE A SMALL FRACTION OF THE ADI

imated daily intakes in the Italian population (n = 3270): C. Le Donne et al. 2017

w- and No- Calorie veetener Users	ACE-K Intake (mg/kg bw/day)	Percent of ADI (ADI=9 mg/kg bw/day; Europe)
l Low-Calorie Sweetener Users		
ean	0.46	5%
th Percentile	2.2	24%

mated daily intakes in Irish pre-school children Martyn et al., 2016

w- and No- Calorie veetener Users	ACE-K Intake (mg/kg bw/day)	Percent of ADI (ADI=9 mg/kg bw/day; Europe)
l Low-Calorie Sweetener Users		
ean	0.51	6
th Percentile	2.0	22%

LOBAL REGULATORY
ANDSCAPE

ICS HAVE BEEN REVIEWED BY SAFETY EXPERTS AROUND THE WORLD

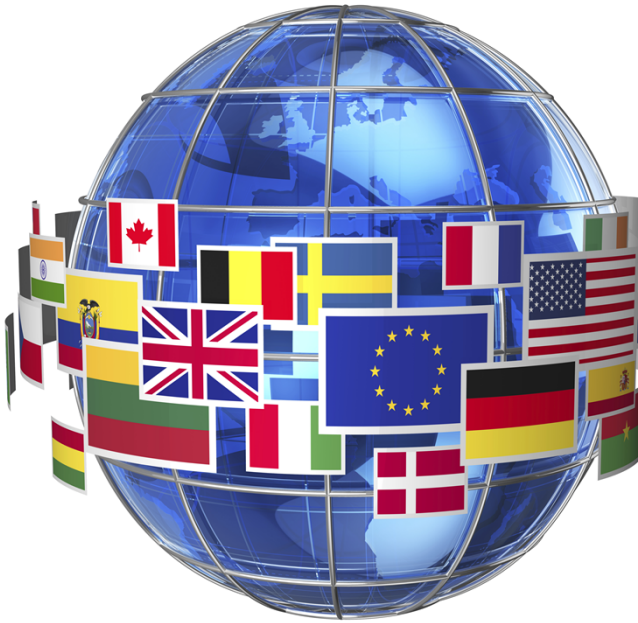
ependent safety reviews by major regulatory authorities

- Joint FAO/WHO Expert Committee on Food Additives (JECFA)
- European Food Safety Authority (EFSA)
- US Food and Drug Administration (FDA)
- Health Canada (HC)
- Food Safety Australia/New Zealand (FSANZ)

Regulatory authorities establish the Acceptable Daily Intake

- Will advise if any special warnings or labeling requirements are needed

All major authorities support the safety for LNCS across all age groups and sensitive sub-populations (e.g. pregnant women, children)



U RE-EVALUATION PROCESS

In the European Union LCS permitted/approved **before 20 January 2009 are required to undergo a thorough new risk assessment** by the European Food Safety Authority (EFSA).

Commission Regulation (EU) No 257/2010 set up a programme for the re-evaluation of approved LCS in accordance with Regulation (EC) No 1333/2008.

Therefore other than aspartame, advantame and steviol glycosides all LCS including acesulfame K, alitame, cyclamate, neotame, NHDC, saccharin, sucralose and thaumatin will be re-evaluated.

The submissions for re-evaluation is required to be submitted by June 2018 and will be evaluated by 2020.

ABELING

erview of Common Practices around the rld

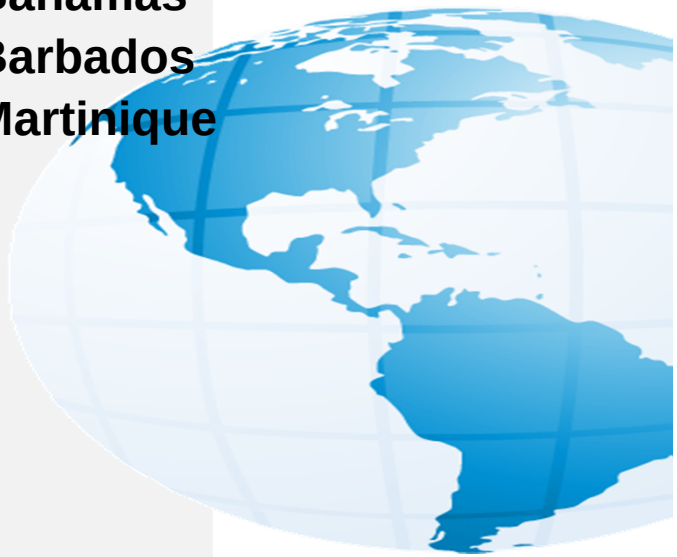
IE MAJORITY OF COUNTRIES AROUND THE WORLD DO NOT REQUIRE ARNING LABEL STATEMENTS FOR LNCS BASED ON AGE OR PREGNANCY

ngapore
hailand
hilippines
etnam
apan
orea
ong Kong
aiwan
hina
ew Zealand
ustralia
zerbaijan
rmenia

Georgia
Kazakhstan
Israel
EU (27 countries)
Tanzania
Zimbabwe
Morocco
Tunisia
Nigeria
Central Africa
Egypt
Iraq

Gulf and Yemen
Iran
Jordan
Lebanon
Syria
United States
Canada
Mexico
Brazil
Peru
Bolivia
Paraguay
Uruguay
Argentina

Colombia
Costa Rica
Aruba
Bahamas
Barbados
Martinique



consumers with phenylketonuria, each geography above requires a statement for aspartame
contains a source of phenylalanine: aspartame)

HENYLKETONURIA IS A RARE CONDITION IN CERTAIN INDIVIDUALS

Phenylketonuria is a rare inherited condition affecting 1 in 10,000 people (USA)

The incidence in India is estimated to be 1 in 18,000 people

Individuals with PKU lack the enzyme that converts phenylalanine into the amino acid tyrosine

People with PKU must manage their intake of phenylalanine from all dietary sources

For the benefit of individuals with PKU, foods and beverages that contain aspartame carry a label statement indicating the products contains phenylalanine. Example: **Contains a Source of Phenylalanine**

Common sources of phenylalanine in the diet include

- meats
- cheese
- poultry
- eggs
- milk/dairy products

UMMARY AND CONCLUSIONS

All LNCS undergo an extensive toxicological program in support of safety

All LNCS are reviewed thoroughly by Regulatory Experts and Authorities around the world who then set the ADI

The ADI covers all sensitive groups including children and pregnant women

Data shows human exposures below the ADI

Only warning labelling required for aspartame related to PKU

IANK YOU!

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