Risk Assessment- Case Studies

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Risk Assessment of Chemicals

Contaminants Additives

Threshold Chemicals - Acceptable Daily Intake

Health based guideline value for Additives - ADI

The Acceptable Daily Intake (ADI) is defined as an estimate of the amount of a food additive, expressed on a bodyweight basis that can be ingested on a daily basis over a lifetime without appreciable risk to health.
"Without appreciable risk" means based on the current knowledge, certainty that no harm will result, even after a lifetime of exposure to the additive concerned.

Risk Assessment

Hazard Identification

Hazard Characterization

Exposure Assessment

Risk Characterization

Back ground

Colours Food - Textile dyes

Project on synthetic food colours (Ministry of Food Processing)
Recommended to reduce permitted levels in selected colours–
Not effected – Illegal use vs legal limits

Artificial sweeteners - Story of Saccharin

Unconditional ADI 0-5.0mg/kgbw (11th &18th JECFA meetings)
Rat study " Excessive and long term ingestion of Saccharine might represent carcinogenic hazard
Temporary ADI 0-2.5mg/kgbw (21st JECFA meeting)

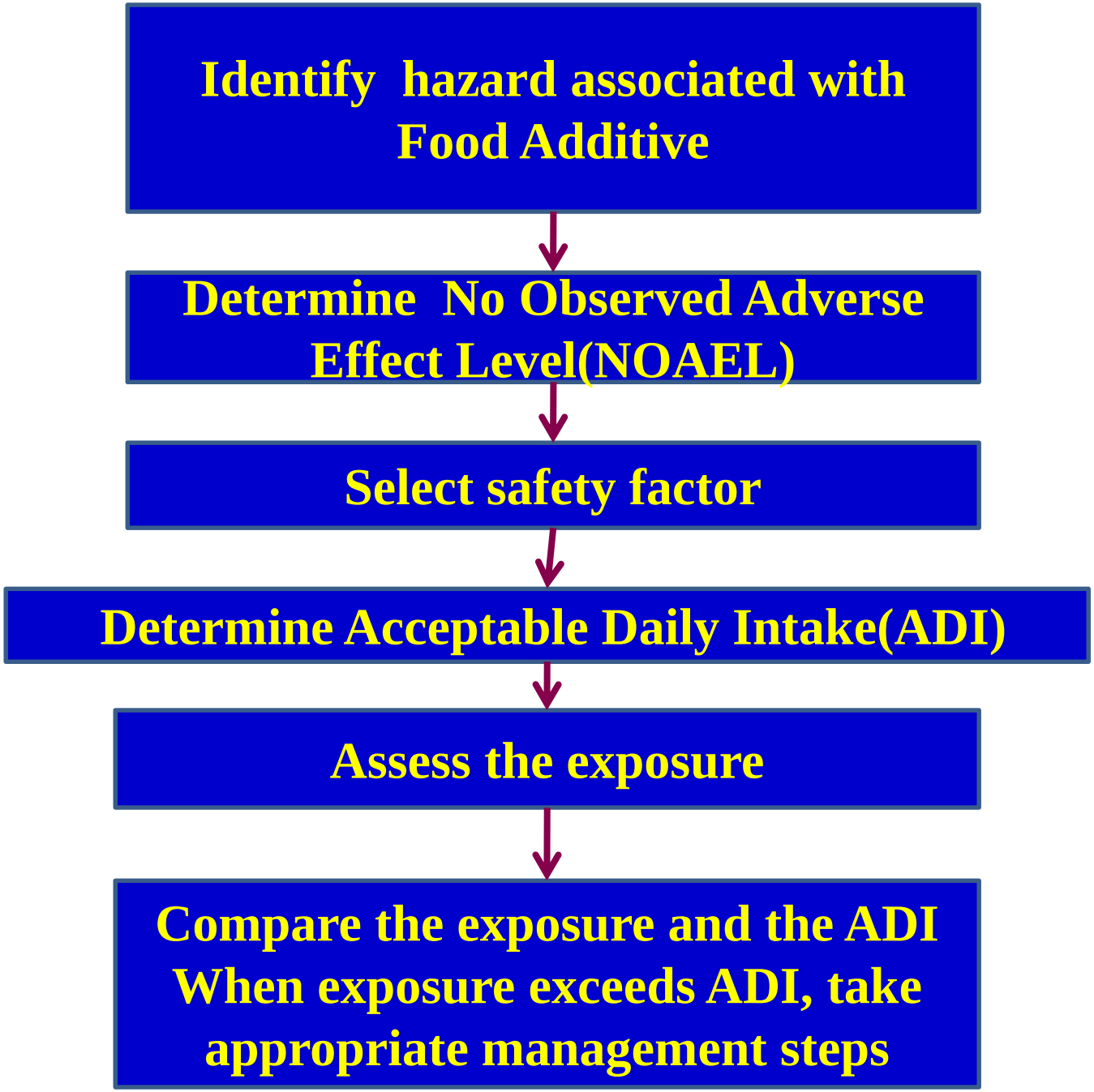
Unconditional ADI 0-5.0mg/kgbw (28th JECFA meeting)

Risk Assessment of Synthetic Food Colours: A Case Study in Hyderabad (Rao & Rao Int. J. Food Safety & Public Health, 2008)

Target population - children

Food Frequency and Laboratory analysis of food samples

Few cases, where ADI of certain colours is crossed on a single day consumption basis, but it was essentially on account of illegal use(beyond permitted limits)


Identify hazard associated with Food Additive
Determine No Observed Adverse Effect Level(NOAEL)
Select safety factor
Determine Acceptable Daily Intake(ADI)
Assess the exposure
Compare the exposure and the ADI When exposure exceeds ADI, take appropriate management steps

Food Colours

Concerns and Perceptions

Colours - Natural vs Synthetic
Permitted vs Non permitted
Regulatory limits vs technological function
Prevention of fraud

S.No	Name of the food colour	INS No	ADI (mg/ kg bw)
1	**Erythrosine** (No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	127	0-0.1
2	**Ponceau 4R** No. of permitted food items = 40; No. of consumption data available permitted food items = 7	124	0-4.0
3	**Carmoisine** (No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	122	0-4.0
4	**Sunset Yellow FCF** (No. of permitted food items = 15; No. of consumption data available permitted food items = 5)	110	0-4.0
5	**Indigo carmine** (No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	132	0-5.0
6	**Tartrazine** No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	102	0-7.5
7	**Brilliant blue FCF** (No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	133	0-12.5
	Fast green FCF No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	143	0-25.0

S.No	Name of the food colour	INS No	ADI (mg/ kg bw)
1	**Canthaxanthin** (No. of permitted food items = 4; No. of consumption data available permitted food items = 2)	**161g**	**0-0.03**
2	**Riboflavin** (No. of permitted food items = 7; No. of consumption data available permitted food items = 2)	**101**	**0-0.5**
3	**Curcumin** (No. of permitted food items = 9; No. of consumption data available permitted food items = 2)	**100ii**	**0-4.0**
4	**Beta carotene** (No. of permitted food items = 20; No. of consumption data available permitted food items = 2)	**160a**	**0-5.0**
5	**Beta - apo - 8' – carotenal** (No. of permitted food items = 10; No. of consumption data available permitted food items = 5)	**160e**	**0-5.0**
6	**Ethylester of Beta apo-8 carotenic acid** (No. of permitted food items = 2; No. of consumption data available permitted food items = 1)	**160f**	**0-5.0**
7	**Annatto extracts** (No. of permitted food items = 22; No. of consumption data available permitted food items = 2)	**160b**	**0-12.0**
8	**Caramel** (No. of permitted food items = 5; No. of consumption data available permitted food items = 2)	**150**	**0-160.0**

Approaches Food Consumption data

Population based - per capita consumption
Not generally useful
for food additives

Household based - Provides consumption
at household level
Not at individual level

Individual based - More closely reflect actual consumption
Bias

Consumption of selected processed foods Rural (g or ml/day)

Food	Mean	Median	95th Percentile
Biscuits	18.06	8.14	52.0
Candies	1.17	0.50	4.57
Carbonated beverages	11.78	6.67	35.71
Chocolates	4.08	2.29	13.71
Malted & other beverages	29.12	5.0	200.0
Ice cream	4.63	1.67	14.29
Jam	1.22	0.86	4.29
Chips	6.74	2.83	22.86

Consumption of selected processed foods Urban-HIG(g/ml/day

Food	Mean	Median	95th Percentile
Biscuits	6.79	5.71	24.0
Candies	2.00	2.00	2.00
Carbonated beverages	26.56	8.30	200.00
Chocolates	4.24	2.67	14.29
Malted & other beverages	52.72	20.00	250.0
Ice cream	7.99	5.00	28.57
Jam	4.62	1.43	20.00
Chips	8.90	4.29	28.57

Assumptions

1. All the colours are used at permitted levels
2. A person consumes all the foods where these additives are added

Food consumption data:

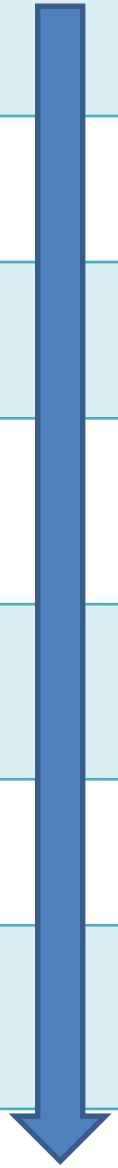
Food consumption data is taken from recently(2012) completed study

2. Data is computed only on foods where the consumption data is available

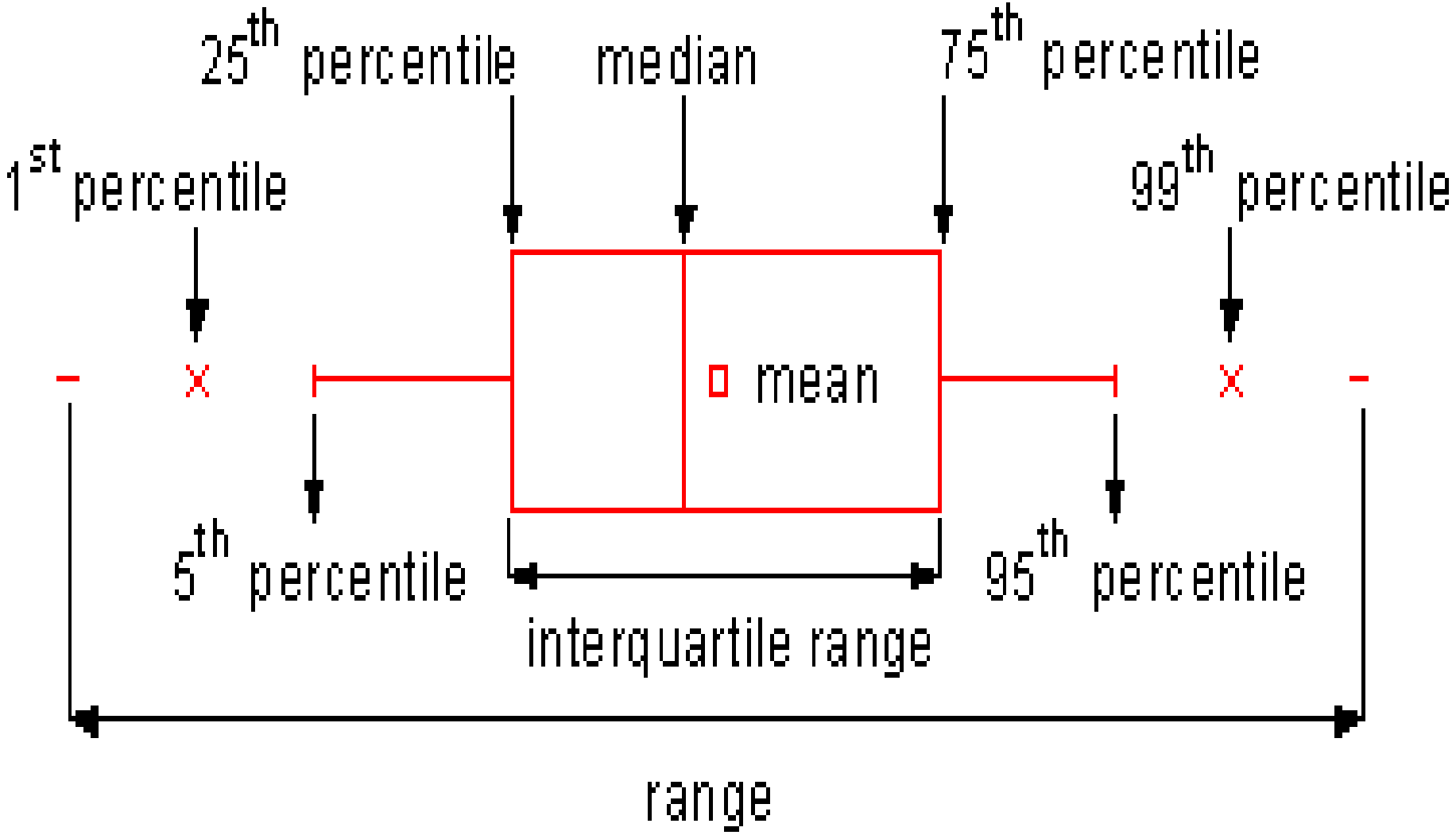
Body weight

Body used for ADI calculation is 50kg

S.No	Name of the food colour	INS No	ADI (mg/ kg bw)	Percentage of ADI at Mean value	Percentage of ADI at 95th percentile value
1	**Erythrosine** (No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	127	0-0.1	96 %	537.6 %
	Ponceau 4R No. of permitted food items = 40; No. of consumption data available permitted food items = 7	124	0-4	3.11 %	15.44 %
3	**Carmoisine** (No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	122	0-4	2.4 %	13.44 %
	Sunset Yellow FCF (No. of permitted food items = 15; No. of consumption data available permitted food items = 5)	110	0-4	2.4 %	13.44 %
5	**Indigo carmine** No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	132	0-5	1.92 %	10.75 %
	Tartrazine No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	102	0-7.5	1.28 %	7.1 %
7	**Brilliant blue FCF** (No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	133	0-12.5	0.7 %	4.3 %
	Fast green FCF No. of permitted food items = 14; No. of consumption data available permitted food items = 5)	143	0-25	0.38 %	2.15 %



S.No	Name of the food colour	INS No	ADI (mg/ kg bw)	Percentage of ADI at Mean value	Percentage of ADI at 95th percentile value
1	**Canthaxanthin** (No. of permitted food items = 4; No. of consumption data available permitted food items = 2)	**161g**	**0-0.03**	**81.3 %**	**285.3 %**
2	**Riboflavin** (No. of permitted food items = 7; No. of consumption data available permitted food items = 2)	**101**	**0-0.5**	**4.88 %**	**17.1 %**
3	**Curcumin** (No. of permitted food items = 9; No. of consumption data available permitted food items = 2)	**100ii**	**0-4**	**0.8 %**	**2.85 %**
4	**Beta carotene** (No. of permitted food items = 20; No. of consumption data available permitted food items = 2)	**160a**	**0-5**	**0.48 %**	**1.71 %**
5	**Beta - apo - 8' – carotenal** (No. of permitted food items = 10; No. of consumption data available permitted food items = 5)	**160e**	**0-5**	**0.48 %**	**1.71 %**
6	**Ethylester of Beta apo-8 carotenic acid** (No. of permitted food items = 2; No. of consumption data available permitted food items = 1)	**160f**	**0-5**	**0.16 %**	**0.57 %**
7	**Annatto extracts** (No. of permitted food items = 22; No. of consumption data available permitted food items = 2)	**160b**	**0-12**	**0.2 %**	**0.71 %**
8	**Caramel** (No. of permitted food items = 5; No. of consumption data available permitted food items = 2)	**150**	**0-160**	**0.3 %**	**1.08 %**

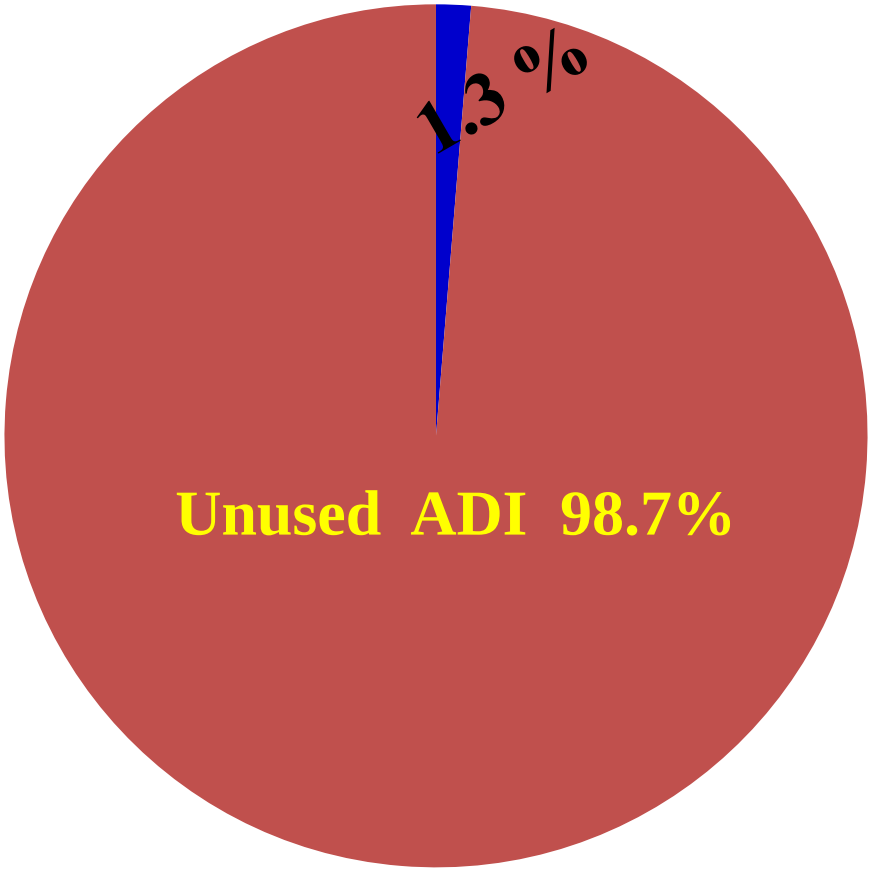

25th percentile
median
75th percentile
1st percentile
99th percentile
mean
5th percentile
95th percentile
interquartile range
range

Southampton Study – Hyper activity in children

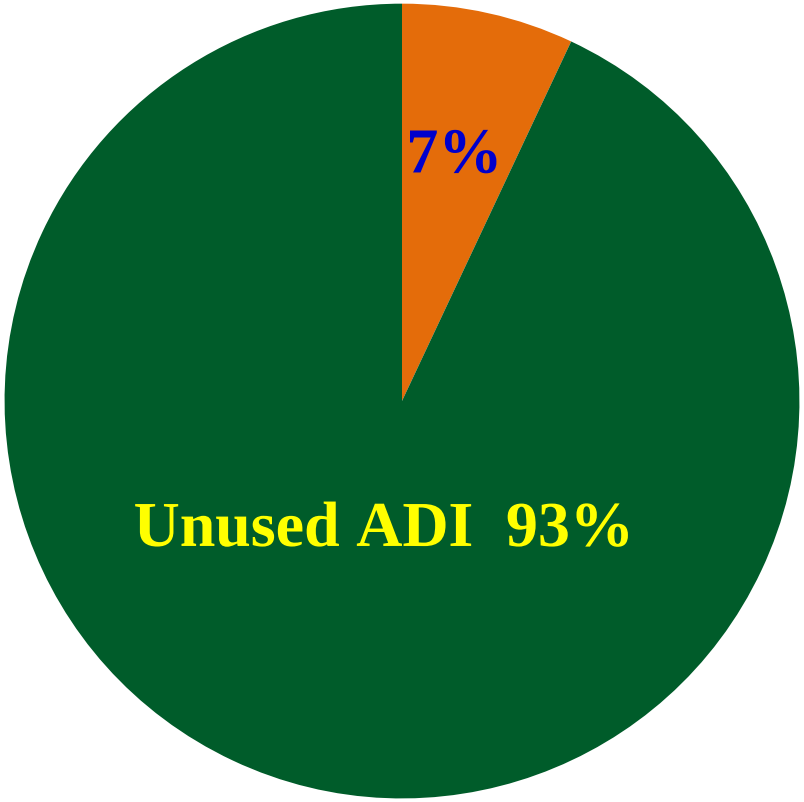
Further evaluation of the Food colours **sunset yellow** (E110), Quinoline **yellow** (E104), Carmoisine (E122), Allura **red** (E129), Tartrazine (E102) and Ponceau 4R (E124)

The European Food Safety Authority (EFSA) has recommended further safety tests for six food dyes – including five of the so-called Southampton Six colours – *although it says currently there is no reason to revise the acceptable daily intake (ADI).*

Percentage of ADI used up for Tartrazine at mean intake of colored food

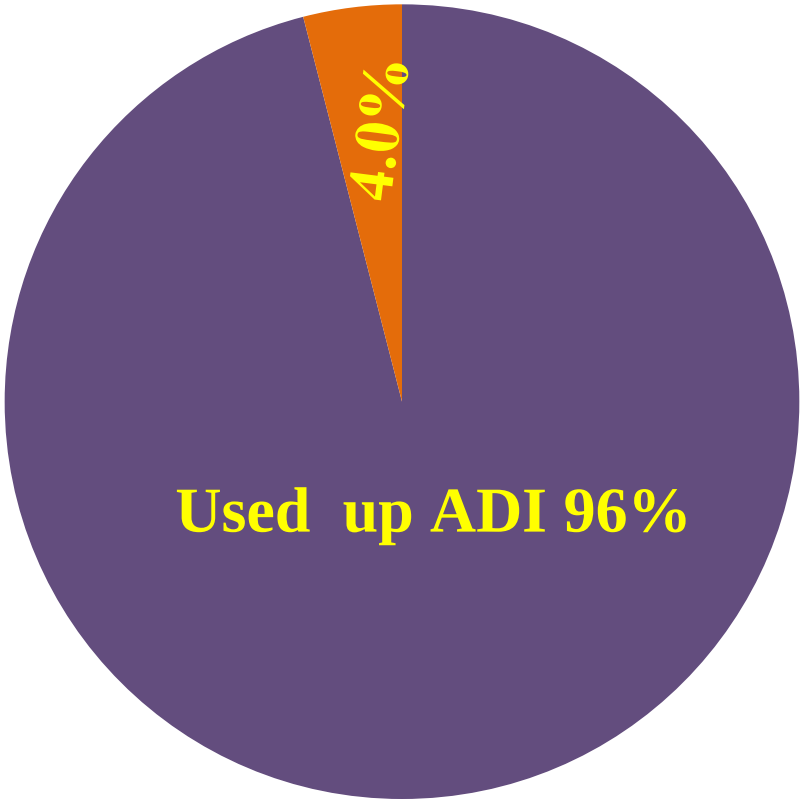


Percentage of ADI used up for Tartrazine at 95th percentile intake of colored food



Exposure assessment of Erythrosine

Percentage of ADI used up for Erythrosine at mean intake of colored food



Erythrosine

Lowest Observed Adverse Effect Level (LOAEL) is 200mg oral dose/14days in humans had increased Thyroid secretions (Hyperthyroidism)

60mg oral dose had no effect -No Observed Adverse Effect Level(NOAEL)
60/60= 1mg/kg bw with a safety factor of 10
ADI 0-0.1mg/kg bw

Evaluated in 2018 and No change in ADI

Erythrosine - Hazard Identification

“The studies on rat showed a rapid onset in the expected hormonal changes of a statistically significant rise in serum levels of thyrotropin, thyroxine (T_4), and 3,3,5'-triiodothyronine (rT_3), and a decrease in serum 3,5,3'-triiodothyronine (T_3) after ingestion of 40 mg/kg erythrosine in the diet. A no-observed-effect level of 0.6 mg/kg erythrosine in the diet corresponding to 30 mg per kg of body weight per day was obtained.
The changes seen in these studies are consistent with the hypothesis that erythrosine inhibits the hepatic conversion of circulating T_4 to T_3, and the resulting decrease in the concentration of T_3 stimulates the serial release of thyrotropin-releasing hormone from the hypothalamus and then thyrotropin from the pituitary.The sustained increases in the levels of thyrotropin produce hyperstimulation of the thyroid, which may be associated with the tumorigenic effects “

(FAS 28-JECFA 37/171)

ADI based on Human volunteers study

"In view of the differences in thyroid physiology between humans and rats the Committee based its evaluation on the previously reported no-observed-effect level derived from human data. Therefore the Committee allocated an ADI of 0-0.1 mg/kg of body weight for erythrosine, based on the no-effect-level at 60 mg per person per day (equivalent to 1 mg per kg body weight per day) and a safety factor of 10"

(FAS 28-JECFA 37/171)

Canthaxanthin – Hazard Identification

Lowest Observed Adverse Effect Level(LOAEL) is 0.30mg/kgbw , based on formation of crystalline deposits in the Retina both in monkeys and humans

No Observed Adverse Effect Level(NOAEL) is 0.25mg/kgbw based human study where they have given 15mg/day which had no effect on the subjects.

ADI NOAEL/10 = 0.03mg/kgbw

Body weights

Body weights of Adult men* (>18yrs) Rural

Percentiles	Body weight (in Kg)
5	41.10
10	43.70
25	49.17
50	55.85
75	63.02
95	76.30

Body weights of Adult men* (>18yrs) Urban

Percentiles	Body weight (in Kg)
5	44.84
10	48.20
25	54.00
50	62.40
75	70.30
95	86.00

Body weights of Adult women* (>18yrs) Urban

Percentiles	Body weight (in Kg)
5	38.50
10	41.50
25	47.90
50	55.30
75	62.90
95	76.50

Body weights of Adult women* (>18yrs) Rural

Percentiles	Body weight (in Kg)
5	34.90
10	37.40
25	41.80
50	48.00
75	55.60
95	69.00

* n= 4029

Reference body weights for Indians

Adult 50kg

Child 15kg

Erythrosine intake - 96% of ADI for Adult
- 316% of ADI for Child

Canthaxanthin - 81% of ADI for Adult
- 268% of ADI for Child

Artificial Sweeteners

Concerns and perceptions

Cancers - policy for permitting any additive – Only threshold chemicals

Artificial/synthetic -Not safe

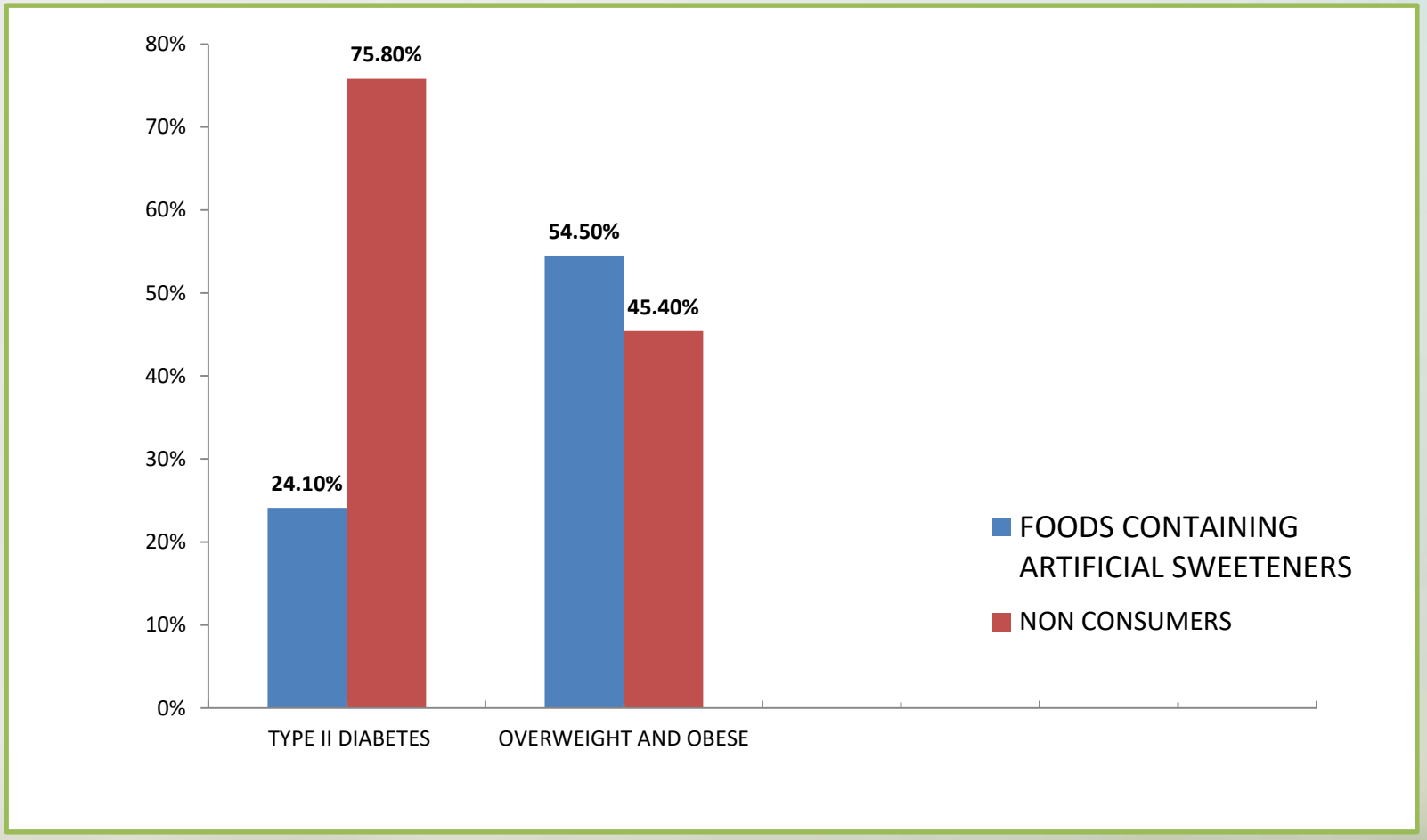
CHARACTERISTICS OF THE SWEETENERS

Sweetener	Sweetness (compared with sucrose)	JECFA ADI (mg/kg body weight/day)	Characteristics
Aspartame	180-200	0-40	white, odorless, crystalline powder, slightly soluble in water ,provides 4 kcal/g
Acesulfame-k	200	0-15	Odorless, white crystalline powder, flavor enhancer, but high concentrations may lead slight after taste.
Sucralose	600	0-15	Since 1998 it was in use as additive in 15 food categories, including tabletop sweetener, White to off-white, odorless crystalline powder, heat and ph stable
Saccharin	300	0-5	White crystals or a white, crystalline powder, odorless or with a faint, aromatic odor, bitter or metallic aftertaste,
Neotame	7000-13000	0-2	White to half white powder, manufactured from aspartame, heat stable & completely eliminated

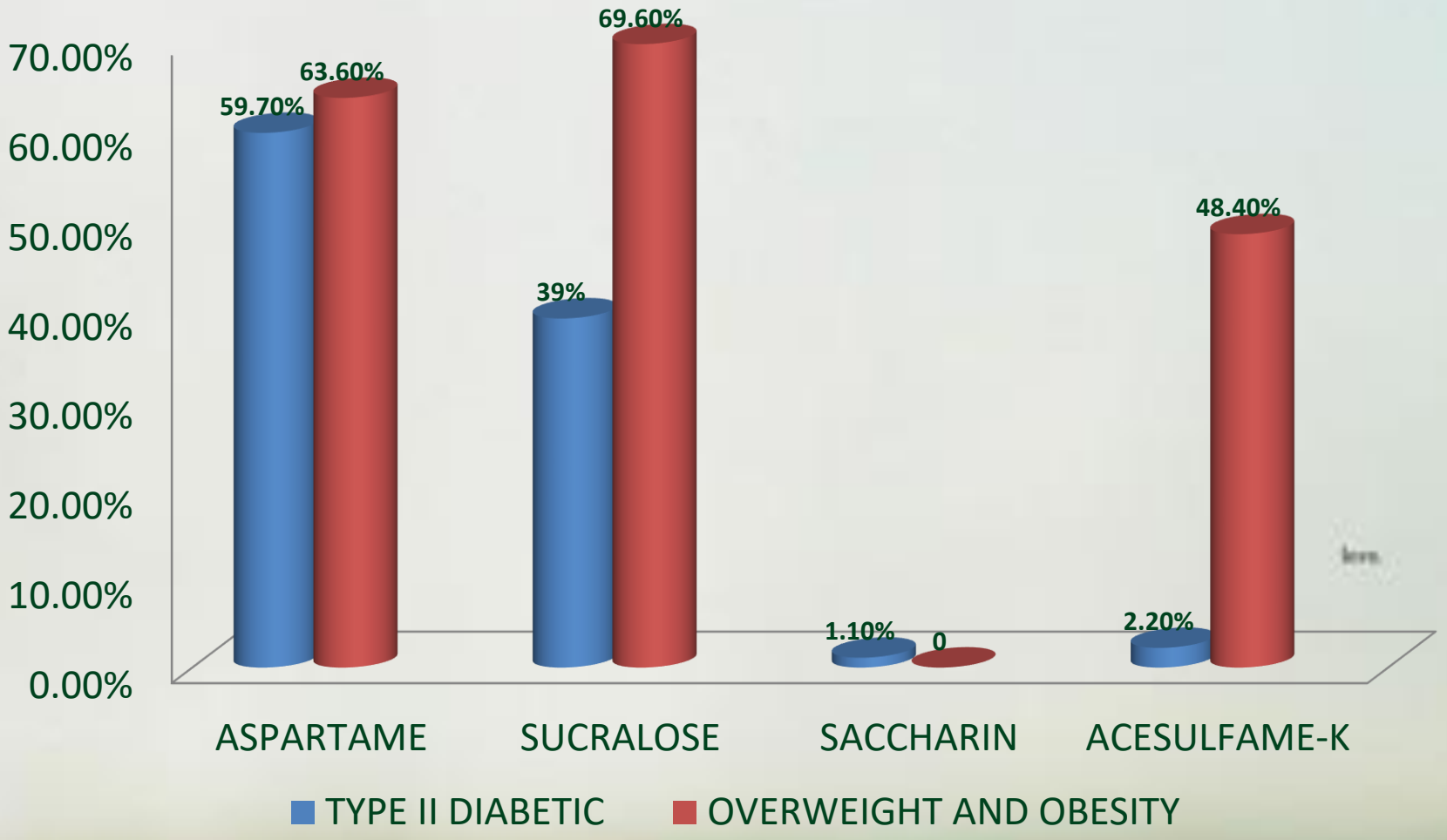
Commonly Prepared Sugar Free Sweets

Sweets	Sweetener used	Weight of each sweet (g)	Amount of sweetener in one unit of sweet (mg)
1.Sugarfree angeer rolls	relish(sucralose)	29.16±3.76	7.29±0.94
2.Sugarfree ragi laddu	relish(sucralose)	45.83±3.76	18.79±1.54
3.Sugarfree badusha	relish(sucralose)	52.66±5.35	21.96±2.23
4.Sugarfree agmeri kalakanda	relish(sucralose)	45±6.32	3.6±0.50
5.Sugarfree kaju barfi	relish(sucralose)	40±3.16	6.67±0.54
6.Sugarfree kajukathli	relish(sucralose)	9.83±0.40	6.67±0.54
7.Sugarfree gondh laddu	relish(sucralose)	50.16±1.60	20.56±0.65
8.Sugarfree mothichurladdu	relish(sucralose)	44.83±2.56	7.62±0.43
9.Sugarfree mysore pak	relish(sucralose)	35±5.17	11.68±1.72
10.Sugarfree sunnunda	relish(sucralose)	42.33±2.58	14.13±0.86
11.Sugarfree kova pure	relish(sucralose)	47.66±2.33	11.91±0.58
12. Sugarfree kalakanda	relish(sucralose)	45±6.32	3.6±0.50

Comparing percentage intake of foods containing artificial sweeteners and non consumers among the type 2 diabetic, overweight and obese individuals



consumption pattern of sweeteners among regular consumers



Comparison of mean daily intake of type 2 diabetic individuals [n=87] with ADI

Sweetener	Percentage consumption (%)	Intake (mg/kg/day) Mean±SD	Range	JECFA (mg/kg/day)	% ADI
Aspartame	52(59.7)	0.85±0.74	0.01-2.89	40	2.1
Sucralose	34(39)	0.41±0.46	0.01-1.87	15	2.6
Saccharin	1(1.1)	0.002±0.0	0-0.002	5	0.04
Acesulfame-k	2(2.2)	0.035±0.007	0.03-0.04	15	0.2

Total number of subjects exceed because, people had more than one sweetener through their foods

Mean daily intake of individual sweeteners among overweight and obese individuals [n=33] and its percentage comparison with ADI

Sweetener	Percentage consumption n (%)	Intake (mg/kg/day) Mean±SD	Range	JECFA (mg/kg/day)	% ADI
Aspartame	21(63.6)	0.65±0.52	0.06-1.38	40	1.62
Sucralose	23 (69.6)	0.41±0.11	0.29-0.61	15	**2.73**
Saccharin	0(0)	-	-	5	-
Acesulfame-k	16(48.4)	0.15±0.05	0.04-0.21	15	1.0

Total number of subjects exceeds, because some people were having more than one sweetener through their diet foods

To conclude

Prioritization of Food Additives for RA based on Health based guideline value

Low ADI + High consumption

Higher authorization + High consumption

Thank you for your attention

Estimates of intakes of BHT (Example)

First level screening by Budget method ----- Exceeded the ADI

Estimates provided by 10 countries - using GSFA levels of use - consistently exceeded ADI

Mean intake	230 %	ADI China
	240%	ADI US
High intake	600-2000 %	ADI

Intake estimates using national levels of use

% of ADI	Method of estimate
30	Poundage method
20-30	Household surveys and sales data
10-30	Model diet
0.1-30	Individual data
0.003	Total diet study (Japan)

Conclusion : Unlikely to exceed ADI

Recommendation: May review MLs potentially contributing to high intake ie Fats and oils free from water, chewing gum & processed fish and fish products