NOTE ON NON SUGAR SWEETENERS(NSS) & ASPARTAME

Highlights of the WHO Report:

1, The World Health Organization (WHO) released a new guideline on NSS, in May 2023 with a conditional recommendation against the use of NSS to control body weight or to reduce the risk of non-communicable diseases (NCDs).

2. The WHO recommendation was based on the findings of a systematic review of the available evidence which suggests that use of NSS does not confer any long-term benefitin reducing body fat in adults or children.

3. Results of the review also suggest that there may be potential undesirable effects from long-term use of NSS, such as an increased risk of type 2 diabetes, cardiovascular diseases, and mortality in adults. However, the WHO report also suggests that the certainty of these findings ranges from very low to low and that is why the recommendation is conditional. A "Conditional" recommendation by WHO means that there is a no certainty or a varying degree of certainty about the statement being made.

4. The guideline further suggests that "Replacing free sugars with NSS does not help with weight control in the long term. People need to consider other ways to reduce free sugars intake, such as consuming food with naturally occurring sugars, like fruit, or unsweetened food and beverages," and that "NSS are not essential dietary factors and have no nutritional value.

Recommendations of the Scientific Panel on the WHO Report:

The WHO's new guideline on non-sugar sweetener (NSS) was deliberated in the 22nd & 23rd Scientific panel meeting of Nutrition and Fortification (held on 23.05.23 & 6.07.23 respectively). Views & Opinion of experts from Medical fraternity, Scientist, Nutritionist and Academicians were also sought. The outcome of the deliberation is listed below:

a. The WHO guidelines are conditional and there is a need for country specific meaningful discussions.
b. There is low to very low positive association found across many of the outcomes and is not prudent to arrive at a conclusion based on this advice.
c. No RCT data is available on cancer and in the absence of evidence it may not be relevant to state that consuming NSS has association with the occurrence of cancer.
d. One of the limitations of this study was the inability to assess the health effects of individual sweeteners with prolonged use such as stevia and monk fruit.
e. The dietary habits of Indians are entirely different and the WHO document has not made any reference/ study conducted on Asian population particularly Indian population.
f. The Weight management in itself is very complex and many confounding factors

are associated with it. The WHO document has not considered any of the important factors such as lifestyle modification, diet control, regular exercise etc.

g. The Food Authority has a separate regulation in place for the weight management for products manufactured domestically /imported to India.
h. To put it in a nutshell the WHO guideline is inconclusive and several important factors have not been considered in the analysis of RCT, Prospective CohortStudies and Case control studies and hence in the current scenario no sufficient/ substantive data is available to revise the existing FSSAI recommendation.
i. The guideline further suggests that "Replacing free sugars with NSS does not help with weight control in the long term. People need to consider other ways to reduce free sugars intake, such as consuming food with naturally occurring sugars, like fruit, or unsweetened food and beverages.

The WHO guideline can be used to educate consumers and create awareness through Eat right India movement and create awareness among the consumers to consume artificially sweetened products in moderation.

Evaluation of the health effects of Aspartame consumption:

1. "WHO's cancer research agency (IARC) to say aspartame sweetener a possible carcinogen -sources" was discussed in the 23rd meeting of Scientific panel on Nutrition and Fortification held on 6th July, 2023.
2. The panel stated that, as per FSS (Food Products Standards and Food Additives) Regulation, 2011, every package containing the Aspartame (Methyl ester), in food and advertisement shall carry the prescribed warning for vulnerable population. Aspartame is thoroughly reviewed and assessed by JECFA. The panel agreed that there is no convincing evidence on the adverse effect of Aspartame with the existing literature /available studies. The Panel further opined that the issue may further be reviewed post obtaining the IARC's hazard identification and JECFA's risk assessment report.

The Summary of findings of the evaluation of aspartame at the International Agency for Research on Cancer (IARC) and Joint Expert Committee on Food Additives (JECFA):

The Summary and conclusions of the Ninety-sixth meeting of the Joint FAO/WHO Executive Committee on Food Additives issued on 14th July, 2023 was presented before the 46th Scientific Committee meeting of FSSAI held on 23rd July 2023.

The Joint Expert Committee on Food Additives (JECFA) in its twenty-fifth meeting established an ADI of 0–40 mg/kg bodyweight for aspartame. This ADI was based on theNo-Observed-Adverse-Effect Limit (NOAEL) of 4000 mg/kg bodyweight/day. This is thehighest dose tested, in a 104-week study in rats exposed to aspartame in the diet (Ishii et al.) and further a 100-fold uncertainty factor is applied to arrive at ADI. The Committee evaluated the biochemical, toxicological and epidemiological studies on aspartame, its metabolites and degradation products. Committee also assessed the estimates of dietary exposure to aspartame for the first time.

Joint FAO/WHO Executive Committee on Food Additives (JECFA) concluded that there was no convincing evidence from experimental animal or human data that aspartame has adverse effects after ingestion. The JECFA noted that aspartame is fully hydrolysed in the gastrointestinal tract into metabolites & no aspartame enters the systemic circulation as such. The Committee concluded that the data evaluated during the meeting indicated no reason to change the previously established acceptable daily intake (ADI) of 0–40 mg/kg body weight/day for aspartame. The Committee therefore reaffirmed the ADI of 0–40 mg/kg body weight/day for aspartame.

1. It was noted that in the oral aspartame exposure studies in humans at doses up to the current ADI, there were no increases in the plasma concentrations of the metabolites of aspartame.
2. Aspartame has been tested in several in vitro and in vivo genotoxicity assays. Considering the conflicting results and the limited quality of the studies, it was concluded that aspartame does not perform a genotoxic action.
3. JECFA evaluated data from 12 oral carcinogenicity studies of aspartame and identified limitations in all of them.
4. It is noted that all the studies apart from those by Soffritti et al. (2005; 2006; 2007; 2010) showed negative results. The Committee considered the positive findings of Soffritti and colleagues, however found that there were limitations in the study design, execution, reporting and interpretation of these studies.
5. Based on the results of the oral carcinogenicity studies of aspartame, the absence of evidence of geno toxicity and a lack of evidence on a mechanism by which oral exposure to aspartame could induce cancer, JECFA concluded that it is not possible to establish a link between aspartame exposure in animals and the appearance of cancer.
6. The Committee noted that statistically significant increases were reported for some cancers, such as hepatocellular, breast and haematological (non-Hodgkin lymphoma and multiple myeloma) cancers, in some cohort studies conducted with aspartame or beverages containing aspartame as an intense sweetener. However, a consistent association between aspartame consumption and a specific cancer type could not be demonstrated. All the studies had limitations in exposure estimation.
7. IARC evaluation noted limitations in all three streams of evidence (human cancer, cancer in experimental animals, and mechanistic evidence). JECFA have not found convincing evidence of a plausible mechanism leading to adverse effects in animals or humans nor a sufficient number of studies demonstrating such effects.
8. Due to limited / not convincing evidence for cancer in humans, The IARC and JECFA did not rule out the possibility of reverse causality, chance, bias and confounding factors such socioeconomic, lifestyle or consumption of other dietary components.

FSSAI's Position:

Definition of NSS in FSSR:

Non Sugar Sweetener(NSS):

The Non Sugar sweeteners or NSS are widely used food additives and are classified either as "Caloric sweeteners" or "Non– caloric sweeteners" based on the caloric value.

Caloric sweeteners: Substances having greater than 2 percent of the caloric value of sucrose per equivalent unit of sweetening capacity. These include Sorbitol, Sorbitol syrup, Mannitol, Isomalt, Polyglycitol syrup, Maltitol, Maltitol syrup, Lactitol and Xylitol.

Non-caloric sweeteners: Substances having less than 2 percent of the caloric value of sucrose per equivalent unit of sweetening capacity. These include Erythritol, Steviol glycoside, Thaumatin, Aspartame, Sucralose, Neotame, Acesulfame potassium, Aspartame-Acesulfame potassium salt and Saccharins.

The Food Safety and Standards Authority of India (FSSAI) has laid down safety limits for non-caloric sweeteners (NSS) such as stevia, acesulfame potassium, aspartame, sodium and calcium saccharin, sucralose and sorbitol as additives to be used in various food products on the basis of risk assessment and ADI (Acceptable Daily Intake) established by JECFA (Joint Expert Committee on Food Additives) and also in in harmonization with Codex.

It may be pertinent to note that FSSAI has not recommended these NSS for weight loss or maintenance of healthy weight, and as a means of controlling blood glucose in individuals with diabetes.

Further, stricter labelling requirements are in place which require due declarations on the food labels along with the names where such sweeteners have been added either singly or in combination. The Food Authority undertakes thorough scrutiny before allowing any non-caloric sweeteners in food products, keeping in view of the Indian scenario, the global regulatory practices & risk assessments carried out by JECFA.

Conclusion:

FSSAI has taken cognizance on the WHO's report in the Indian context. All the major highlights of the report and the related Scientific facts about the Non-Sugar sweeteners were discussed. It was found that country specific studies are needed to explore the NSS/ Aspartame's impact on metabolic processes, as well as its links to other diseases. FSSAI is in agreement with JECFA & IARC conclusions & accord the response of other global regulatory bodies. In the absence of substantive established evidence on the safety of NSS/ Aspartame, FSSAI is retaining the existing limits. However, the WHO's guidelines on NSS shall be used to provide guidance to public & health professionals to reduce their daily intake of simple sugars, promote healthy diets and prevent overweight & obesity and diet-related Non Communicable Diseases(NCD). WHO's report should be used to educate and sensitize

consumers, create awareness and engage people to consume NSS/artificially sweetened products and other foods high in sugar, salt, and fats (HFSS) in moderation.

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1. Dr. S N Jha, Chairperson of SC
2. Dr. Anu Appaiah, Independent Member
3. Dr. Shashank Joshi, Independent Member
4. Dr. Vasudeva Singh, Independent Member
5. Dr. Alka Rao, Chairperson, Scientific Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials (SP-01)
6. Dr. Paresh Govindlal Shah, Chairperson, Scientific Panel on Pesticide Residues (SP-02)
7. Prof. Bikash Medhi, Chairperson, Scientific Panel on Antibiotic Residues (SP-03)
8. Dr. Dinesh Kumar, Chairperson, Scientific Panel on Genetically Modified Organisms and Foods (SP-04)
9. Dr. Sukhadeo B Barbuddhe, Chairperson, Scientific Panel on Biological Hazards (SP-06)
10. Prof. Alok Dhawan, Chairperson, Scientific Panel on Contaminants in the Food Chain (SP-07) *(online)*
11. Dr. SubbaRao M Gavaravarapu Chairperson, Scientific Panel on Labelling & Claims/Advertisements (SP-08)
12. Dr. Kaushik Banerjee, Chairperson, Scientific Panel on Methods of Sampling and Analysis (SP-09)
13. Dr. Joykrushna Jena, Chairperson, Scientific Panel on Fish and Fisheries Products (SP-10)
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16. Prof. Pankaj Kumar Shukla, Chairperson, Scientific Panel on Meat and Meat Products including Poultry (SP-13) *(online)*
17. Dr. Ravinder Kumar Malik, Chairperson, Scientific Panel on Milk and Milk Products (SP-14)
18. Dr. Ram Rajasekharan, Chairperson, Scientific Panel on Oils and Fats (SP-15)
19. Dr. TSR Murli, Chairperson, Scientific Panel on Sweets and Confectionery (SP-16)
20. Dr. C.V. Rode, Chairperson, Scientific Panel on Water and Beverages (SP-17)
21. Dr. Sirimavo Nair, Chairperson, Scientific Panel on Nutrition and Fortification (SP-18)
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Documents / Publications:

1. Use of non-sugar sweeteners WHO guideline ISBN 978-92-4-007361-6 (electronic version)
2. WHO's cancer research agency to say aspartame sweetener a possiblecarcinogen-sources.(https://www.reuters.com/business/healthcare- pharmaceuticals/whos-cancer-research-agency-say-aspartame-sweetener- possible-carcinogen-sources-2023-06-29/)
3. Summary of findings of the evaluation of aspartame at the International Agency for Research on Cancer (IARC) Monographs Programme's 134th Meeting, 6–13 June 2023 and The Joint FAO/WHO Expert Committee On Food Additives (JECFA) 96th Meeting, 27 June–6 July 2023
4. Joint FAO/WHO Expert Committee on Food Additives, Ninety-sixth meeting (Safety evaluation of certain food additives), 27 June–6 July 2023, summary and conclusions, Issued on 14 July 2023

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1. Anna Palomar-Cros et al.,consumption of aspartame and other artificial sweeteners and risk of cancer in the Spanish multicase-control study (MCC- Spain):Int J Cancer 2023 Sep 1;153(5):979-993. doi: 10.1002/ijc.34577. Epub 2023 Jun 16.

2. B A Magnuson et.al, Aspartame: a safety evaluation based on current use levels, regulations, and toxicological and epidemiological studies: Crit Rev Toxicol. 2007;37(8):629-727. doi: 10.1080/10408440701516184.
3. Susan A Elmore et.al, Pathologists' perspective on the study design, analysis, and interpretation of proliferative lesions in lifetime and prenatal rodent carcinogenicity bioassays of aspartame: Food Chem Toxicol.2023 Jan;171: 113504.doi: 10.1016/j.fct.2022.113504.
4. Shoumeng Yan et.al.Can Artificial Sweeteners Increase the Risk of Cancer Incidence and Mortality: Evidence from Prospective Studies:Nutrients.2022 Sep 10;14(18):3742. doi:10.3390/nu14183742.