

# HOT OFF THE PRESS

# "WHAT DOES DR. B THINK OF ASPARTAME BEING CLASSIFIED AS A POSSIBLE CARCINOGEN BY THE WORLD HEALTH ORGANIZATION?"

There are so many fresh, interesting studies that I'd like to break down, but this newsletter comes to you by popular demand.

We've received message after message asking,

> ***"What does Dr. B think of aspartame being classified as a possible carcinogen by the World Health Organization?"***

## LET'S GET RIGHT INTO IT.

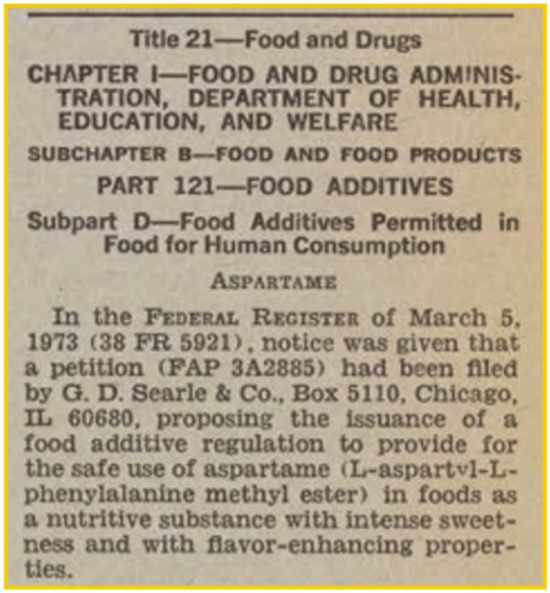
# WHAT THEY STUDIED

Aspartame is an artificial sweetener, perhaps the most consumed artificial sweetener on the market. In the US, more than 6,000 manufactured (ultra-processed) products, including:

- Diet or zero-sugar beverages, including Diet Coke
- Sugar-free gelatin, such as Sugar-free Jell-O
- Diet drink mixes like Crystal Light
- Sugar-free gums like Trident
- Tabletop sweeteners like Equal and Nutrasweet

The majority of aspartame consumption comes from diet sodas, accounting for 90% of the exposure in some populations. Aspartame was first approved by the Food and Drug Administration in 1974.

*(Check this out, **I tracked down the yellow, dated pages** from the announcement... There's no reference to websites or social media handles and it's printed on this stuff called paper. )*



Title 21—Food and Drugs

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

SUBCHAPTER B—FOOD AND FOOD PRODUCTS

PART 121—FOOD ADDITIVES

Subpart D—Food Additives Permitted in Food for Human Consumption

ASPARTAME

In the FEDERAL REGISTER of March 5, 1973 (38 FR 5921), notice was given that a petition (FAP 3A2885) had been filed by G. D. Searle & Co., Box 5110, Chicago, IL 60680, proposing the issuance of a food additive regulation to provide for the safe use of aspartame (L-aspartyl-L-phenylalanine methyl ester) in foods as a nutritive substance with intense sweetness and with flavor-enhancing properties.

There has been plenty of controversy around aspartame through the years.

You can't sell that many Diet Cokes and not get people asking questions like, "Should we really be guzzling this many Diet Cokes?" or "This tastes like chemicals. Are you sure there's nothing to be concerned about?" Through the years, the answers to these questions depended on who you asked.

The FDA has maintained the safety of aspartame, and they continue to. But for the first time, the International Agency for Research on Cancer (IARC) has weighed in on this food additive.

# WHAT ARE THE HEADLINE FINDINGS

It was nearly impossible to miss the headlines.

*Aspartame Is a Possible Cause of Cancer in Humans, a W.H.O. Agency Says*

The F.D.A. and the powerful beverage industry protested the new findings, and a second W.H.O. group stood by its standard that the sweetener is generally safe.

Give this article 621

**Aspartame is Possibly Linked to Cancer in Humans, the WHO Says**

**New York Times**

BUSINESS

Aspartame may cause cancer, global health body says

One of the world's most common, and most studied, sweeteners comes under the microscope again. It is determined to be a 'possible carcinogen' and yet acceptable daily intake remains unchanged.

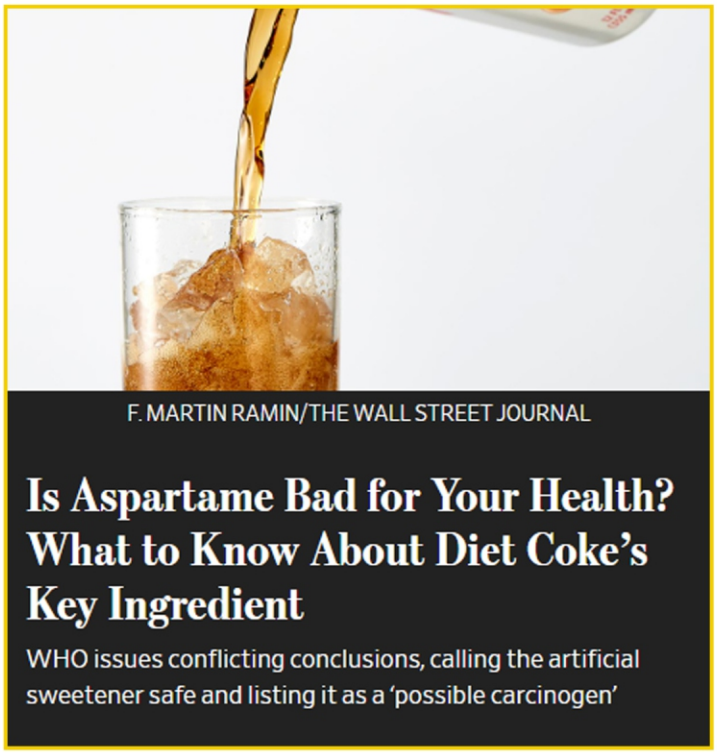
By Laura Reiley

July 13, 2023 at 6:33 p.m. EDT

0:36 / 2:35

**Aspartame designated possible carcinogen by World Health Organization's IARC**

**Washington Post**



F. MARTIN RAMIN/THE WALL STREET JOURNAL

**Is Aspartame Bad for Your Health? What to Know About Diet Coke's Key Ingredient**

WHO issues conflicting conclusions, calling the artificial sweetener safe and listing it as a 'possible carcinogen'

[Is Aspartame Bad for Your Health? What to Know About Diet Coke's Key Ingredient]

Wall Street Journal


[Does Aspartame Cause Cancer? What to Know]

Time

# HERE'S WHAT HAPPENED...

The IARC is the specialized cancer agency of the World Health Organization. After a complete review of the literature (7000 studies reviewed, 1300 studies included), the agency designated aspartame in Group 2B, which means it is "possibly carcinogenic to humans."

As you can see below, the IARC classifies potentially carcinogenic substances in 1 of 4 categories according to their confidence of carcinogenicity. In other words, the strength of evidence.

## GROUP 1

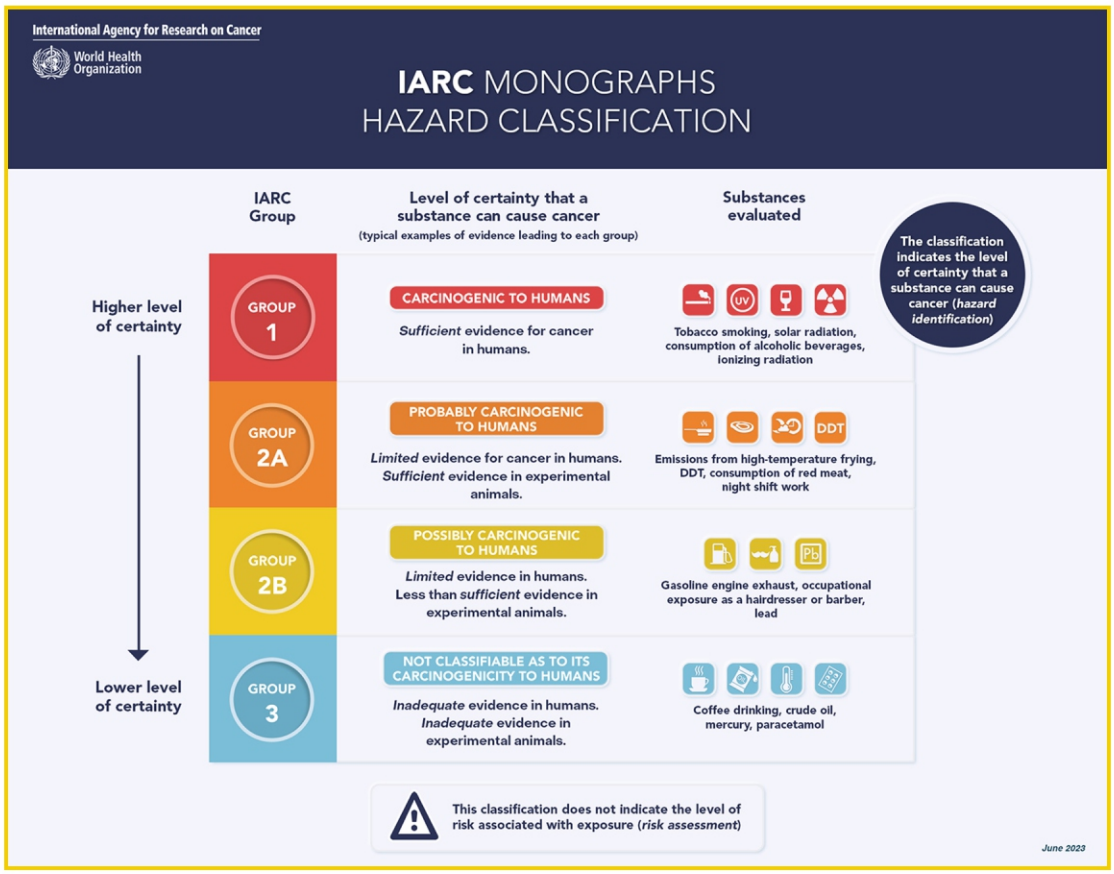
Group 1 is the highest confidence, which includes tobacco use but also alcohol consumption and sunlight.

## GROUP 2A

Group 2A is "probably carcinogenic to humans", and Group 2B (the third group) is "possibly carcinogenic."

## GROUP 2B

Group 2B is massive and includes about half of the 1000ish substances classified by the agency.



But what's interesting is that the IARC isn't the only WHO organization that released a statement on aspartame.

In what seems to be a first of its kind, a completely separate agency within the WHO, the Joint Expert Committee on Food Additives (JECFA), synchronized their assessment and the two independent agencies released a statement together, including a Q&A and while singing Kumbaya, which you can read **here**.

Notably, the assessments were independent with the IARC going first (June 6-13) and the JECFA following June 27-July 6.

## SO WHAT DID THE JECFA HAVE TO ADD?

Well, the JECFA had previously reviewed aspartame decades ago and established an acceptable daily intake of 0-40mg/kg body weight for aspartame. The JECFA's statement was to say that they reviewed the same studies that the IARC had reviewed and that they were not changing their position. You can consume up to 40mg/kg of your body weight in aspartame daily and be perfectly safe.

### TRANSLATION

**An average sized person has just been authorized to drink 14 cans of Diet Coke per day.**

Maybe it's just me... but it feels like these two statements are a bit in conflict with one another.

If you're wondering how to make sense of that, let me tell you what nearly every scientist has said when they were asked about this. The IARC is tasked with assessing risk for developing cancer. It's made up of cancer experts from across the globe (see them listed below).

The meeting also had representatives from the US National Cancer Institute, the US Food and Drug Administration, Health Canada, and the European Food Safety Authority. There were also some "observers" present... I'll let you know who they are in a bit.

IARC Monographs **Working Group Members** E Riboli (UK) – Meeting Chair; FA Beland (USA); DW Lachenmeier (Germany); MM Marques (Portugal); DH Phillips (UK); E Schernhammer (Austria) – Subgroup Meeting Chairs; A Afghan (Canada); R Assunção (Portugal); G Caderni (Italy); JC Corton (USA); GA Umbuzeiro (Brazil); D de Jong (The Netherlands); M Deschasaux-Tanguy (France); A Hodge (Australia); DD Levy (USA); D Mandrioli (Italy); ML McCullough (USA); SA McNaughton (Australia); T Morita (Japan); AP Nugent (UK); K Ogawa (Japan); AR Pandiri (USA); CM Sergi (Canada); M Touvier (France); L Zhang (USA)

*Declaration of interests* All Working Group Members declare no competing interests

**Invited Specialists** J Ishihara, School of Life and Environmental Science, Azabu University, Japan

*Declaration of interests* The research unit of JI receives support, in the form of a grant, for dietary exposure assessment studies from Kagome Co. Ltd, involving competing interests for aspartame

**Representatives** D Evans, Health Products and Food Branch, Health Canada, Canada; S Francke, Office of Food Additive Safety (OFAS), US Food and Drug Administration, USA; F Lodi, European Food Safety Authority (EFSA), Italy; S Ross, National Cancer Institute (NCI), National Institutes of Health (NIH), USA

*Declaration of interests* All Representatives declare no competing interests

Anyway, the IARC are notoriously conservative in their risk assessments, and when they classify a substance in these 4 categories it's based upon *hazard*, not risk.

**Hazard means the possibility of harm, but doesn't indicate the likelihood.**

For example, getting into a car and driving to the supermarket is a potential hazard. You could get into a car accident. That's not likely to happen, but it's possible. Driving after not sleeping in the last 48 hours is a hazard too, but obviously the likelihood is way higher for a car accident.

The JECFA is an agency within the Food and Agriculture Organization of the WHO, meaning it's essentially a food regulatory and safety arm of the WHO. Their task is to assess for adverse effects from food additives, which may include cancer but could also include diabetes or other things. Their job is to determine if a product is safe to be on the market, and if so what the acceptable levels of consumption are. So in this case, the JECFA wasn't moved by the evidence and stands by their prior acceptable daily intake of 40mg/kg body weight.

So the IARC is saying cancer is "possible" and the JECFA is saying fuhgeddaboudit and most scientists are essentially saying that the IARC classification isn't big news and doesn't necessarily change how we feel about aspartame.

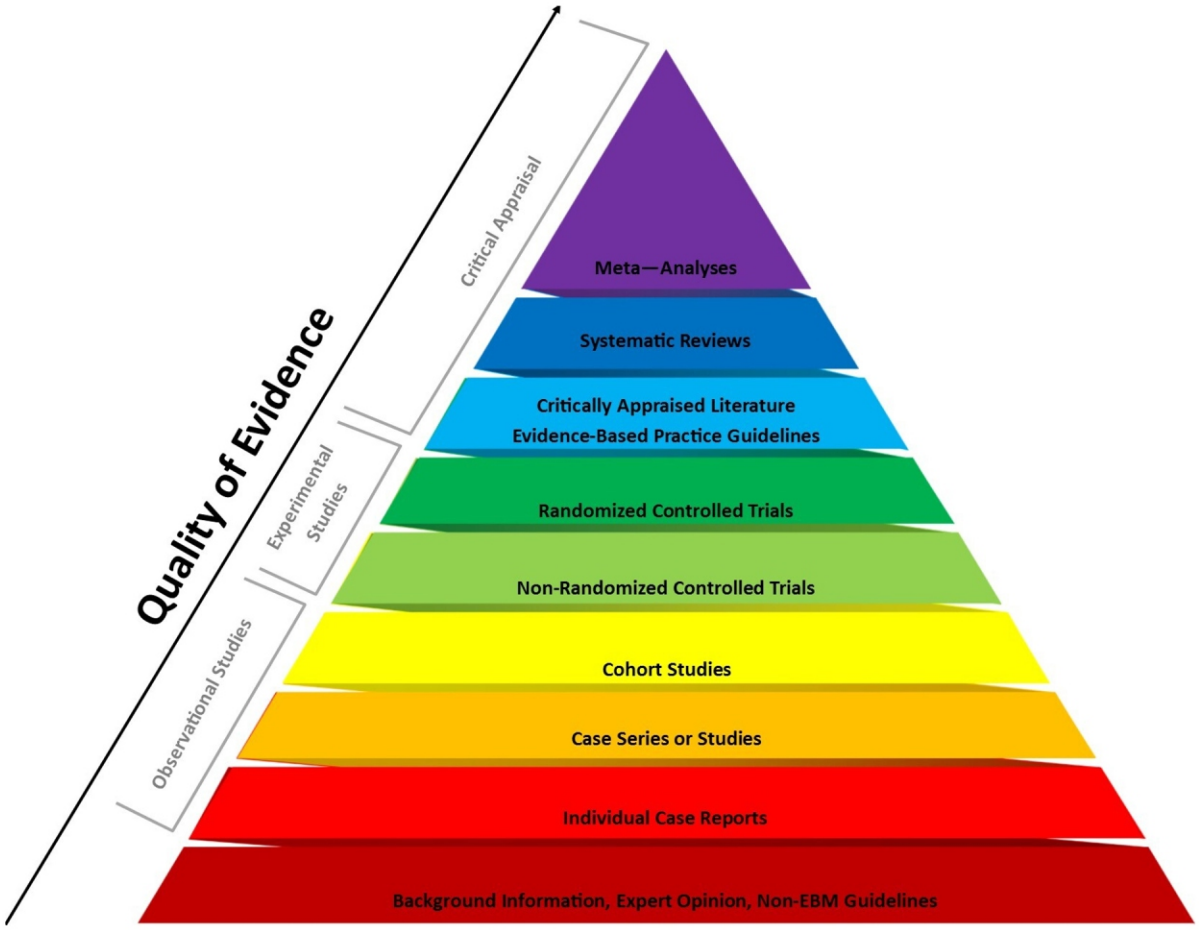
**But did they read the complete documents?** Because I did, and I think there's a lot more to this story.

# WHAT THE STUDY REALLY SHOWED

## I'M GOING TO BREAK THIS INTO 3 PARTS.

Before we jump in, just remember that it's very hard to PROVE that something causes cancer because the exposure will occur for decades prior to the manifestation of cancer and you have to isolate that particular exposure and separate it out from ALL the other things that that person was exposed to during the decades preceding the cancer diagnosis.

To deal with this, we look at the quality of the evidence (see the hierarchy of evidence below), the consistency (are we seeing the same thing in different places), dose response (does the risk increase with higher doses?), and we want to see different scientific techniques pointing in the same direction. In other words, when mechanistic, animal model, and human research are all pointing in the same direction we need to really take it seriously.



# WHAT THE IARC FOUND IN THEIR REPORT. YOU CAN *READ IT HERE*.

New human research connecting aspartame consumption to increased risk of cancer.

## LIVER CANCER

There were four prospective cohorts (three studies) assessing the likelihood of liver cancer or liver cancer mortality with aspartame consumption. This included a large cohort study involving 10 European countries, a study pooling two large US cohorts, and another large US prospective cohort. All three studies found aspartame associated with increased risk of cancer incidence or cancer mortality. Per the IARC working group "All three studies were of high quality and controlled for many potential confounders."

## NUTRINET SANTE

This is a French prospective cohort study that started in 2009, is still ongoing, and is an excellent source of information because it's thorough and also has more than 100,000 people in it. In a **2022 study**, they found among 102.865 French adults aspartame intake was associated with increased overall risk of cancer, but more specifically breast cancer and obesity-related cancers (such as colorectal, stomach, liver, esophageal, breast, ovarian, endometrial and prostate cancers). Notably, there was a dose response in all cases – more aspartame was associated with higher risk. Also notably, the intake in the high risk group was just 47mg/day, which is less than drinking a single Diet Coke and is MUCH LOWER than the amount allowed by the JECFA. Once again, this is a high quality study that controls for many potential confounders.

There was also evidence for cancer in animal model studies, including rats developing hepatocellular cancer.

There was also mechanistic evidence. *"The IARC evaluation identified consistent and coherent evidence of oxidative stress and suggestive evidence of chronic inflammation and of alteration of cell proliferation, cell death, or nutrient supply, all in experimental systems."*

The IARC acknowledges that there were members of the group that felt that this evidence would have supported a Group 2A, *"Probably carcinogenic) designation. Nonetheless, the overall evidence was graded as "limited", which led to the designation of Group 2A "Possibly carcinogenic."*

## DR. B'S TAKE

### I ACTUALLY DON'T HAVE A PROBLEM WITH THEIR FINAL CONCLUSION.

Clearly, aspartame hasn't met the standard for Group 1, so it would have been Group 2A or 2B. There's a hump that you need to get over in order to classify something as Group 2A "Probable" that requires a higher level of evidence, which is the reason that you see half of the substances in Group 2B "Possible."

That said, I personally would vote for aspartame to be Group 2A because we have multiple high quality cohort studies from different places showing similar findings, we have animal model studies to back it up, and we have mechanistic studies to further back it up.

I fully acknowledge, to classify aspartame as Group 2A would have set off a FIRESTORM. Let's not be naive... they know this. It doesn't mean that this is the reason they didn't classify it as Group 2A, but it is a bias that may have impacted their decision making.

Beyond the classification, I think the level of exposure needs to be considered. In the NutriNet-Sante study, the exposure was 20-40 times below the accepted daily intake that the JECFA has established.

Finally, I want to call attention to the connection between liver cancer, insulin resistance and type 2 diabetes. Insulin resistance (requiring more insulin to achieve the same level of blood sugar control) is the root cause of type 2 diabetes and is exploding.

Current estimates are that 38% of Americans have prediabetes and 10% have Type 2 diabetes. Insulin resistance doesn't just promote poor blood sugar control, it also leads to the deposition of fat in the liver, known as non-alcoholic fatty liver disease, which is soon to be the leading cause of liver transplant and is fueling the explosion of hepatocellular (liver) cancer. Point being, insulin resistance is a major risk factor for liver cancer.

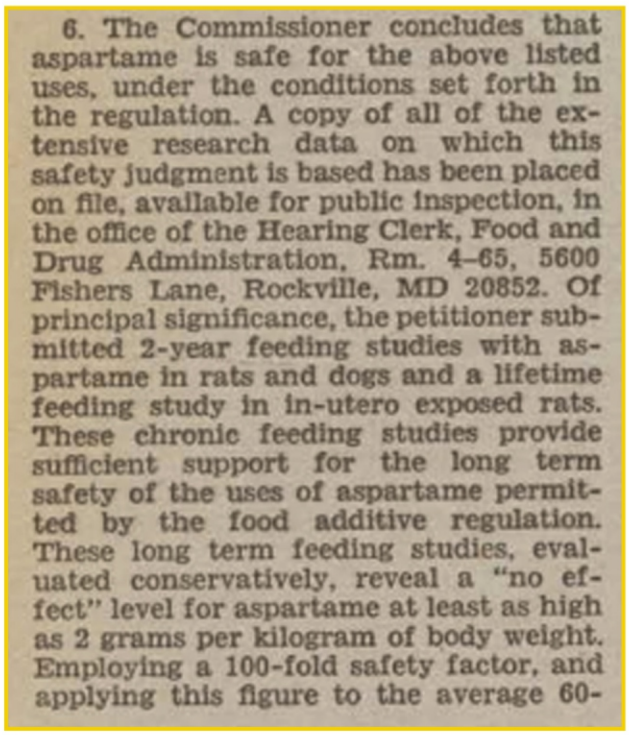
## WHAT THE JECFA FOUND IN THEIR REPORT. YOU CAN *READ IT HERE*.

The committee assessed the same studies as the IARC and emphasized the origins of the ADI (acceptable daily intake) for aspartame. It was at their 25th meeting (this is their 96th meeting, by the way) and the committee at that time reviewed a 104-week study in rats exposed to aspartame at a dose of 4000mg/kg body weight per day.

**The rats did okay. But rats aren't humans.**

So to play it safe, they applied an arbitrary 100-fold uncertainty factor. This is how you get 40mg/kg for the ADI. 4000 in a rat study, divided by 100 because rats aren't humans equals 40.

By the way, the 104-week rat study **was published in 1981**. But clearly this data existed well before 1981 because it is also the principal reference in the 1974 FDA approval of aspartame. Note that the same rat study used to approve aspartame in 1974 remains the principal defense of its safety in 2023. You're probably doing the same thing as me right now — calculating how many years it's been.



6. The Commissioner concludes that aspartame is safe for the above listed uses, under the conditions set forth in the regulation. A copy of all of the extensive research data on which this safety judgment is based has been placed on file, available for public inspection, in the office of the Hearing Clerk, Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20852. Of principal significance, the petitioner submitted 2-year feeding studies with aspartame in rats and dogs and a lifetime feeding study in in-utero exposed rats. These chronic feeding studies provide sufficient support for the long term safety of the uses of aspartame permitted by the food additive regulation. These long term feeding studies, evaluated conservatively, reveal a "no effect" level for aspartame at least as high as 2 grams per kilogram of body weight. Employing a 100-fold safety factor, and applying this figure to the average 60-

What about the new data? The multiple human prospective cohorts, the mouse and rat studies showing the cancers developing, the mechanistic studies fulfilling biological plausibility? ***"The evidence of an association between aspartame consumption and cancer in humans is not convincing."***

They also looked at non-cancer outcomes such as the risk of developing type 2 diabetes. They acknowledge that population-based studies associate aspartame consumption with a greater risk of type 2 diabetes. ***"An association between aspartame consumption and the evaluated non-cancer health end-points is not convincing."***

## THUS, AFTER A REVIEW OF THE DATA, HERE IS THEIR SUMMARY STATEMENT:

***"Overall, the committee concluded that there was no convincing evidence from experimental animal or human data that aspartame has adverse effects after ingestion."***

The committee concluded that there was no reason to change the previously established ADI of 0-40mg/kg body weight for aspartame.

It's worth acknowledging that this gives us insights into our process around food safety and approval for entry into the market. A small amount of research is required to get approval, the food is then treated as categorically safe (far beyond what the initial evidence actually showed), and any change to the status of that food is rare despite accumulating evidence of concern.

# DR. B'S TAKE

Let me be the first to say that I appreciate academic debate, healthy skepticism, and peer review. These are important contributors to academic quality and integrity. If no one pushes back it means we are in an echo chamber, and an echo chamber is dangerous because it can lead to unchecked radicalization and distortion.

In this case, the committee gets to have the last word. There really isn't debate, it's simply their response and our choice on whether or not to accept that response.

Repeatedly they use the language "not convincing." What does this even mean? I assume they're trying to say that they are expert scientists and the evidence hasn't yet achieved a level of breadth, consistency, and quality to merit a change in their position based upon their assessment.

But it is difficult for me (or I would imagine any reasonable person who actually reads these documents) to believe that these multiple studies are meaningless when their original position that they are so unwilling to modify is based upon a rat study from 1974.

Without a clear breakdown leveling the evidence for and against safety, it starts to feel like "Not convincing" is a cheap and easy way to dismiss the accumulating evidence and not have to actually deal with it. They do cite criticisms of epidemiology research, but these are criticisms that exist for ALL epidemiology studies. You could literally use the same argument to say that the evidence that tobacco causes cancer is "Not convincing."

They owe us a better explanation than this. I can't have confidence in "just trust us, we're the experts" as the justification for not altering the safety thresholds when 1 in 6 people are dying from cancer and 6,000,000 to 10,000,000 *pounds* of this stuff enter our food supply every year. You can produce more than 2,200 cans of Diet Coke with 1 pound of aspartame.

# TRANSPARENCY, INTEGRITY, TRUST AND CONFIDENCE IN THESE AGENCIES.

To start, there are a myriad of topics and studies that were not mentioned in either report.

- The microbiome is not mentioned even once, despite the overwhelming evidence that aspartame alters the gut microbiome, such as **this study** where alteration of the gut microbiome promoted insulin resistance in rats.

- A **2023 study** found that long-term aspartame intake was associated with increased visceral fat (the kind that promotes insulin resistance) along with intramuscular and subcutaneous fat as well as greater body mass index, weight, waist circumference. Powerfully, this is a study of 3088 people who started off when they were 25 years old and healthy body weight (on average) and were followed for 25 years!

- A recent **2021 review article** raises safety concerns beyond just cancer risk and disruption of the metabolism.

The approval of aspartame by the FDA is one of the most controversial in history and has the makings of a Netflix documentary. A **Virginia Tech review** alleges that a study in which 98 out of 196 infant mice died after exposure to aspartame was overlooked by the FDA. This review provides a history of the controversy surrounding aspartame's approval by the FDA, with references, and it is quite eye opening and thought provoking to say the least. Donald Rumsfled of all people makes a guest appearance. I didn't see that one coming!

The IARC meeting allowed "Observers" who, in their Declaration of Interests, report funding by The American Beverage Association, The Calorie Control Council, and The International Council of Beverages Associations. Why are they there? And why are they *allowed* to be there? I think we all know why they are there. They professionally represent the interests of those organizations. Aspartame is a big money business. The people in the aspartame industry want to protect their business, and money is not a barrier, but really what you want is influence and power that exists in the room where it happens. We are bearing witness to industry lobbying, folks.

**Observers** A Agudo, Catalan Institute of Oncology, Spain; S Barlow, Consultant, UK; S Borghoff, ToxStrategies LLC, USA; S Elmore, Elmore Pathology LLC, USA; T Galligan, Center for Science in the Public Interest (CSPI), USA; B Magnuson, Health Science Consultants, Canada; F Wu, Michigan State University, USA

*Declaration of interests* SB is employed by ToxStrategies LLC, a consulting firm that has provided research services to The American Beverage Association and The Calorie Control Council. The International Council of Beverages Associations has sponsored her travel to the IARC Meeting, June 2023. SE is a consultant for The American Beverage Association. TG has issued written comments on the safety of aspartame in response to regulatory dockets issued by the US Department of Health and Human Services and Department of Agriculture. BM is employed by Health Science Consultants, which has received consulting fees by The Calorie Control Council for critical review of studies on aspartame. The Calorie Control Council also sponsored BM's attendance to the IARC Meeting. All other Observers declare no competing interests.

At least the IARC provided "Declarations of interest." The JECFA does not provide a conflict of interest statement, and trying to even identify who the people are is extremely difficult. I spent 20 minutes trying to figure out who the chairperson is and really didn't get anywhere.

**Members**

Dr A. Agudo, Unit of Cancer and Nutrition, Catalan Institute of Oncology, Barcelona, Spain
Dr S. Barlow, Brighton, East Sussex, United Kingdom of Great Britain and Northern Ireland
Dr D. Benford, Cheddington, Buckinghamshire, United Kingdom *(Chairperson)*
Dr R. Cantrill, Bedford, Nova Scotia, Canada *(Vice-chairperson)*
Dr M. DiNovi, Baltimore (MD), United States of America (USA)
Dr N. Fletcher, Food Standards Australia New Zealand, Kingston, Australia
Dr D.E. Folmer, Division of Science and Technology, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, United States Food and Drug Administration, College Park (MD), USA *(Joint Rapporteur)*
Dr S.M.F. Jeurissen, Department for Food Safety, Centre for Nutrition, Prevention and Health, National Institute for Public Health and the Environment, Bilthoven, Netherlands (Kingdom of the)
Ms K. Laurvick, Food Standards, United States Pharmacopeia, Rockville (MD), USA
Dr J.-C. LeBlanc, Laboratory for Food Safety, French Agency for Food, Environmental and Occupational Health and Safety, Maison-Alfort, France
Dr U. Mueller, Perth, Western Australia, Australia *(Joint Rapporteur)*
Dr J. Schlatter, Zurich, Switzerland
Dr F. Wu, Food Science and Human Nutrition, Agricultural, Food, and Resource Economics, Michigan State University, East Lansing (MI), USA

# DR. B'S TAKE

## MAYBE I'M NAIVE AND TOO IDEALISTIC, BUT THE FDA, IARC AND JECFA ARE SUPPOSED TO BE AGENCIES *FOR THE PEOPLE.* THEY ARE SUPPOSED TO REPRESENT US AND WHAT IS BEST FOR US.

**First of all,** it's important that they actually fulfill that purpose. Accusations that they overlooked research that was available to them, if true, suggests they are either incompetent or they have corrupted motivations. I don't think they are incompetent. To continue to overlook or dismiss new research without adequate communication to justify your reasons is to repeat that original sin.

**Second,** if you care about integrity and your reputation, why would you allow agents of bias to overtly exist in the room? We know why the lobbyists are there. Why is contact between lobbyists and committee members allowed at any point, let alone during the proceedings where decisions are made? That undermines our ability to trust their process. Again, I know the members are smarter than this, yet this dirty practice is pervasive, we all know it's happening, and we either accept it, overlook it, or are regrettably accepting it in silence.

**Third,** transparency is a requirement for trust. This applies to all relationships, including these types of relationships with scientists and agencies. If they cared about garnering our trust, they would actually go out of their way to be as transparent as possible. When you make it exceedingly difficult to know who is even in the room, what their conflicts of interest are, and what was said it suggests that transparency is not a priority when all of these things are easily achievable.

To be clear, I am not saying that I automatically reject the statements made by these agencies. That would mean that because I have concerns about transparency and integrity, I am automatically assuming the opposite of what is said by these agencies. I'm pretty sure we all know at this point that assumptions generally aren't a strong strategy. What I AM saying is that when it's an important topic, we should stop and take the time to dig just a little bit deeper on our own.

Call it trust but verify or healthy skepticism, but it's really just an exercise in confidence and finding trustworthy sources in pursuit of the truth. A good start is reading the actual reports by the agencies involved and then asking yourself, "Does this seem reasonable?"

# WHAT YOU SHOULD DO ABOUT IT

## WE'VE COVERED A LOT, BUT I THINK THE ANSWER IS REALLY SIMPLE...

Let's each take a step back for a moment and do an exercise. Pretend we're starting over with a clean slate. Let's put ALL the evidence on the table... The evidence from the rat study used to approve aspartame half a century ago that continues to be used to defend its safety today. And the evidence from humans, animals, microbes and mechanistic laboratory studies that suggest reasons to be concerned about the safety of aspartame.

As I asserted earlier, we look at the quality of the evidence (see the hierarchy of evidence graphic above), the consistency (are we seeing the same thing in different places), dose response (does the risk increase with higher doses?), and we want to see different scientific techniques pointing in the same direction.

**Remember, this isn't a choice between aspartame and sugar. You have option number 3 as well, which is NEITHER. And also, this can be shades of gray. There's a big difference between multiple cans of Diet Coke daily and the occasional can.**

**Okay, with a fresh start and applying those measures, where is the scale tilting for you? Wherever that is, now you know what to do.**