

Sweet Misery Fact Check

Part II

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This is part of my “What Does the Science Say” series which lives at <http://whatdoesthesciencesay.wordpress.com>

There is a comment-enabled blog edition available at <http://whatdoesthesciencesay.wordpress.com/2012/08/03/sweet-misery-fact-check-part-2/>

There is an HTML version available at <http://tinyurl.com/sweetfact2>

A PDF version is available at: <http://whatdoesthesciencesay.files.wordpress.com/2012/08/sweetmiseryfactcheckpart2.pdf>

In the first part ([read here](#)) of my “fact check” on the *Sweet Misery* documentary, I mainly covered the claims that it leads to neurological disorders or is otherwise inherently unsafe. In this second part, the focus turns to the process of aspartame approval. The research for this turned out to be interesting, especially as occasionally the claims in the documentary would have a small nugget of truth buried in them. Sometimes they may even be wholly true, but still essentially meaningless. It is quite clear that aspartame does not lead to brain tumors. So claims that there were mismanaged studies that *could* have demonstrated this in the 70s are pointless, as we now know that aspartame does *not* cause cancer.

In this part I will generally only cover claims for which I can find some sort of documentation one way or another. Frequently the speakers in the documentary will say that they spoke to so-and-so at the FDA or Searle, or were shown some document, but no evidence is provided nor is there necessarily a way of disproving the statement. There are also claims about behind the scenes shady dealings of Donald Rumsfeld and other leaders of Searle and the FDA. But I have to consider it speculation and hearsay without some any evidence to back them up.

Claim: The “Bressler Report” found a 115-week DKP rat study to be fatally flawed

Around minute 27 of the documentary, Russell Blaylock discusses a 115 week DKP (diketopiperazine) rat study that the FDA had concerns with due to some inaccuracies in the collection and reporting of data. He mentions that the “Bressler Report” -- the results of an investigation lead by Chicago division of the then-Bureau of Foods investigator Jerome Bressler -- found that the DKP (and other) study was “horribly done research” and that there were tons of discrepancies. Assuming that the linked document on wnho.net is in fact the real Bressler

report¹, then these are accurate statements. However, as best I can tell [reading the actual report](#), Bressler never indicates that the discrepancies change these actual conclusions in a drastic way (Bressler 1977 ²).

Page 68 has the summary of the some of the lesions and masses that were considered significant that were inconsistent with the submitted FDA study. It indicates that “for the most part” the pathology reports are “in agreement” with those of Searle. The report does find that the incidence of uterine polyps in the medium dose was 15% rather than 12%. This makes them potentially dose-related to the levels of DKP in the diet (which would seem to indicate that the rats did in fact consume the DKP and not avoid it). In the report summary, the “throwing out” of the tumors isn’t noted as significant.

On the face of it, it seems strange that when Bressler went to Searle to investigate the raw data, virtually none of the people who performed the study were available or had left Searle. Dr. K.S. Rao, the head of the study, had left and refused to be interviewed. While this seems fishy, it may be also be perfectly normal. Bressler was doing his investigation three years after the study had been submitted to the FDA (1974), with the study actually starting in 1971. There is a good chance that people were brought on from universities as interns, and that researchers were simply contractors there for the single study.

Claim: Rao / Waisman monkey study was covered up

Around minute 30, former FDA Investigator Arthur Evangelista begins discussing the “covered up” [monkey study](#) performed by K.S. Rao and Harry Waisman. He mentions that it had methodological issues. What he doesn’t mention is that Waisman *died* partly through the study, which led to it being terminated early. In other words, the study was *never finished* and yet Searle submitted what it had. Nonetheless, even based on the partial results, the FDA still opted to use it as the basis for the labelling for Phenylketonurics found on anything containing aspartame (much to the dismay of the Quaker company which pointed out that other protein-based components of its cereals contained much more phenylalanine than the aspartame had, making the warning confusing) due to the exhibition of seizure activity in medium and “high” dose groups. Note that even the “low” dose group was 32 times the estimated maximal intake (GAO ³). A later similar study did not exhibit the same seizure activity as it spread out the food intake over a more normal period (rather than one massive spike at once... which the monkeys

¹ I am a bit skeptical of the introductory portion which claims that the “worst 20%” were actually held back by the FDA and that portion has been restored in this version of it. As far as I can tell, the “missing” 20% is actually the portion of the review that covered two other aspartame studies, not the DKP study.

² Bressler, Jerome. 7 August 1977. Review of “115 Week Oral Tumorigenicity Study in the Rat, conducted with SC-19192 (diketopiperazine)”. Visited 16 July 2012. <<http://www.dorway.com/bresslercomplete.pdf>>

³ GAO (United States General Accounting Office). “Food And Drug Administration: Food Additive Approval Process Followed for Aspartame”. June 1987. GAO/HRD-87-46.

often didn't finish) (Reynolds⁴). So, if anything, the criticised (by all) Rao/Waisman study found more problems with aspartame (specifically, the phenylalanine content) than actually appear to exist.

Evangelista also mentions that "1 or 2" died (it was one, and the cause was unknown). There were no seizures in the low dose group, which corresponds to about 32x the estimated maximal intake of aspartame. The seizures occurred in the medium and high dose (100 and 120 times maximal daily intake) and the authors note that this can be induced with the equivalent amount of phenylalanine by itself (so this is a known effect of phenylalanine, nothing special for aspartame here) (RAO p.11 ^{5,6}). Another key point is that the low dose group never has the seizure, so there was apparently no "build up" of seizure-inducing chemicals (a favorite canard of the anti-aspartame folks).

Claim: Ralph Walton's review of peer-reviewed aspartame studies show 97 non-industry independent studies find aspartame to be dangerous

In minute 32, Walton refers to his "independent review" of the peer-reviewed aspartame studies, finding that the positive ones were Searle-funded and the "independent" ones turned out against aspartame. [I have covered this](#) one before, [as have others](#)⁷. Virtually none of the studies he cites as "independent" are even studies, and certainly not peer-reviewed. Additionally, very few of them even directly address aspartame. For example, he will point to studies showing that large amounts of methanol can be bad. We know this. And this has very little to do with aspartame. The couple that could be considered to directly address aspartame with negative consequences haven't been reproduced or are of low methodological quality.

Specifically, it seems that only five of the mentioned studies could be considered to be peer-reviewed and directly relatable to aspartame:

1. Camfield PR, Camfield CS, Dooley JM, et. al., Aspartame Exacerbates EEG Spike Wave Discharge in Children With Generalized Absence Epilepsy: A Double-Blind Controlled Study. *Neurology* 1992;42:1000-1003.

⁴ Reynolds WA, Bauman AF, Stegink LD. "Developmental Assessment of Infant Macaques Receiving Dietary Aspartame of Phenylalanine" in "Aspartame: physiology and biochemistry" by Lewis D. Stegink. *I believe that Stegink was associated with Searle in some capacity.*

⁵ Rao KS, McConnell RG, Waisman HA. "SC-18862: 52 Week Oral Toxicity Study in Infant Monkey". October 1972. *Note: Far as I can tell this was never published in a journal, so I have to assume that [dorway.com](#) has an accurate version of it*

⁶ Pedantic note. Throughout the internet and even in the documentary people refer to the Rao study as "SC-18862". That is not the number of the study but rather the technical name (at the time) for aspartame. I would hazard a guess that it refers to "Searle Company".

⁷ aspartame.net "Aspartame Information replies to the New York Times". 12 February 2006. Visited 15 July 2012. NOTE: aspartame.net is created by Ajinomoto North America, the makers of aspartame.

2. Mahalik MP and Gautieri RF, Reflex Responsiveness of CF-1 Mouse Neonates Following Maternal Aspartame Exposure. *Research Communications in Psychology, Psychiatry & Behavior* 1984;9(4):385-403
3. Pinto JM, Mahea TJ, Administration of Aspartame Potentiates Pentylenetetrazole and Fluorothyl-Induced Seizures in Mice. *Neuropharmacology* 1988;27(1):51-55.
4. Trocho C, Pardo R, Rafecas I, Virgili J, Remesar X, Fernandez-Lopez JA, Alemany M, Formaldehyde Derived From Dietary Aspartame Binds to Tissue Components In Vivo. *Life Sciences* 1998;63(5);337-349.
5. Van Den Eeden SK, Koepsell TD, Langstreth WT Jr, et a., Aspartame Ingestion and Headaches: A randomized Crossover Trial. *Neurology* 1994;44(10):1787-93.

The Camfield study (as mentioned in the title) only applies to children with a specific form of epilepsy. As noted in an American Academy of Pediatrics article reviewing “inactive ingredients” in various pharmaceuticals, they simply recommend that children who have *untreated* epilepsy avoid aspartame in large doses (AAP 1997 ⁸). A later study by Rowan and Shaywitz was unable to reproduce seizure activity in a controlled study of 16 adults and 2 children.

The Mahalik study was unable to be reproduced following the same methods by McAnulty et al (McAnulty 1989 ⁹). The primary difference in their methods is that Mahalik et al did not use concurrent controls, but rather used historical controls. Note that McAnulty appears to have been employed by the NutraSweet company.

The Pinto study, like the Camfield one, relates to seizure activity, specifically around the phenylalanine content. As has been noted in other articles, aspartame is actually a relatively low source for phenylalanine and the results really only apply, potentially, to sufferers of PKU.

The Trocho study is about the formaldehyde/methanol concentrations. I discuss this in my first [aspartame article](#). But in short, Tephyl et al notes that this study does not really apply to actual animals. Formaldehyde has never been demonstrated to build up on the body (and is a normal metabolic byproduct throughout the day from fruit juices), even when large direct doses of methanol are given to monkeys.

The Van Den Eeden study found that among people who self-report headaches after aspartame consumption, a subset of them actually seem to get more headaches when given aspartame versus placebo.

But if you follow the first link you can look at the studies he cites and decide for yourself. I’ve classified them by what type of study they are (peer-reviewed study, letter or case study) and whether they find aspartame to be “harmful”.

⁸ “Inactive” Ingredients in Pharmaceutical Products: Update (Subject Review)’ *PEDIATRICS* Vol. 99 No. 2 February 1, 1997 pp. 268-278 (doi: 10.1542/peds.99.2.268)

⁹ Absence of developmental effects in CF-1 mice exposed to aspartame in utero. McAnulty PA, Collier MJ. *Life Science Research, Eye, Suffolk, England*. The NutraSweet Company. Accepted 9 March 1989. Available online 27 September 2004. [http://dx.doi.org/10.1016/0272-0590\(89\)90265-0](http://dx.doi.org/10.1016/0272-0590(89)90265-0)

Claim: The Commissioner of the FDA (illegally) overruled the Board of Inquiry decision regarding aspartame approval

It is true that the Commissioner of the FDA did overrule the Board of Inquiry's decision following the Task Force's investigation. In his view, there was ample evidence of safety and no real evidence for brain cancer (which was their final fear). The concern of some of the board members was that there were not enough rats in the study to detect a 5% increase in chance of brain cancer. At the time that the GAO investigated the approval process, the National Toxicology Program's standards were still only barely above what Searle had already done (in other words, even then in 1987 there was not a requirement to be certain of detecting 5% increase) (GAO p.55-59 ¹⁰). In the documentary, James Turner claims that the Commissioner was violating law when he overturned the decision, but this does not appear to be the case. According to Title 21, the Public Board of Inquiry is a *scientific* not a *legal* body (CFR ¹¹).

Another interesting tidbit is that the documentary (around minute 55) says that it was a "clear conflict of interest" that Searle paid for an independent analysis (by UAREP, a consortium of nine universities) of the studies submitted to the FDA. In actuality, the FDA simply required them to foot the bill for the analysis. It was in no way sponsored by Searle (GAO pp.30-31).

The Missing Executive Order

I hesitate to say "and then things get weird", considering what this article is reviewing. But then things get weird. About an hour into the video, Turner claims that the first action by Ronald Reagan upon coming into office in 1981 was to sign an Executive Order removing the ability of the FDA to stop the marketing of aspartame. No such Executive Order exists. [Regan's earliest one was signed on January 28th](#) (Federal Register ¹²). Naturally, [Betty Martini claims the order was signed between the 20th and 26th](#) and has been covered up. Why the entire government would choose to cover up just that one Executive Order is beyond me. Frankly, it is this exact type of thing that should make you question the entire documentary (assuming you weren't already, as we have reached the end of the 2nd part of the series of articles). Absence of evidence is not evidence of anything.

Conclusions

¹⁰ GAO (United States General Accounting Office). "Food And Drug Administration: Food Additive Approval Process Followed for Aspartame". June 1987. GAO/HRD-87-46. <<http://www.gao.gov/assets/150/145477.pdf>>

¹¹ CFR (Code of Federal Regulations) Title 21, Subpart B, S. 13.30. <http://tinyurl.com/cfr21-13> (Visited August 26, 2011). *I am not certain that at the time of aspartame approval the Board had more authority.*

¹² National Archives. Federal Register:Executive Orders Disposition Tables. Ronald Regan - 1981". <http://www.archives.gov/federal-register/executive-orders/1981-reagan.html>. Visited August 25, 2011.

The next, and hopefully final, part will discuss the story of a woman convicted of murdering her husband who has become a cause celebre for anti-aspartame crusaders who believe it was actually an aspartame overdose that led to his death (despite the fact that no such thing has ever been demonstrated to ever occur).