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## THE STRAIGHT FACTS ABOUT ASPARTAME AND OTHER LOW-CALORIE SWEETENERS

Transcript: A Presentation from  
**Dr. George Blackburn** and **Dr. Bernadene Magnuson**

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### **George L. Blackburn, MD, PhD**

Dr. Blackburn is the S. Daniel Abraham Associate Professor of Nutrition and Associate Director of the Division of Nutrition at Harvard Medical School, where he is also serving as Chief of the Nutrition/Metabolism Laboratory and Director of the Center for the Study of Nutrition Medicine. He is an honorary member of the American Dietetic Association and an American Society for Nutrition Fellow.



### **Bernadene Magnuson, PhD**

Dr. Magnuson is Assistant Professor of Nutrition and Food Science at the University of Maryland, where she conducts research on food toxicology, diet and cancer prevention and teaches food science and food toxicology. She recently served on an expert panel review of the safety of aspartame.

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**[Title Slide]**

**J. Koelemay:** Hello, everyone. I'm Joan Koelemay, a registered dietician with the Beverage Institute for Health and Wellness of the Coca-Cola Company and your host for today's Webinar: "Straight Facts on Aspartame and Other Low Calorie Sweeteners," featuring obesity expert Dr. George L. Blackburn and food toxicologist, Dr. Bernadene Magnuson.

We are proud to sponsor this event, which brings together dietetic professionals and two of today's leading experts to explore the science, safety and usefulness of low calorie sweeteners in weight management. Since this is an extensive topic, we have asked our speakers to focus primarily on aspartame, the most common low calorie sweetener used in foods and beverages today.

Dr. Blackburn will address the impact of low calorie sweeteners on appetite and food intake, as well as their beneficial role in helping clients achieve their weight management goals. Toxicologist Bernadene Magnuson will discuss aspartame metabolism and provide the science that dispels common myths about its safety.

**[Slide 2]**

Dr. Magnuson is on faculty at the University of Maryland where she teaches courses on food science and food toxicology. Her research includes both food toxicology and diet and cancer prevention. Dr. Magnuson is an active member of the Institute of Food Technologists and the Society of Toxicology and has offered numerous peer review articles, book chapter abstracts and professional articles relates to diet, food toxicology and cancer.

Recently, she was the lead author of an expert review on the safety of aspartame, published in critical reviews of toxicology in October 2007.

Dr. Magnuson will discuss the findings of that paper and their expert review panel in her presentation. And now, here's Dr. Magnuson.

**[Slide 3]**

**Dr. B. Magnuson:** Thank you very much for that introduction and welcome, everybody. I am going to discuss today the findings of the expert review on the safety of aspartame. You can see on the screen the expert panel that were the co-authors of this report. These are internationally recognized toxicologists from around the world that each contributed significantly to the findings of this report.



**[Slide 4]**

Aspartame, of course, is one of the high intensity low-calorie sweeteners that is on the market. Questions regarding the safety of aspartame have continued to surface in the press and in the Internet since the introduction in the marketplace. Recently, two long-time lifetime exposure studies that were conducted in Italy also brought the question of aspartame safety into the realm of the scientific community.

Therefore, the goal of this expert review panel was to look at all scientific studies that have been conducted on aspartame and to assess the safety of the current consumption levels of aspartame. Therefore, what I'm going to talk about today is both the consumption levels and how we assess those, as well as our findings on the safety of the levels of aspartame that are currently being consumed.

**[Slide 5]**

The breakdown products of aspartame are shown on the screen. It is broken down during storage to the dipeptide, that is the two amino acids joined together - aspartylphenylalanine. That dipeptide also can cyclize and form a cyclic dipeptide called diketopiperazine. Another of the breakdown product is methanol and of course, it can also breakdown completely into the two individual amino acids.

**[Slide 6]**

Aspartame is very stable under dry conditions. But with long-term storage in beverages, it can break down. It also breaks down under conditions of high temperature and high pH or alkaline conditions. It is for this reason that aspartame is not recommended for baked or cooked products.

The breakdown products of aspartame are shown on the screen. It is broken down during storage to the dipeptide, that is the two amino acids joined together - aspartylphenylalanine. That dipeptide also can cyclize and form a cyclic dipeptide called diketopiperazine. Another of the breakdown product is methanol and of course, it can also breakdown completely into the two individual amino acids.

An important factor is that all of the breakdown products are not sweet. So, the consumer is immediately aware of the fact that the product has broken down because there is a loss of sweetness. This, in itself, is what we call a self-limiting factor, that individuals will probably not consumer the product. However, because there is a possibility that they may, these products have also been evaluated for their safety. That was also reviewed in this safety evaluation.



**[Slide 7]**

Before aspartame was allowed to be marketed, there was a pre-market safety evaluation submitted to scientific authorities. In order to have the pre-market safety evaluation, the producer of aspartame had to produce a comprehensive battery of studies. These includes acute or very short-term studies, sub-chronic and long-term toxicity studies, carcinogenicity or evaluation of cancer potential, genetic toxicity, the effect on reproduction, the effect on teratogenicity, which is birth defects. These were all done in rodents, as well as other species such as rabbits and dogs.

There's also been many human studies that have been conducted, looking at the blood chemistry, the effect in target populations that are likely to be high consumers of aspartame, including diabetics or children. This data has been reviewed by every major international food authority in the U.S. That would be FDA; also Health Canada, the European Union and JACFA in Europe have also evaluated the safety of aspartame.

Aspartame is approved for use in over 130 countries around the world.

**[Slide 8]**

One of the uses of all of that data that was presented in terms of the safety of aspartame was to establish what's called an ADI value. This is the acceptable daily intake. It is the amount that is considered safe to consume everyday for a lifetime without any adverse effects.

What is important for you to understand is this does not mean that if you consume more than the acceptable daily intake that you will automatically have an effect. What the acceptable daily intake means is that as long as you're consuming that much or less, we are very confident that there will be no adverse effects. The reason for that safety or that confidence in the ADI value is because it is a very conservative estimate. Let me explain how we determined ADI.

The amount that animals can consume everyday within a chronic or long-term study without there being any observed effect; so that means no change in any of the parameters, the many biochemical parameters, pathological evaluation and so on. As long there is no observed effect, that has been called the "no observed effect" level for the animal. We then apply safety factors, and this safety factor is usually 100, based on the difference of approximately ten fold at male curve from susceptible to resistant or different types of individuals and another ten fold safety factor to account for potential differences between humans and animals.



**[Slide 9]**

So what that means is you start with a level that has absolutely no effect in animals and divide that by at least 100. That becomes your acceptable daily intake value. FDA has set the ADI at 50 milligrams per kilogram body weight. Now, let me show you what that means in terms of serving of food containing aspartame.

What you'll see on this slide is the number of servings that you would have to consume to get to that ADI of 50 milligrams per kilogram body weight. Of course, it depends on the individual's body weight. So for an adult weighing approximately 150 pounds, they could consume 20 carbonated soft drinks that are sweetened aspartame before they got to the amount of the acceptable daily intake. For a child, of course, because they weigh less, then you divide that for about six soft drinks, and you can see the other examples. Tabletop sweeteners, you're looking at 97 packets of sweetener. Even those people who have a really, really sweet tooth none of them do I know that actually use that amount.

So, when you look at these numbers, you can see why we do not have anybody that actually reaches the ADI.

**[Slide 10]**

We wanted to confirm that though by looking at what are the current consumption levels of aspartame. To do that, we looked at a number of different applications and you see here various applications that have been approved for use of aspartame.

**[Slide 11]**

The process of the review I'm going to now talk about - the study that we did, how we actually undertook it, both the process of looking at all the literature and how we evaluated the current consumption level of aspartame. So to find all of the studies that have been conducted on aspartame and ensure that we're looking at every study that has been published or reported, we searched scientific literature databases that are very comprehensive - not only U.S., but international - also all patents, the various reports that have been reported to contain information on the safety of aspartame.

We also reviewed all reports that were submitted to the FDA's Federal Register. We had access to all of the unpublished regulatory submission reports. So in the earlier slide where I showed you all of the studies that were submitted for pre-market safety evaluation, we had access to all of those and reviewed the results from those studies as well.



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We ended up with many, many different studies to look at. Over 500 articles are actually cited in this report. The ones that are not cited included those where the primary topic of the study was to look at the sensory properties of aspartame, or how it would best be modified or formulated in different product applications. So for example, is it best with different blends or what pH and so on? We did not spend any time looking at those. We also did not look at or include any articles that talked about potential health benefits of consumption of aspartame.

**[Slide 12]**

The purpose of this review was really just to focus on the safety questions. So while you're looking at the studies on the affects of aspartame at various doses, you have to be able to put that into perspective as well. How does that compare to what we are currently consuming?

So, we conducted a current analysis of the consumption of aspartame. The purpose of this was to make sure we were using the most recent food intake data that is available. The consumption of aspartame, of course, has been studied years ago, but we know that our diet is changing and consumption of low calorie sweeteners is probably increasing. Therefore, we used food intake data from the NHAINES Examination Survey that was conducted in 2001-2002. That gave us data on the amount of products containing aspartame that were being consumed by individuals that completed this evaluation or this food intake report.

In order to be able to determine or estimate/calculate the amount of aspartame, you need to look not only at how much of a particular product a person is consuming, but also how much aspartame is in that product. To assess the amount of aspartame or to enter into our calculations what the aspartame content of foods were we made a number of assumptions, and those are listed here.

First of all, if there was a typical use level reported from industry, we would use the most current information in terms of the amount of aspartame added to various foods. Sometimes we didn't have that information and so we would find levels that were reported in the literature. If that was not the case, we then assumed the amount in the food is the highest level that is allowed.

The other important assumption that was made is that we assumed that all sweetened, artificially sweetened or products were sweetened by aspartame. Of course, that is an overestimation because we know many of the food products used other types of sweeteners or used blends.



**[Slide 13]**

However, using those assumptions, we came up with an estimate of the current consumption of aspartame. These values that are on your screen now are based only on individuals who reported consuming low calorie sweetener, a product containing a low calorie sweetener. So those are what we call “users only.” We did not include individuals who did not consume any of these products.

So looking only at users, what you see is that the average consumption of aspartame is around five milligrams per kilogram body weight. The 90<sup>th</sup> and 95<sup>th</sup> percentile are those individuals that are the very high consumers, the high-end users. So, you would expect those to increase. What you see, even with the 95<sup>th</sup> percentile consumers, the consumption is still less than about 15 milligrams per kilogram body weight per day.

So if you remember that the acceptable daily intake, the amount that you can consumer every day with no adverse effects is 50 milligrams per kilogram body weight, you can see that we are well, well below that acceptable daily intake. That in itself is an indicator that it would be highly unlikely that we would find any adverse effects occurring at these levels.

**[Slide 14]**

The summary then of our look at the consumption of aspartame is that in fact, yes, the intake of aspartame has increased in recent years. However, this change is not that dramatic. In past years, it’s been seen around three or four milligrams per kilogram per day. It still remains well below the acceptable daily intake, even for high intake populations. There is overestimation of consumption by the nature of how NHANES is conducted and is using users only and also because of the some of the assumptions that I described earlier. Therefore, even worst-case scenario predictions with very high users suggest that product intake will not reach that acceptable daily intake level.

**[Slide 15]**

So let’s now move into talking about how we use aspartame, and I want you to have a good understanding of how aspartame is absorbed into the gastrointestinal tract and how is it used in our body because I believe that it is really important for you to understand that before we move into looking at what are the reports on the safety of aspartame.

What you’ll see is aspartame enters the intestinal lumen or is in the gastrointestinal content and as it is in the intestinal lumen, several things can happen. There are digestive enzymes called esterases that will break off that ester from aspartame and produce methanol and the dipeptide. So, you’ll see



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methanol and aspartame, phenylalanine dipeptide. Enzymes called peptidases, which can cleave that peptide, then act on that to produce the two individual amino acids - aspartic acid or aspartylphenylalanine.

All of those products - aspartame, methanol, the dipeptide and the two individual amino acids - can enter into the mucosal cell through various uptake mechanisms. Within the mucosal cell, and those are the cells that line the surface of your gastrointestinal track, aspartame also can go through the very same steps. So it can, again, be broken down into methanol and dipeptide and then into the two individual amino acids.

What is very important for you to understand is that aspartame itself never leaves the mucosal cell. It is always broken down into methanol and the two amino acids before it enters the blood stream. So this is very important to understand when you're looking at some of the safety factors or safety studies, I'm sorry, because in some studies, scientists are taking aspartame as a whole compound and adding it into cells in culture or directly injecting it into the animal and looking at effects. That is not a physiological exposure because other than the mucosal cells of the gastrointestinal tract, no other cells actually see aspartame in its entirety. It is always broken down into the methanol and those amino acids.

**[Slide 16]**

First of all, I'm going to just talk about where else do we get those components of aspartame - phenylalanine, aspartic acid and methanol. These, as many of you would already know, are very common components in a wide number of foods. You'll see there the amount in phenylalanine and aspartic acid, methanol, that you would consume or result from the consumption of one beverage sweetened with aspartame.

In comparison, as we know, any protein-containing foods, such as milk, cheese, meat, have those amino acids in a much greater amount than you would obtain from aspartame. So aspartame really is just supplementing the other diet sources of those amino acids.

**[Slide 17]**

Let's talk for a few minutes about the metabolism of methanol. Methanol enters the body and is broken down into formaldehyde. I'm going to spend a fair bit of time talking about methanol and formaldehyde because these two components are often referenced in articles on the Web and so on as the causative or potential causative factors for potential adverse effects of aspartame. The reason is that it is well established that both of these compounds if consumed or



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if you're exposed to them in very high amounts over a short period of time can result in adverse effects.

What you'll see though is that we are well able to handle small amounts, such as the amount that would be found in tomato juice or in a soft drink sweetened with aspartame. Methanol, as we say, is broken down into formaldehyde. Formaldehyde is, in itself then, used in a number of biochemical pathways for the synthesis of amino acids and nucleic acids. Formaldehyde also can be further broken down to formic acid. Formic acid is also integral into a number of various biochemical pathways, again, used for purine synthesis, or it can be directly excreted into the urine. Formic acid that does not enter either of those pathways or excreted is broken down into carbon dioxide and water and just excreted as those components normally are.

**[Slide 18]**

The critical factor in looking at methanol metabolism is the amount that we can handle. So we can see methanol is converted by a very common liver enzyme called alcohol dehydrogenase. This enzyme is active in the metabolism of a variety of different alcohols, and it is broken down, as I said before, into formaldehyde.

The important thing is formaldehyde; the half-life of formaldehyde is very, very short. It only is in our body for about one and a half minutes and then it is very rapidly broken down into formic acid. So there is no accumulation of formaldehyde. It is the accumulation of the breakdown product of formaldehyde called formic acid. That is responsible for the toxicity of both formaldehyde and methanol.

As I said, we're exposed to methanol in our foods and various other products constantly. So there is a normal range of formic acid in our blood, and you can see that on this screen. It is once we start entering or exceeding our ability to metabolize methanol or formaldehyde that you can start to have adverse effects.

The amount of methanol that has to occur before you start seeing adverse effects is over 100 milligrams per deciliter of blood. So we can actually consume up to two grams of methanol, an adult can, without any adverse effects because of our ability to rapidly metabolize it through these pathways to carbon dioxide and water. I'm going to show you some data on what are the levels that are associated, or what levels that we see in the blood following consumption of aspartame. We'll come back to this in a minute.

**[Slide 19]**

First, I want to talk about the formaldehyde metabolism. Again, formaldehyde is not a foreign compound to us. It is a constituent of many foods. It is



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produced in the body upon demethylation of various foods and of drugs and even some common products that we consume all the time such as caffeine. So one cup of coffee actually produces 30 milligrams of formaldehyde. So, probably for most of us, myself for sure, I will have my little dose of formaldehyde every morning with my cup of coffee and my liver and so on complete handles that without any problem. It is, in fact, an essential component for, one, carbon metabolism and is a substrate for the synthesis of nucleic acids that are used for the synthesis of DNA.

In fact, some calculations are that we have over 50,000 milligrams or 50 grams of formaldehyde is produced and metabolized every day by an adult human body. Our liver is very, very good at metabolizing formaldehyde and can metabolize 22 milligrams of formaldehyde per minute for formic acid and carbon dioxide and water.

**[Slide 20]**

So this will explain the results that we're going to see on the next slide. When individuals, healthy adults were given various doses of aspartame and the effect of those doses of aspartame on methanol, formaldehyde and formic acid in the blood were evaluated, you can see, first of all, never do you find formaldehyde because formaldehyde, as I said, is broken down so quickly it is not detectable.

The levels of methanol that are produced, you can see on this slide. Even at doses of 200 milligrams per kilogram, and remember, just to put that into context, the average daily consumption over a whole day is five milligrams per kilogram. Even with 200 milligrams per kilogram of aspartame, the peak methanol concentration does not reach even three milligrams per deciliter. There is never any change in the blood formic acid level.

Just a reminder that I said before that the lowest level of blood methanol before you even start to see any kinds of toxicity is over 100 milligrams per deciliter. So a blip of three milligrams per deciliter really is just that, just a blip as the methanol is being metabolized.

So the question was also, what about healthy infants? Their liver, is it still as functional and as capable of metabolizing aspartame, and what you can see there is actually, again, methanol just does a little blip at around one milligram per deciliter. Formic acid is never detected and neither is formaldehyde.

So those first two rows were acute studies, given one dose. So the other question was, "Well, what if you are consuming aspartame-containing products every day over the course of eight hours?" So in this situation, adults were given 600 milligrams every hour for eight hours. At that level, there was no change in blood methanol or formic acid levels. I also just want to note that this also has been studied, the safety of aspartame and effect on these parameters have also been studied in individuals with liver disease, with other



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potentially impaired problems of metabolism and again, at the levels that are being consumed, there is no effect on methanol or formic acid levels.

**[Slide 21]**

So with that background in mind, let's look actually at the toxicity studies and our evaluation of the safety of aspartame. This panel looked at reports on a wide, wide variety, every possible study in terms of the safety of aspartame and you'll see this list on this slide. Today what I'm going to focus on are chronic bioassays and specifically the question of cancer and aspartame because that is one that has been in the press lately. Also, the question of neurotoxicity or the effect on the brain because, again, this is one that is often mentioned in these Internet myths and the question of safety during reproduction. I've given you some background in terms of human clinical studies, and I will just quickly review, as well, the epidemiological studies that have been done on aspartame.

**[Slide 22]**

There have been many, many long-term studies with aspartame in animals. It is the most well studied food additive that we have in the market. You can see here that we have had five long-term studies with rats, three with mice, three with transgenic mice models. Now, these are genetically engineered to be especially or highly susceptible to the induction of cancer. These were done by the National Toxicology Program. There have also been studies done with hamsters, one with dogs. All of those were conducted to assess the ability of aspartame to induce or to cause cancer. There have also been two additional studies done in rats to assess whether or not aspartame could promote or enhance the development of cancers that may already be pre-existing in an animal.

**[Slide 23]**

The findings were that 14 of those 15 animal studies had negative findings. That means that the results were that there's no evidence of a carcinogenic or cancer causing effect on aspartame. The two studies on cancer promotion were also negative.

The one study that was positive was conducted by the Ramazzini Foundation. They concluded that aspartame has carcinogenic potential. This study has been very intensely reviewed both by this panel, as well as numerous other food authorities around the world. All of the panels that have looked at this study have come to the same conclusion. Those are that the study had numerous methodological problems and the interpretation of the results had numerous errors.



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Overall, the study provided no credible evidence to other scientists that aspartame is carcinogenic or able to cause cancer. Overall, the conclusion is there is no need to further review the safety of aspartame by the food authorities and in addition, there is no need to revised previously established acceptable daily intake values.

**[Slide 23]**

Other studies that are being conducted I'm going to highlight are those on pregnancy and development of infants, or of the fetus. Aspartame also has been very intensely studied in these types of animal model studies; so studies to look at the affect on reproduction, the ability of animals, does it affect the ability of the animal to mate, to become pregnant, any affect on pregnancy or the outcome of pregnancy, the ability of the animal to lactate, produce milk, to successfully feed her pups and so on and then the development of those pups. These have been looked in rats, mice, hamsters and rabbits.

In humans, studies on the affect of lactation have been studied. In animals, there was no affect at doses up to 4,000 milligrams per kilogram per day in rodents and up to 1,600 milligrams per kilogram per day in rabbits. Those are the highest doses that were tested. That's why we have that limitation on them.

In humans, there was no change in the composition of breast milk. So what we were looking for there is there any change in the amino acid composition, or any other parameter as a result of consuming aspartame. There was no change in breast milk composition. So overall, the conclusion is that there's no evidence that aspartame, at the levels that are being consumed today, would have any adverse effects on pregnancy or development.

**[Slide 24]**

The question of headaches is one that comes up very frequently. There have been several scientific studies that have been conducted and there are some conflicting results. Most show no effect. So in these studies, individuals who feel they are susceptible to the induction of headaches are given aspartame or a placebo and followed to see whether or not there is induction of headache. As I said, both show no effect.

However, some small studies have been positive, suggesting that there may be a susceptible subset of the population that experiences headaches. There is no known mechanism. When we talk about the metabolism of aspartame and what are the breakdown products and how the body handles it, there's no biological explanation for how this could result in a headache.

It is also a very difficult question to study because, of course, there's no objective measurement. The only person that can actually know whether or not



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the individual has a headache is the individual themselves. We cannot measure the onset or the duration. So, with these studies, there's the power of suggestion. There are a lot of issues that make it very difficult to study and that is one possible explanation for why we have inconsistent results.

**[Slide 25]**

The affect of aspartame on the brain has also been one that has been a question. I found this to just be a fascinating area of research. When I undertook this study, I had no idea there had been so much work done on this topic. There have been animal studies that have been done, feeding animals up to 4% of the diet and at that level; there was no affect on any neuronal function or the brain function, ability for animals to learn various different tasks, to any change in their behavior.

This had no effect on these parameters even though there are changes in the blood and brain amino acid levels. You would expect that if you're giving those two amino acids at the level, up to 4% of the diet, it would be anticipated that you would see some changes in those amino acid levels. So what is important to understand is even though you can have a biochemical change, that can occur without there being any functional or adverse effect, and that is because we are well adapted to utilize different nutrients for various functions.

Human studies have also been done. We've looked at normal children and I always get a kick out of this. I don't know how they actually classify these, but hyperactive children, children with inborn error of metabolism, PKU - that means that they're unable to use phenylalanine at high levels in their diet - also, aggressive school boys, sugar sensitive children and airline pilots and also a number of healthy adults. Oh, I guess, actually, I should have put those airline pilots with healthy adults. Sorry - not the children, healthy adults, adults with Parkinson's disease and intervals with depression.

In the human studies, again, no effect in all of the studies that look at behavior or learning capabilities except for one small study where they did find a change. So overall, we have very good confidence that there is very little affect of aspartame on learning or behavior.

**[Slide 26]**

The ability to induce seizures has also come up as a question and has been intensely studied in a wide number of various animal models to induce convulsions and seizures in animals. Over and over again, there is no affect on aspartame when given up to doses of 1,000 milligrams per kilogram per day.

In addition to convulsions and seizures, genetically, epilepsy ... rats were evaluated as well and no effect was found. Human studies have been conducted and, of course, at doses much lower. But still, 34 to 50 milligrams



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per kilogram per day, which is upwards around ten times the current consumption levels and no effect on seizures were observed. Children have been evaluated, as well as adults.

**[Slide 27]**

So I'm now going to move from those types of clinical studies and animal studies to epidemiological studies where we're looking at what is out there in terms of effect on populations that have been consuming aspartame. One of the questions of the safety of aspartame on the brain was really stirred up again by one report, one epidemiological study that was on the first row of the table that you're seeing now by Dr. Olney where they reported that the incidence of brain tumors increased after aspartame was placed on the market.

This has been a very controversial study. The data that was used were reports of brain tumor just from nine different locations in the U.S. An important factor is that the consumption of aspartame by those individuals was never measured or confirmed. That, however, prompted a number of subsequent studies. The first one that was done by Gurney in 1977 looks specifically at a case control study where they did do dietary recalls. They found no association between consumption of aspartame and brain tumors.

There have been several others that I'm not going to go into detail, but you can see on this table. The important thing is that consistently, there has been no association between the actual consumption of aspartame and the induction of brain tumors.

The largest one that has been completed was from the National Cancer Institute where we had almost 500,000 subjects and again, they conclusively demonstrate no association between brain tumors or between counters of the blood, and that was also done in response to that Italian study I mentioned earlier. This epidemiological study confirmed no association. There's also very recently been another one from Italy by Gallus. Again, consistently no association between cancer development and sweetener consumption.

**[Slide 28]**

So let's wrap up now with a summary of what I've said. The metabolism of aspartame is very well understood and the breakdown products, methanol into two amino acids, are metabolized and follow the same pathway of those components from other common foods. The consumption, even at levels higher than expected under typical conditions, so those worst case scenarios that I talked about, has virtually no impact on the levels of blood constituents such as amino acids, methanol levels or glucose.

This is a well-studied sweetener whose safety is clearly documented and well established. I hope I've convinced you that there have been extensive



laboratory testing, animal experiments and epidemiological studies done, as well as human clinical trials.

**[Slide 29]**

There is no credible link between the consumption of aspartame at levels found in the human diet and conditions related to the nervous system or behaviour or any other symptom or illness.

Lastly, there's no evidence of genetic toxicity and no credible evidence that aspartame is carcinogenic. Studies show that it did not increase hunger in those who used it. To the contrary; there are indications that it may be an effective tool as part of an overall weight management program. You have heard, of course, much more of that from our other expert, Dr. Blackburn.

**[Slide 30]**

So the overall conclusion of this expert panel is that aspartame is a well characterized, thoroughly studied, high intensity sweetener that has a long history of safe use in the food supply and can help reduce the caloric content of a wide variety of foods. I've given you here the reference for this full report, which is quite a lengthy document, over 100 pages - so it's good bedtime reading - in critical reviews in toxicology. I'd just like to thank you, again, for your attention.

**[Slide 31]**

**J. Koelemay:** Great. Thank you very much, Dr. Magnuson. That was a wonderful presentation, and I know that the registered dieticians and other health professionals listening to the Webinar can definitely use the information you provided in helping their clients better understand and feel safe about the use of low calorie sweeteners in their diets.

I have a couple of questions I just want to clarify with you as we wrap up here. One of the questions that came to us prior to the event was asking the number of milligrams of aspartame in a diet soft drink. I have found that information and I want to share that with everyone on the record here.

In Diet Coca-Cola, which has the highest amount of aspartame in Coca-Cola products, and that's because aspartame is the sole sweetener in Diet Coke where in our other diet beverages there is a blend of aspartame and other sweeteners such as AceK. There's 125 milligrams per eight ounces in a Diet Coke. So for those of you who want to do that math, when we were looking at the ADI slides, that's just over six cans for a child of 50 pounds to meet that ADI. So those numbers, if you do the math, that balances out just about perfectly. I wanted to address that for everyone.



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Dr. Magnuson, thank you, again, for your comments. I know you were part of a very large panel that addressed this issue, and I have one other question for you. This panel was sponsored by the maker of aspartame. Is that correct?

**Dr. B. Magnuson:** That's correct.

**J. Koelemay:** Can you address that? Did you know that they were the sponsor when you conducted your analysis?

**Dr. B. Magnuson:** Sure. Thank you for asking me about it so I have the opportunity to address it. The producer of aspartame, one of the largest producers is Ajinomoto. They came to the private consulting firm that I was working with, Murdock Group, and asked us to conduct this review.

The criteria were, first of all, that we had free hand to come up with any conclusion. So it was what is called an unrestricted support. The only criterion is that the findings were given to them before to the press. The other important factor is that the expert panel was chosen by the Murdock Group and the identity of the panelists was never given to the sponsor until after the paper was published.

Similarly, the panelists did not know who the sponsor was until the paper was submitted for publication. So it was sort of a double blind, if you will, and it was only after the paper was submitted for publication did the sponsor know who the expert panel was and vice versa. The other important thing to consider is that this report also underwent extensive peer review by the critical reviews in toxicology. This is one of the top journals in toxicology and they also had world-renowned reviewers look very carefully and they also had world-renowned reviewers look very carefully at this paper before it was published

**J. Koelemay:** Then another e-mail question that I know you are going to be addressing via email was asking a little more information about the Ramazzini study. I know you went into that at the beginning of your presentation. Could you just sum that up again specifically on that topic in terms of the issues and the concerns that were raised by the Ramazzini study in Italy?

**Dr. B. Magnuson:** Sure. This was a very large study that was conducted by the Ramazzini Institute and what they did was feed a large number of animals different doses of aspartame until their natural death. So unlike the traditional toxicology study where there is a preset, usually two years, where all the animals are terminated and the evaluation of pathology are done then, this group uses rather unconventional protocol and allows the animals to live until they die naturally.

One of the biggest problems with that study is that there was a very large problem with infection in the animals that the infection rates amongst different groups was inconsistent and highly variable.



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So the conclusions were that a lot of the pathologies and the results that were found were probably secondary to these chronic lung infections and other problems in their animal studies that were not well controlled for.

In all other studies that are conducted in various toxicology laboratories, it is a requirement that you start with healthy animals, drug-free animals and you do not have that complication of infection. So that's why despite a large study, every authority that has looked at those and reviewed their slides, as well as our group found that the study is just not valid in terms of the conclusions that it has drawn.

**J. Koelemay:** Then one last question. We're looking at an ADI of aspartame at 50 milligrams per kilogram of body weight in the U.S. As I understand it each sweetener has its own ADI established. Does that mean that if you consumer aspartame and sucralose, the sucralose does not count against the ADI for aspartame? Is that how that works?

**Dr. B. Magnuson:** No. Each one is done individually and I think that if there was any evidence or similar metabolism; I mean if there was any evidence of potential interaction that potentially could be considered. But each of these sweeteners really is very different from each other in terms of how they're metabolized. There's really no, at least in my mind, I can't think of why the intake of one should affect the intake of another.

**J. Koelemay:** The reason I'm asking; well, first, if our audience interested in us pursuing a similar talk on sucralose, we certainly will do that, but also that if a patient or a client feels that they're sensitive to aspartame, that there are alternative sweeteners that, as you said, are metabolized differently, that have their own ADI and that they can use, and if they want to limit aspartame use, they can certainly choose beverages with Splenda or sucralose and other sweeteners. I think that that's also important to understand, that they aren't all the same and that they're each metabolized differently. Thank you for clarifying that.

**Dr. B. Magnuson:** No problem.

**J. Koelemay:** Again, thank you, everyone. Our time is up and I think the presentation was extremely well done. All this information will be available on the Beverage Institute Web site as podcast and transcripts very shortly, as soon



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as we can get all of that done. So again, thank you, again, Dr. Magnuson for this information and have a great day.

The Beverage Institute For Health & Wellness is a scientific organization, within The Coca-Cola Company, dedicated to increasing understanding of the role that beverages play in nutrition and health around the world.