COMPLAINT NUMBER	20/147
ADVERTISER	Tru Niagen NZ
ADVERTISEMENT	Tru Niagen NZ Print
DATE OF MEETING	11 August 2020
OUTCOME	Not Upheld in part & Settled in part No further action required

Summary of the Complaints Board Decision
The Complaints Board did not uphold a complaint about a newspaper advertisement for Tru Niagen dietary supplement. The Board said the advertisement was not misleading and the Advertiser had provided sufficient substantiation to support the health benefit claims made. The Board agreed there were errors in the graph in the advertisement. However, in light of the self-regulatory action taken by the Advertiser in agreeing to remove this graph, the Board ruled this part of the complaint was Settled.

Advertisement
The newspaper advertisement for Tru Niagen dietary supplement says in part it "supports healthy levels of NAD (nicotinamide adenine dinucleotide) ... When we take TRU NIAGEN our NAD levels rise. A daily dose of TRU NIAGEN supports healthy levels of NAD in cells so they can function at their best."

Summary of the Complaint
The Complainant was concerned the advertisement was misleading and makes unsubstantiated claims about how the use of Tru Niagen can benefit health.

Issues Raised:
- Social Responsibility
- Mandatory Information
- Natural Health and Dietary Supplements
- Safety and Effectiveness
- Scientific Language
- Truthful Presentation

Summary of the Advertiser's Response
The Advertiser defended the advertisement. They acknowledged the errors in the graph but said they do not think they cause the advertisement to be misleading. They said they only make three claims in the advertisement:

1) That NAD+ declines with age and under metabolic stress
2) That Tru Niagen supports NAD+ levels
3) Healthy NAD+ levels are required for healthy cellular function

Relevant ASA Codes of Practice

The Acting Chair directed the Complaints Board to consider the complaint with reference to the following codes:

THERAPEUTIC AND HEALTH ADVERTISING CODE

Principle 1: Social Responsibility: Therapeutic and Health advertisements shall observe a high standard of social responsibility particularly as consumers often rely on such products, devices and services for their health and wellbeing.

Rule 1 (a) Mandatory information: Advertisements shall contain the following mandatory information to encourage responsible prescribing, recommendation, sale and use. This information shall be set out in a way (legible / audible) that ensures it can be readily understood by the audience to whom it is directed.

Natural Health Products and Dietary Supplements
Any mandatory information as required by the applicable legislation and the following statements:

- Name and address of the advertiser
- *Always read the label and use as directed.*

For products that contain vitamins and / or minerals, the following additional statement (or words to this effect).

- *Vitamins and minerals are supplementary to and not a replacement for a balanced diet.*

Rule 1 (b) Safety and effectiveness: Advertisements shall not contain any claim, statement or implication that the products, devices or services advertised:

- are safe or that their use cannot cause harm or that they have no side effects or risks.
- are effective in all cases
- are infallible, unfailing, magical, miraculous, or that it is a certain, guaranteed or sure cure
- are likely to lead persons to believe that;
    - they are suffering from a serious ailment, or
    - harmful consequences may result from the therapeutic or health product, device or service not being used.

Rule 1 (d) Scientific language: The use of scientific language in advertisements is acceptable providing that it is appropriate to, and readily understood by, the audience to whom it is directed.

Principle 2: Truthful Presentation: Advertisements shall be truthful, balanced and not misleading. Advertisements shall not mislead or be likely to mislead, deceive or confuse consumers, abuse their trust, exploit their lack of knowledge or without justifiable reason, play on fear. This includes by implication, omission, ambiguity, exaggerated or unrealistic claim or hyperbole.

Rule 2 (a) Truthful presentation: Advertisements shall be accurate. Statements and claims shall be valid and shall be able to be substantiated. Substantiation should exist prior to a claim being made. For medicines and medical devices, therapeutic claims must be consistent with the approved indication(s) (for medicines) or the listed intended purpose (for medical devices).

The Complaints Board agreed that while the Complainant had referred to the Advertising Standards Code, all of the matters raised in their complaint could be dealt with under the Therapeutic and Health Advertising Code.

Relevant precedent decisions
In considering this complaint the Complaints Board referred to three precedent decisions, Decision 16/007, which was Not Upheld, 17/096 which was Upheld in part and Settled in part and 18/251 which was Upheld in part, Settled in part and Not Upheld in part.

The full versions of these decisions can be found on the ASA website:
https://www.asa.co.nz/decisions/

Decision 16/007 concerned a Health 2000 brochure advertisement which included a "Clinicians Hi Dose Vit C" supplement which referred to the effect of Vitamin C on the immune system.
The Complaints Board said the Advertiser substantiated the claims about the effect of Vitamin C on the immune system. It said the Complainant had taken an extreme interpretation of the advertisement and when considered in its entirety the advertisement was unlikely to mislead consumers.

Decision 17/096 concerned a website advertisement for NZfulvic (www.nzfulvic.com) which promoted the various health benefits of consuming the "mineral rich" dietary supplement. The NZfulvic Benefits page (www.nzfulvic.com/benefits) showed a bottle of the product surrounded by several health benefit claims. The website also included a testimonial about weight loss.
Noting the removal of the testimonial from the website, the Complaints Board ruled this part of the complaint was Settled. The Complaints Board found the remaining claims were not supported to the level required for health benefit claims and were likely to mislead consumers. The claims were also found to use scientific language which was unlikely to be clearly understood by the general consumer and the advertisement had not been prepared with the high standard of social responsibility to consumers and society required of therapeutic and health advertisements.

Decision 18/251 concerned a website advertisement for BePure Health Ltd, www.bepure.co.nz , which promoted health and wellness and offered "Scientific, Holistic Health" by selling multi-vitamins, fish oil, urine tests and nutrition programmes.

The Complaints Board said sufficient substantiation had not been provided for the claims regarding:

- Comprehensive Stool Parasitology Testing with Analysis,
- IGG/IGA Elisa Testing,
- 15 tips to support fertility including dietary supplement products and techniques to address oestrogen dominance, low progesterone and excess testosterone,
- The accuracy and reliability of the quality (previously "gold standard") functional health testing.

The Complaints Board agreed these parts of the complaint were Upheld.

The Complaints Board noted the amendments the Advertiser made to the website advertisement regarding: the BePure Programmes, Functional Tests (for Mood, Sleep and Oxidative Stress, Cellular Energy and Nutrients) and the home collection urine tests. The Complaints Board agreed the amendments had addressed the misleading claims issues raised by the Complainant and agreed these parts of the complaint were Settled.

The Complaints Board said a sufficient response had been provided by the Advertiser for the claims regarding the purpose of the functional health Gut and Liver Health Screening,

Hormone Balance Test and the Adrenal Function Test and agreed these parts of the complaint were Not Upheld.

Complaints Board Discussion

Consumer Takeout

The Complaints Board agreed the likely consumer takeout was Tru Niagen supports NAD levels in the body, which decrease with age. These NAD levels can open our bodies up to the usual range of age-related concerns. This product is backed by science.

Therapeutic and Health Advertising Code

The Complaints Board noted that under the Therapeutic and Health Advertising Code:
"Only medicines with consent to distribute in New Zealand and medical devices can claim to have a therapeutic purpose in advertisements" and "Health Benefit claims in advertisements for a Natural Health Product and Dietary Supplement must be supported by scientific or traditional substantiation."

Did the advertisement make any therapeutic or health benefit claims?

The Complaints Board agreed the advertisement did not make any therapeutic claims but did make a health benefit claim: that Tru Niagen supplementation supports healthy levels of NAD. The Board said this advertisement is similar to advertisements for other dietary supplements. It doesn't make any specific claims about the product itself but rather it describes the role of NAD in the body and how Tru Niagen supports this role.

Has the relevant mandatory information for a dietary supplement been provided?

The Complaints Board agreed the relevant mandatory information for a dietary supplement had been provided. The Board noted the advertisement included the name and address of the advertiser, the text "Always read the label and use as directed" and "Vitamins are supplementary to a balanced diet".

Is the advertisement in breach of Rule 1(b) Safety and effectiveness?

The Complaints Board agreed the advertisement was not in breach of Rule 1(b) Safety and effectiveness. The Board said the advertisement did not claim that the product was "effective in all cases".

Is the advertisement misleading?
Have the claims made in the advertisement been substantiated?

The Complaints Board agreed the advertisement was not misleading. The Board said the Advertiser had provided sufficient substantiation to support the claims made in the advertisement.

Is the use of data misleading?
Is the use of scientific language appropriate?

The Complaints Board agreed there were errors in the graph and noted the comments made by the Advertiser: "We acknowledge there were errors in the Advertisement and that "protein" was mistakenly abbreviated to "pro" and "ng" was erroneously recorded as "µg" on the graph's Y axis. (See Appendix 2).

However, in light of the self-regulatory action taken by the Advertiser in agreeing to remove this graph from the advertisement, the Board ruled this part of the complaint was Settled.

With regard to its consideration of the advertisement as a whole and the likely consumer takeout, the Complaints Board confirmed the errors in the axis labelling on the graph did not make the overall advertisement misleading.

Does the advertisement observe a high standard of social responsibility?

The Complaints Board agreed the advertisement did observe a high standard of social responsibility. This is because the advertisement was not misleading,

The Complaints Board said the advertisement was socially responsible, taking into account context, medium, audience and product and was not in breach of Principle 1, Rule 1(a), Rule 1(b), Principle 2 or Rule 2(a) of the Therapeutic and Health Advertising Code.

The Complaints Board said the complaint about a breach of Rule 1(d) was Settled.

Outcome
The Complaints Board ruled the complaint was **Not Upheld in part and Settled in part.**

No further action required.

APPEAL INFORMATION

According to the procedures of the Advertising Standards Complaints Board, all decisions are able to be appealed by any party to the complaint. Information on our Appeal process is on our website www.asa.co.nz. Appeals must be made in writing via email or letter within 14 calendar days of receipt of this decision.

APPENDICES

1. **Complaint**
2. **Response from Advertiser**
3. **Response from Media**

Appendix 1

COMPLAINT

Complaint about the "Tru Niagen" advertisement placed in The Press (Christchurch) on 25 April (p. A6), 2 May (p. A7) and 9 May 2020.

Contraventions of the Advertising Standards Code
Principle 2 (Truthful Presentation)
Rules 2(b) Truthful presentation, 2(c) Use of data, and 2(e) Advocacy advertising.

The graph is poorly and misleadingly presented. Therefore, the evidence "is not easily understood" (guideline to rule 2(b)). The labelling of the vertical axis of the graph is incomplete. For instance, what is the meaning of "pro"? Most members of the public would have no idea of the meaning of "µg / mg". The guidelines to rule 2(c) state that "scientific language" should be "readily understood", in this case, by the public. Therefore rule 2(c) has been contravened. In what material has NAD been measured? It is not stated. There is no citation to the study from which this data has been taken so the public cannot check its truthfulness. The evidence is therefore not "readily available and obtainable" (guideline to rule 2(e)).

I have found that the graph has been taken from the following research paper: Massudi H and others. 2012. Age-associated changes in oxidative stress and NAD+ metabolism in human tissue. PLoS ONE, vol. 7, issue 7, e42357, pp. 9. Below is the figure from the paper which is the source of the graph in the advert.

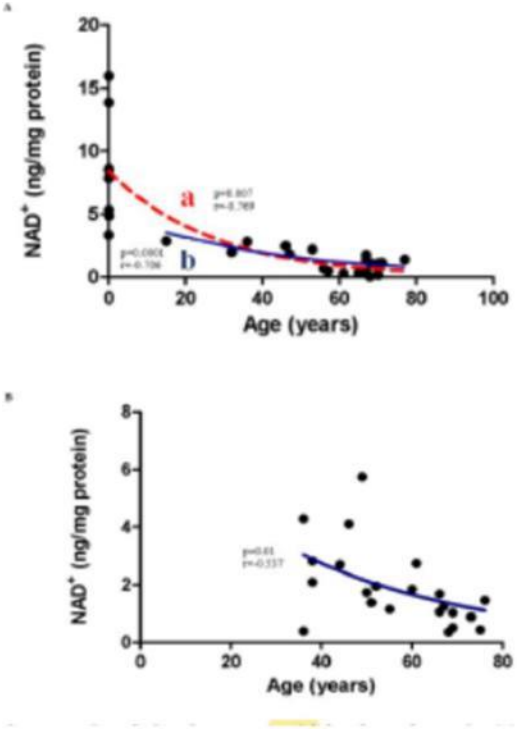

Figure 4. Correlation between NAD+ levels and Age in (A) Males (B) Females. (A) NAD+ concentrations decline with age in males. NAD+ levels decreased significantly in males aged between 0–77 years (line a; $p = 0.0007$; $n = 27$). Pearson's correlation coefficient for a normally distributed population, $r = -0.769$. The post-pubescent data for male subjects also showed a decline in NAD+ levels with age (line b; $r = -0.706$; $p = 0.0001$; $n = 19$). An exponential (first-order) least squares fit was used to generate the nonlinear trend lines (line a and b). **(B) NAD+ concentrations decreased significantly with age (36–76) in post-pubescent females ($p = 0.01$; $n = 22$).** Pearson's correlation coefficient for a normally distributed population, $r = -0.537$. An exponential (first-order) least squares fit was used to generate the nonlinear trend line.
doi:10.1371/journal.pone.0042357.g004

It can be seen that "pro" in the advert means "protein". The label on the vertical axis states that this is measured in nanograms per milligram (ng / mg) and not micrograms per milligram (µg / mg) as shown in the advert. This is a clear "untruth" (rule 2(b)) albeit a minor one. There is no indication of the value at which the vertical axis starts. It could be zero, it could be 1, it could be 4 or whatever. The "0" displayed clearly relates to "Age" on the horizontal axis and not to the vertical axis. The vertical axis scale could be linear or it could be exponential. This is all "misleading" and might even "exploit [consumers] lack of knowledge" (rule 2(b)).

The study is based on measurements of skin cells only. This is not mentioned in the advert. The advert implies by omission that it applies to the whole body. Results in skin cells do not necessarily reflect what might occur in other organs (this is "exaggeration" and "omission" under rule 2(b)).

Two graphs are presented in the research paper, one for males (top) and one for females (bottom). The graph in the advert appears to be an approximate merger of the two but does not say so ("inaccuracy", "omission" under rule 2(b)).

The entire study used only 48 participants. There were no females below the age of 30. There was only one male teenager. There were no participants in their 20s. Despite this the text immediately above and below the graph makes claims about teenagers and people in their twenties: "NAD is plentiful while we are teenagers" and "once we get into our twenties, NAD levels gradually start to decline". This is entirely scientifically invalid. It is quite possible that teenagers and people in their twenties have a huge range in their NAD levels as is apparent in the graph (top) for newborn male children (range about 4 - 16 ng / mg NAD). Therefore, the claims made are "false representation" (rule 2(b)) and "overstate the significance of any results" (rule 2(c)).

All the other claims made in the advertisement derive from their claims about the data displayed in this graph. The fourth line below the graph states: "Until recently, this decline in NAD was thought to be an irreversible consequence of ageing". As argued above, the graph does not indicate an irreversible decline in ageing because of the lack of data for teenagers and people in their twenties and because there is no data for females below the age of 30. The final line of the conclusions in Massudi and others (2012) states that the "...therapeutic benefit of this approach in humans is yet to be established", this approach being an increased intake of NAD. It is the latter that the advertisement is aiming to encourage by purchase of Tru Niagen.

Contraventions to the Therapeutic and Health Advertising Code

1(a) Mandatory information

The points made above about the graph and associated text also apply here. The information is not "set out in a way that ensures it can be readily understood by the audience to whom it is directed."

1(b) Safety and effectiveness

As explained above, the advertisement uses data from a study of skin cells to claim a "decline in NAD.....thought to be an irreversible consequence of ageing". It then goes on to imply that

the use of Tru Niagen would benefit "Heart and blood vessel cells, brain and nerve cells, bone cells, reproductive and hormone-producing cells, our liver and kidney cells, immune cells..." Rule 1(b) states that there should be no claim or implication of a product to be "effective in all cases" as is done here in the advert.

1(d) Scientific language
The points made above about the graph and associated text also apply here. The scientific language is not "readily understood by the audience to whom it is directed".

2(a) Truthful presentation
The points made above about the graph and associated text also apply here. The claims cannot be substantiated as is required by this rule.
Additionally, although the advert states that its claims are backed by "170 scientific studies" there is no advice as to how a member of the public could find any of these. The address of their web-site is provided (www.truniagen.co.nz) and it supplies authors and dates of three studies with human subjects, and authors and dates of six studies with non-human models. However, full citations are not provided and there are no active links to the full publications. Therefore, members of the public would be unable to substantiate the claims.

Final comment
I have been able to find a full copy of one of the two most recent (2018) studies on human subjects (Martens CR and others. 2018. Chronic nicotinamide riboside supplementation is well-tolerated and elevates NAD+ in healthy middle-aged and older adults. Nature Communications 9: 1286, 11 pp.). Nicotinamide riboside (NR) is Niagen the trade name of which is Tru Niagen. Although the results of this study appear to support some claims made in the advert, it is important to note that the authors also state: 1) that their study was an "exploratory analysis", 2) that it was a "small initial intervention trial", 3) "Finally, we wish to emphasize certain limitations of this initial trial on chronic NR supplementation in humans. Because the physiological outcomes in this study were designed to be exploratory in nature...".

In an interview (https://www.sciencedaily.com/releases/2018/03/180329083313.htm) two of the authors of Martens and others (2018) stressed that the study was "small and pilot in nature". Also, Martens stated: "We are not able to make any definitive claims that this compound is safe or going to be effective for specific segments of the population "What this paper provides us with is a really good stepping stone for future work".

These statements confirm that much of the advert is hyperbole and exaggeration and the science that might truly and strongly support the claims has yet to be performed.

Appendix 2

RESPONSE FROM ADVERTISER, TRU NIAGEN NZ

RE: Response to complaint … re advertisement in The Press (Christchurch) on 25 April (p. A6), 2 May (p. A7) and 9 May 2020 (“the Advertisement”).

Dear Members of the Advertising Complaints Board,

TRU NIAGEN New Zealand has elected to defend the complaints set out by [The Complainant] in his letter to dated 15 May 2020 (“the Letter”). For ease of reference, we address each of [his] complaints in the same order they are set out in the Letter.

1.) Principle 2 (Truthful Presentation) - Rules 2(b) Truthful presentation, 2(c) Use of data, and 2(e) Advocacy advertising:

We have broken [The Complainant's] submission in relation to Principle 2 of the Advertising Standards Code ('the Code") into parts as follows:

Graph & units of measurement
We acknowledge there were errors in the Advertisement and that "protein" was mistakenly abbreviated to "pro" and that "ng" was erroneously recorded as "µg" on the graph's Y axis. However, we do not believe that these mistakes to measuring units would have misled the average consumer or materially changed the way in which the Advertisement was interpreted. There was no intention to deceive or mislead the public, rather this was a mistake in copywriting which will be rectified in future advertising.

Alternatively, we would be agreeable to removing the units of measurements entirely, so that it's clear that the graph is just a general representation of the decline of NAD+ levels with age – which is the purpose of its inclusion in the Advertisement (rather than depicting the results from one particular study).

Scientific references
On one hand, [The Complainant] is stating in the Letter that scientific language used should be understandable and on the other he is asking for citations to scientific literature and studies for consumers to check truthfulness.

From the advice we have received from various TAPS adjudicators, including scientific references and links to study results is not appropriate in consumer advertising and could lead to greater confusion to the most members of the public. Therefore, we refute [The Complainant's] assertion that there has been a breach of principle (2)(e).

Scientific data
Our understanding of the Code and from the advice we've received through the TAPS pre-approval process, is that the information displayed in advertisements should not be so technical that the average New Zealander would become confused and then more easily misled by scientific jargon.

The purpose of including the graph in the Advertisement was to simply illustrate to readers that NAD+ levels decline with age. This was in no way meant to be deceiving and is widely accepted scientific fact.

We disagree that there has been false representation (2(b)) or an over statement of significance of any results (2(c)) and would refer you to a selections of studies (listed below) evidencing the decline in NAD+ levels in multiple tissue types with age. We have highlighted sections of particular relevance below and in further detail in the full studies **attached** to the covering email.

Age-Associated Changes In Oxidative Stress and NAD⁺ Metabolism In Human Tissue

Hassina Massudi,[1,2] Ross Grant,[1,2,] Nady Braidy,[1,3] Jade Guest,[1,2] Bruce Farnsworth,[2] and Gilles J. Guillemin[1,4]*

Published online 2012 Jul 27. doi: 10.1371/journal.pone.0042357

https://pubmed.ncbi.nlm.nih.gov/22848760/

Nicotinamide adenine dinucleotide (NAD(+)) is an essential electron transporter in mitochondrial respiration and oxidative phosphorylation. In genomic DNA, NAD(+) also represents the sole substrate for the nuclear repair enzyme, poly(ADP-ribose) polymerase (PARP) and the sirtuin family of NAD-dependent histone deacetylases. Age associated increases in oxidative nuclear damage have been associated with PARP-mediated NAD(+) depletion and loss of SIRT1 activity in rodents. In this study, we further investigated whether these same associations were present in aging human tissue. Human pelvic skin samples were obtained from consenting patients aged between 15-77 and newborn babies (0-1 year old) (n = 49) previously scheduled for an unrelated surgical procedure. DNA damage correlated strongly with age in both males (p = 0.029; r = 0.490) and females (p = 0.003; r = 0.600) whereas lipid oxidation (MDA) levels increased with age in males (p = 0.004; r = 0.623) but not females (p = 0.3734; r = 0.200). PARP activity significantly increased with age in males (p<0.0001; r = 0.768) and inversely correlated with tissue NAD(+) levels (p = 0.0003; r = -0.639). These associations were less evident in females. A strong negative correlation was observed between NAD(+) levels and age in both males (p = 0.001; r = -0.706) and females (p = 0.01; r = -0.537). SIRT1 activity also negatively correlated with age in males (p = 0.007; r = -0.612) but not in females. Strong positive correlations were also observed between lipid peroxidation and DNA damage (p<0.0001; r = 0.4962), and PARP activity and NAD(+) levels (p = 0.0213; r = 0.5241) in post pubescent males. This study provides quantitative evidence in support of the hypothesis that hyperactivation of PARP due to an accumulation of oxidative damage to DNA during aging may be responsible for increased NAD(+) catabolism in human tissue. The resulting NAD(+) depletion may play a major role in the aging process, by limiting energy production, DNA repair and genomic signalling.

Changes in Oxidative Damage, Inflammation and [NAD(H)] with Age in Cerebrospinal Fluid

Jade Guest, [1,2] Ross Grant, [2,3,] Trevor A. Mori, [4] and Kevin D. Croft [4]* *Published online 2014 Jan 14. doi: 10.1371/journal.pone.0085335*

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3891813/

An extensive body of evidence indicates that oxidative stress and inflammation play a central role in the degenerative changes of systemic tissues in aging. However a comparatively limited amount of data is available to verify whether these processes also contribute to normal aging within the brain. High levels of oxidative damage results in key cellular changes including a reduction in available nicotinamide adenine dinucleotide (NAD^+), an essential molecule required for a number of vital cellular processes including DNA repair, immune signaling and epigenetic processing. In this study we quantified changes in [NAD(H)] and markers of inflammation and oxidative damage (F2-isoprostanes, 8-OHdG, total antioxidant capacity) in the cerebrospinal fluid (CSF) of healthy humans across a wide age range (24–91 years). CSF was collected from consenting patients who required a spinal tap for the administration of anesthetic. CSF of participants aged >45 years was found to contain increased levels of lipid peroxidation (F2-

isoprostanes) (p=0.04) and inflammation (IL-6) (p=0.00) and decreased levels of both total antioxidant capacity (p=0.00) and NAD(H) (p=0.05), compared to their younger counterparts. A positive association was also observed between plasma [NAD(H)] and CSF NAD(H) levels (p=0.03). Further analysis of the data identified a relationship between alcohol intake and CSF [NAD(H)] and markers of inflammation. The CSF of participants who consumed >1 standard drink of alcohol per day contained lower levels of NAD(H) compared to those who consumed no alcohol (p<0.05). An increase in CSF IL-6 was observed in participants who reported drinking >0–1 (p<0.05) and >1 (p<0.05) standard alcoholic drinks per day compared to those who did not drink alcohol. Taken together these data suggest a progressive age associated increase in oxidative damage, inflammation and reduced [NAD(H)] in the brain which may be exacerbated by alcohol intake.

Implications of NAD⁺ Metabolism in the Aging Retina and Retinal Degeneration

Oxid Med Cell Longev. 2020; 2020: 2692794.

Published https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7238357/ online 2020 May 9. doi: 10.1155/2020/2692794

Ravirajsinh N. Jadeja,[1] Menaka C. Thounaojam,[2,3] Manuela Bartoli,[2,3] and Pamela M. Martin[1,2,3]

Although not completely understood with respect to underlying mechanisms, the relevance of NAD⁺ metabolism to aging and longevity has been known for decades. Recent studies have brought to the forefront once again the importance of NAD⁺ metabolism in these processes. The age-dependent decline in NAD⁺ levels has been demonstrated to occur in animal models and humans, in multiple organs including the brain, liver, muscle, pancreas, adipose tissue, and skin [6, 14, 76, 77]. Our recent work coupled with that of others has added the retina, specifically photoreceptor, ganglion, endothelial, and retinal pigment epithelial (RPE) cells, to this growing list of tissues/cell types [24, 25, 67, 68, 72]. Not only do NAD⁺ levels decline with increased age but also an extensive metabolic study conducted by Wang et al., using the cornea, RPE/choroid, and lens, confirmed significant difference in metabolites present within aged (73 weeks old) mouse tissues compared to those present in mice of a relatively young age (6 weeks old) [78]. Together, these data suggest that there is a universal age-dependent decrease of cellular NAD⁺ across species and that most if not all tissues and cell types, excluding possibly only those cells in which mitochondria are absent (e.g., red blood cells), are impacted, to some degree, by the consequent metabolic alterations that emanate. The decrease in NAD⁺ levels is attributed to an imbalance between NAD⁺ synthesis and consumption given that the expression and activity of enzymes critical to NAD⁺ synthesis decline with increasing age despite the fact that the obligatory requirement for NAD⁺ remains high.

2.) Therapeutic and Health Advertising Code:

1(a) Mandatory information

All required mandatory information under this section of the Therapeutic and Health Advertising Code was included in this Advertisement and a TAPs approval number was issued.

Therefore we assert the Advertisement was not in breach of this section.

1(b) Safety and effectiveness
As we have covered the issue of declining NAD+ levels above, we will turn to [The Complainant's] next assertion that the Advertisement implies that Tru Niagen would be benefit "*Heart and blood vessel cells, brain and nerve cells, bone cells, reproductive and hormone-producing cells, our liver and kidney cells, immune cells*..."

We refute that we have made a "*claim or implication of a product to be effective in all cases",* rather the purpose Advertisement is to educate (without confusing) the reader about the crucial role NAD+ plays in every cell in your body (whether it be skin cells, eye cells, brain or muscle cells etc).

It is also accepted scientific fact that NAD+ is the central coordinator of cellular metabolism and that without NAD+, redox reactions required for energy production could not take place. This is taught in every high school and university in the country.
The R. Jadeja study on retinal degeneration begins:

> *Nicotinamide adenine dinucleotide (NAD+) was discovered in 1906 as a coenzyme involved in yeast fermentation [1]. We now know it to be an important cofactor, required for at least 500 different enzymatic reactions in the body including those central to key metabolic pathways such as glycolysis, fatty acid (β) oxidation, the tricarboxylic acid (TCA) cycle, and oxidative phosphorylation as the redox interplay between the oxidized (i.e., NAD+) and reduced forms of NAD (i.e., NADH) governs the activity of critical enzymes in these pathways [2, 3]. NAD+ is also consumed in the processes of protein deacetylation and ADP-ribosylation by sirtuin and poly (ADP-ribose) polymerase (PARP), respectively [2, 4]. Further, the NAD glycohydrolases, CD38 and CD157 (BST1), consume NAD+ through the conversion of NAD into ADP-ribose (ADPR) or cyclic-ADPR [5]. Thus, the facilitation of biologic processes central to the maintenance of the living mammalian (e.g., metabolism, DNA repair, and gene expression) hinges upon the availability of NAD+.*

1(d) Scientific language
We restate our comments above in relation to scientific information/jargon.

2(a) Truthful presentation
The advice we received from the TAPs adjudicator was that while we could include reference to scientific studies (although not mandatory for consumer advertising), active links to full studies are not allowed on our website as they're deemed too technical for the average consumer to interpret and thus would lead to confusion.

As such, we do not believe the Advertisement was in contravention of this section.
However, if it is the Board's advice that we do include active inks to studies on our website, we are agreeable to doing so.

We also note that all ongoing and published scientific studies (preclinical and clinical) in relation to NR and NAD+ can be found online at www.aboutnad.com.

Final comment
[The Complainant] starts that *"I have been able to find a full copy of one of the two most recent (2018) studies on human subjects*" and then goes on to cite comments from the Martens 2018 study that *"Although the results of this study appear to support some claims made in the advert, it is important to note that the authors also state: 1) that their study was an "exploratory analysis", 2) that it was a "small initial intervention trial".*

We must point out that [The Complainant] is wholly mistaken here and has not in fact found or cited the most recently published studies which reconfirm the claims in the Advertisement that Tru Niagen/NR supports healthy levels of NAD+ in humans.

Please refer to excerpt from the latest safety study titled **Safety and Metabolism of Long-term Administration of NIAGEN (Nicotinamide Riboside Chloride) in a Randomized, Double-Blind, Placebo-controlled Clinical Trial of Healthy Overweight Adults**:

Dietrich Conze, Charles Brenner & Claire L. Kruger . *Scientific Reports* **volume 9**, Article number: 9772 (2019) Published: 05 July 2019

> *"To date, NR has also been tested in six clinical trials. The first clinical trial of NR established the safe oral availability of single doses and the timecourse by which NR elevates the human blood NAD metabolome. The second trial provided additional safety data for healthy people taking NR for 8 days. The third and fourth trials addressed NR safety in healthy people either taking 500 mg NR twice daily for 6 weeks or combination of up to 500 mg NR and 100 mg pterostilbene per day for 8 weeks…… A fifth clinical trial documented the safety and tolerance of ingesting 2 grams NR per day for 12 weeks in obese men and post hoc analyses suggested that there was an improvement in fatty liver in the NR-treated group44. In a sixth clinical trial, single 500 mg doses of NR depressed markers of oxidative damage while increasing NADPH and exercise performance in older individuals.*
>
> *All tissues produce NAD^+ from nicotinamide (NAM) or the recently identified NAD^+ precursor, nicotinamide riboside (NR)5 Some tissues can produce NAD^+ from tryptophan de novo and nicotinic acid (NA)2, although the generation of NAD^+ from tryptophan is much less efficient than from the vitamin precursors of NA, NAM, or NR, which are collectively termed vitamin B3. NAD^+ can also be supported by dietary precursors6. For example, pellagra, a disease of deficiency of NAD^+ precursors, can be prevented or treated with approximately 15 mg/day of NA or NAM or with 60-times as much tryptophan7. Importantly, despite homeostatic systems and dietary intake of NAD^+ precursors, it is now known that the levels of NAD^+ co-enzymes are continuously challenged by metabolic stress. In the overfed and type 2 diabetic mouse livers, levels of NADPH are strikingly depressed8, whereas in noise-induced hearing loss9, heart failure10, peripheral nerve damage11, central brain injury12 and the liver of a lactating mouse13, NAD^+ levels are compromised. Moreover, NAD^+ levels have been reported to decline in response to DNA damage14, alcohol metabolism15, and aging16,17, and the expression of nicotinamide phosphoribosyltransferase (NAMPT), the enzyme required for NAM salvage, declines with aging18 and chronic inflammation19. Thus, considering the relationships between NAD^+, metabolic stress and aging, nutritional scientists are now investigating whether the ingestion*

of higher levels of a B3 vitamin should be part of an evidence-based approach to optimize health2.

To evaluate the kinetics and dose-dependency of NR oral availability and safety in overweight, but otherwise healthy men and women, an 8-week randomized, double-blind, placebo-controlled clinical trial was conducted. Consumption of 100, 300 and 1000 mg NR dose-dependently and significantly increased whole blood NAD^+ (i.e., 22%, 51% and 142%) and other NAD^+ metabolites within 2 weeks. The increases were maintained throughout the remainder of the study. There were no reports of flushing and no significant differences in adverse events between the NR and placebo-treated groups or between groups at different NR doses.

We also include links to other studies with relevant excerpts (see below):

Published: December 6, 2017 https://doi.org/10.1371/journal.pone.0186459

An open-label, non-randomized study of the pharmacokinetics of the nutritional supplement nicotinamide riboside (NR) and its effects on blood NAD+ levels in healthy volunteers

Sophia E. Airhart, Laura M. Shireman,Linda J. Risler, Gail D. Anderson, G. A. Nagana Gowda, Daniel Raftery, Rong Tian, Danny D. Shen, Kevin D. O'Brien

- *The co-primary objectives of this study were to determine the human pharmacokinetics (PK) of oral NR and the effect of NR on whole blood nicotinamide adenine dinucleotide (NAD+) levels*

- *Oral NR was well tolerated with no adverse events. Significant increases comparing baseline to mean concentrations at steady state (Cave,ss) were observed for both NR (p = 0.03) and NAD+ (p = 0.001); the latter increased by 100%. Absolute changes from baseline to Day 9 in NR and NAD+ levels correlated highly (R2 = 0.72, p = 0.008).*

- *Because NR increases circulating NAD+ in humans, NR may have potential as a therapy in patients with mitochondrial dysfunction due to genetic and/or acquired diseases.*

Published: 24 November 2017

Repeat dose NRPT (nicotinamide riboside and pterostilbene) increases NAD^+ levels in humans safely and sustainably: a randomized, double-blind, placebo-controlled study

Ryan W. Dellinger, Santiago Roel Santos, Mark Morris, Mal Evans, Dan Alminana, Leonard Guarente & Eric Marcotulli

npj Aging and Mechanisms of Disease **volume 3**, Article number: 17 (2017)

NRPT is a combination of nicotinamide riboside (NR), a nicotinamide adenine dinucleotide ($NAD^{+)}$ precursor vitamin found in milk, and pterostilbene (PT), a

polyphenol found in blueberries. Here, we report this first-in-humans clinical trial designed to assess the safety and efficacy of a repeat dose of NRPT (commercially known as Basis). NRPT was evaluated in a randomized, double-blind, and placebo-controlled study in a population of 120 healthy adults between the ages of 60 and 80 years. The study consisted of three treatment arms: placebo, recommended dose of NRPT (NRPT 1X), and double dose of NRPT (NRPT 2X). All subjects took their blinded supplement daily for eight weeks. Analysis of NAD^+ in whole blood demonstrated that NRPT significantly increases the concentration of NAD^+ in a dose-dependent manner. NAD^+ levels increased by approximately 40% in the NRPT 1X group and approximately 90% in the NRPT 2X group after 4 weeks as compared to placebo and baseline. Furthermore, this significant increase in NAD^+ levels was sustained throughout the entire 8-week trial. NAD^+ levels did not increase for the placebo group during the trial. No serious adverse events were reported in this study. This study shows that a repeat dose of NRPT is a safe and effective way to increase NAD^+ levels sustainably

Published: 29 March 2018

Chronic nicotinamide riboside supplementation is well-tolerated and elevates NAD^+ in healthy middle-aged and older adults

Christopher R. Martens, Blair A. Denman, Melissa R. Mazzo, Michael L. Armstrong, Nichole Reisdorph, Matthew B. McQueen, Michel Chonchol & Douglas R. Seals

Nature Communications **volume 9**, Article number: 1286 (2018)

Nicotinamide adenine dinucleotide (NAD^+) has emerged as a critical co-substrate for enzymes involved in the beneficial effects of regular calorie restriction on healthspan. As such, the use of NAD^+ precursors to augment NAD^+ bioavailability has been proposed as a strategy for improving cardiovascular and other physiological functions with aging in humans. Here we provide the evidence in a 2 × 6-week randomized, double-blind, placebo-controlled, crossover clinical trial that chronic supplementation with the NAD^+ precursor vitamin, nicotinamide riboside (NR), is well tolerated and effectively stimulates NAD^+ metabolism in healthy middle-aged and older adults. Our results also provide initial insight into the effects of chronic NR supplementation on physiological function in humans, and suggest that, in particular, future clinical trials should further assess the potential benefits of NR for reducing blood pressure and arterial stiffness in this group

In addition, we anote that [The Complainant] contacted Nobel Prize Winner, Sir John Walker of the University of Cambridge in regards to the Advertisement.

Here is the response from Sir John Walker (a full copy of the correspondence is **attached** to the covering email):

Dear [The Complainant]

It is true that NAD is an essential component in conversion of energy in food-stuffs into a form that is used to sustain all our activities. It is known that NAD levels decline with increasing age (the graph) and that nicotinamide riboside (TruNiagen), which is part of the vitamin B3 complex, is a precursor of NAD and that its ingestion boosts those levels. I take 500 mg of TruNiagen every day."

John-

Professor Sir John Walker FRS, FMedSci
MRC Mitochondrial Biology Unit
University of Cambridge
The Keith Peters Building
Cambridge Biomedical Campus
Hills Road
Cambridge
CB2 0XY

Finally, [The Complainant] comments *that "these statements confirm that much of the advert is hyperbole and exaggeration and the science that might truly and strongly support the claims has yet to be performed."*

We strongly disagree with this statement as the only claims made in the Advertisement are:

1.) That NAD+ declines with age and under metabolic stress;
2.) That Tru Niagen supports NAD+ levels
3.) Healthy NAD+ levels are required for healthy cellular function

We believe we have sufficiently addressed all three of these claims in this letter.

However, to lend further weight to our position, we would point out that Tru Niagen has received regulatory approval in many other jurisdictions around the world including the US, EU, Hong Kong, Singapore, Canada, UK and most recently Australia.

Compellingly, the dossier of scientific literature submitted to the TGA in Australia was considered strong enough to result in the approval for sale of Tru Niagen as an over the counter dietary supplement, but for approval of the following indications that Tru Niagen/NR:

- Increases NAD+
- Maintain/support energy levels
- Maintain/support general health and wellbeing
- Helps convert (state food) into energy
- Maintain/support body tissue repair/regeneration

Of particular relevance to this matter is the approved claim "maintains/supports body tissue repair and regeneration", to which we would draw your attention to the fact that the approved claim "supporting body tissue repair/regeneration" was not limited to certain cell/tissue types, but was left open to encompass <u>all</u> tissue types. Please find **attached** a copy of the TGA indications to the covering email.

Chromadex Corp, the manufacturer of Tru Niagen prides itself on its rigorous scientific research, good manufacturing practice and adherence to regulatory guidelines in all jurisdictions. The company continues to invest heavily in the science to explore the full potential of its flagship ingredient NIAGEN. The company is guided in this pursuit by a scientific advisory board that includes world-leading research scientists, two of which are Nobel prize

winners. As a company, we are always open to scientific questioning and debate made in good faith.

Thank you for the opportunity to present our case in this instance.

Appendix 3

RESPONSE FROM MEDIA

No response was received from The Press.