Meeting

Draft scientific opinion on the Tolerable Upper Intake Level 2 for vitamin B6

This is a paper for discussion.

This does not represent the views of the Committee and should not be cited.

Introduction

1. EFSA published a public consultation on a draft Opinion on the Tolerable Upper intake Level (TUL) for vitamin B6 on 13th January 2023, which will be closing on the 10th February 2023 (see Annex A for link). The COT are being asked to review this draft opinion and provide any comments which will then be fed back to EFSA. If Members have any further comments, there will be a document provided in the Teams folder or they can be sent directly to the Secretariat. Please provide any comments by Thursday 9th February.

2. This paper provides a brief overview of the draft EFSA Opinion. Due to the limited time available to review the draft Opinion, most of the paper below has been taken from the draft EFSA opinion along with additional information as appropriate. The dietary intake assessment (sections 2.3 and 3.4) has not been considered in this paper, although Members are welcome to provide comments which can be forwarded to EFSA. The paper largely focusses on peripheral neuropathy as this was the endpoint used to establish the proposed TUL as well as previous Health Based Guidance Values (HBGV) for vitamin B6. In addition to the draft opinion there are three annexes covering the protocol, intake assessment and intake data.

Background

3. The European Commission asked the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) to deliver a scientific opinion on the tolerable upper intake level (UL) for vitamin B6. The assessment is being done in the context of setting maximum levels for vitamins and minerals in fortified and food supplements and other nutrients will be reviewed in due course. It is noted that for nutrients for which there are no, or insufficient, data on which to base the establishment of an UL, an indication should be given on the highest level of intake where there is reasonable confidence on the absence of adverse effects.

EFSA draft opinion

4. There is a well established relationship between excess vitamin B6 intakes and the development of peripheral neuropathy. It is the critical effect on which the previous TULs of 25 mg/day was established by the Scientific Committee on Food in 2000 and of 10 mg/day by the UK Expert Group on Vitamins and Minerals (EVM) in 2003. The context of the assessment and reviews by other bodies are covered in sections 1.4 and 1.5 of the draft opinion respectively. This includes the key studies used to set HBGVs. In general, the studies are the same but the interpretation and handling of the limited dataset differ with recommended HBGVs ranging from 10-100 mg/day for adults.

5. The problem formulation is given as follows (section 2.1)

- What is the maximum level of total chronic daily intake of vitamin B6 (from all sources) that is not expected to pose a risk of adverse health effects to humans? (Hazard identification and hazard characterisation).
- What is the daily intake of vitamin B6 from all dietary sources in European Union (EU) populations? (Intake assessment)
- ·What is the risk of adverse effects related to the intake of vitamin B6 in EU populations, including attendant uncertainties? (Risk characterisation)

6. It is stated that the hazard identification and hazard characterisation relate to the identification of adverse health effects of a given nutrient and the qualitative and quantitative evaluation of the adverse health effects associated with the nutrient, including dose-response assessment and derivation of a UL, if possible. This section also contains a number of sub-questions.

7. The review focusses on 2 endpoints, the development of peripheral neuropathy and developmental toxicity. Other endpoints identified in the search are also considered briefly.

8. Section 2.2.2 covers the methodology used in the review including evidence appraisal, synthesis and integration.

9. Sections 3.1 and 3.2 cover the chemistry of vitamin B6 and the ADME aspects. Vitamin B6 is a generic descriptor term for all 3-hydroxy-2-methylpyridine derivatives exhibiting biological pyridoxine activity. This covers three vitamers that differ by the one-carbon substitution at the fourth position of the pyridine ring: the alcohol pyridoxine (PN), the aldehyde pyridoxal (PL), and the amine pyridoxamine (PM) as well as their phosphate esters, i.e. pyridoxine 5'-phosphate (PNP), pyridoxal 5'-phosphate (PLP) and pyridoxamine 5'-phosphate (PMP).

ADME

10. The bioaccessibility of vitamin B6 is nearly complete but may be reduced (25-30%) by thermal processing. The vitamers PL, PN, and PM are absorbed without modification while their phosphorylated forms of the vitamers need to be dephosphorylated by alkaline phosphatase first. The absorption of PN hydrochloride (the most widespread form of vitamin B6 used in food supplements) from supplements is almost complete with 95% absorption being reported. Overall, vitamin B6 absorption from mixed diets has been estimated to be around 75%.

11. In the liver, the vitamers are re-phosphorylated by pyridoxal kinase. PNP and PMP are subsequently oxidised with the involvement of pyridoxine and pyridoxamine 5´-phosphate oxidases to PLP, which is the principal active vitamer. Before secretion into the circulatory system from hepatocytes, PLP is bound to the lysine residues of proteins, mainly albumin, which is the main transport protein.

12. PLP constitutes 70-90% of total vitamin B6 in plasma at normal intakes, with PL and 4-PA being the other major vitamers. At high vitamin B6 intakes, PL becomes the predominant vitamer in plasma, since only a limited amount of PLP can be bound to albumin and the remaining PLP is dephosphorylated to PL. At high PN intakes, both pyridoxal kinase and pyridoxine 5´-phosphate oxidase become saturated which impedes the conversion of PN to PNP and to PLP. Therefore, PN which has been shown to be cytotoxic in in vitro experiments on cultured neuronal cells and which is usually not present in plasma, starts to appear in circulation, and may accumulate after long term supplementation. Free PN may also be detected in some individuals after PLP supplementation, possibly owing to the presence of proteins with pyridoxal reductase activity in those

individuals.

13. When reaching the target tissue, PLP disassociates from albumin and is dephosphorylated by alkaline phosphatase. After entering cells, it is re-phosphorylated by pyridoxal kinase. The uptake of vitamin B6 after dephosphorylation is thought to occur via a saturable process. Thus the intracellular concentrations of PLP are tightly regulated. Both pyridoxal reductase and PLP-binding protein are thought to prevent adverse reactions of the aldehyde moiety of PL/PLP with non-specific cellular amino acids and amines.

14. The main route for B6 elimination is the urine, with 4-pyridoxic acid (PA) being the main urinary metabolite. The EFSA Panel noted that large inter-individual differences in the metabolism of vitamin B6 have been reported.

Biomarkers

15. Plasma PLP concentrations are considered to be a reliable marker of vitamin B6 intake and status as they correlate well with vitamin B6 intakes through habitual diets. Plasma PLP concentrations of 30 nmol/L as a population mean are indicative of adequate vitamin B6 status. Urinary 4-PA excretion was considered a marker of short-term intake (i.e. 5-7 days) but not of vitamin B6 status. The concentration of total vitamin B6 in plasma, the concentration of PL and PMP in plasma or red blood cells (RBCs), the concentration of PLP in RBCs, as well as ratios of concentrations of vitamin B6 vitamers in plasma, were deemed not to be suitable biomarkers of vitamin B6 intake and/or status at normal levels of intake. However, it has been suggested that plasma concentrations of PN, PL and 4-PA might be useful markers of high vitamin B6 exposure. With respect to plasma PLP concentrations at high vitamin B6 intakes, it has been observed that they do not increase linearly but start to level off. Plasma PLP concentrations decline with age, possibly owing to changing metabolism with age, during pregnancy, to a greater extent than can be explained by the expanding blood volume, and in inflammatory conditions. They are also influenced by albumin concentrations, alcohol consumption and alkaline phosphatase activity. Genetic variations in alkaline phosphatase activity also affect plasma PLP concentrations in both directions. The contribution of vitamin B6-producing colonic bacteria to plasma PLP concentrations is unknown, but differences in gut microbiota may also explain some interindividual differences in plasma PLP concentrations following similar vitamin B6 intakes.

Hazard identification

16. The relationship between B6 and the development of peripheral neuropathy is well established in humans and animals.

17. A number of studies were excluded from the assessment, notably those where the doses exceeded 500 mg/day since this was a dose that the SCF had already deemed to be toxic.

Human data

18. Four studies were used by the EFSA panel in the evaluation of the lower bound level of daily vitamin B6 intake that is associated with the development of peripheral neuropathy. These were a prospective cohort study (Shrim et al., 2006), two retrospective studies (Brush et al., 1988; Chaudhry and Cornblath, 2013) and one case control study (Dalton and Dalton, 1987) along with nutrivigilance data from Member states. These are discussed in section 3.5.1.1

19. Limited conclusions could be drawn from the prospective cohort study by Shrim et al. (2006) or Chaudary et al. (2003). The EFSA panel described the Brush et al., 1988 and Dalton and Dalton, 1987 studies as below.

20. In the retrospective study by Brush et al. (1988), 630 women suffering from Pre-menstrual syndrome (PMS) initially took 40 -100 mg/day vitamin B6 and subsequently mainly 120 and 200 mg/day. The women reported no symptoms of peripheral neuropathy. The total duration of vitamin B6 exposure was 6 months in 46% of individuals and longer than one year in 19.5% (the duration of exposure to different vitamin B6 dosages was not reported). In a follow-up of the study which was described by the SCF in 2000 and which covered three additional years, five cases of dizziness and six cases of mild tingling were noted in 336 women taking 200 mg/day vitamin B6 (duration not reported). The EFSA Panel considered that the follow-up of the study shows the occurrence of symptoms of peripheral neuropathy at supplemental doses of 200 mg/day vitamin B6 consumed for an unknown period of time.

21. In the case control study described by Dalton and Dalton (1987), which was the study used by the SCF (2000) for the setting of the UL, 172 women with PMS, attending the same private practice, were recruited. The women were taking vitamin B6 supplements (range 18 ng/mL (>72.8 nmol/L). Women were asked to report symptoms indicative of peripheral neuropathy and in positive cases women were followed-up by a neurological examination (not further described). A total of 103 women (60%) had neurological symptoms (paraesthesia, bone pains, hyperaesthesia, muscle weakness, fasciculation and numbness; cases), while 69

women did not have symptoms (controls). Serum PLP concentrations were above the upper limit of testing of 34 ng/mL (137.5 nmol/L) in 70% of cases and 55% of controls. The average vitamin B6 intake was 117 ± 92 mg/day (measure of spread not further specified) in cases and 116±6 mg/day in controls. Cases had, however, taken supplements on average for longer than controls (mean 2.9 ± .9 vs. 1.6 ± 2.1 years, p 0.01) without reporting on latency periods. Doses of 50 mg/day (lower bound not reported) were consumed by 43 women (cases and controls combined) and 48% of these women showed symptoms of peripheral neuropathy. Exposure was > 6 months in all cases. With increasing doses, the percentage of women suffering from peripheral neuropathy increased, except in the highest dose group which, however, also included the smallest number of participants. The percentage of women with symptoms were 60%, 77% and 51% of 65, 42 and 22 women in the groups consuming 50-100 mg/day, 100-200 mg/day and 200-500 mg/day, respectively (data calculated by EFSA based on information provided in the publication). Following withdrawal of vitamin B6 supplements, 55% of women reported partial or complete recovery after 3 months and after 6 months all had recovered. The Panel notes that the SCF (2000) had previously used the average supplemental intake in this study of around 100 mg/day as a RP for the derivation of the UL. This was based on the observation that cases had taken vitamin B6 supplements on average for longer at the same mean intakes, indicating that an inverse relationship between dose and time to onset of symptoms existed at these mean intakes. The Panel, however, considers that this study not only shows an inverse relationship between dose and time to onset of symptoms, but also a dose-dependent increase in the percentage of women with symptoms of peripheral neuropathy occurring at supplemental vitamin B6 intakes of 50 mg/day (lower bound but not reported) when consumed for > 6 months.

22. The EFSA panel also considered a number of case reports and series along with nutrivigilance data. These are described on pages 30-31 and in Table 6. Overall, the Panel considered that there is evidence that symptoms of peripheral neuropathy may occur at supplemental vitamin B6 intakes that are below the RP of 100 mg/day used by the SCF (2000) to establish the UL. The EFSA panel made the following observations.

- In the case control study by Dalton and Dalton (1987), 48% of women who had taken vitamin B6 supplements at doses 50 mg/day for more than 6 months (the lowest dose group) showed symptoms of neuropathy and the percentage of women affected increased with increasing doses.

- A woman was positively rechallenged with 50 mg/day supplemental vitamin B6, taken for four months, following recovery from neuropathy that had originally developed after consumption of 75 mg/day vitamin B6 for two years (Dalton and Dalton, 1987). There is uncertainty whether vitamin B6 plasma concentrations had returned to normal between the two challenges. However, there was one year between the easing of symptoms and the rechallenge.
- A man developed neuropathy (Blackburn and Warren, 2017) following energy drink consumption. These energy drinks had provided a total of 31 mg/day vitamin B6. However, information on the latency period, the overall duration of consumption, the composition of the implicated energy drink other than vitamin B6 and other dietary habits is lacking.
- Dalton (1985) reports that 23 women with symptoms of neuropathy had consumed between 50 and 300 mg/day vitamin B6. It is unclear if these cases partly or fully overlap with the cases described by Dalton and Dalton (1987) and it is unknown how many women had consumed the dose of 50 mg/day.
- The Dutch nutrivigilance system reports that 33 cases for which information on both the dose and the latency period were available had taken supplements that contained ≤50 mg/day vitamin B6.
- The French nutrivigilance system indicates cases of peripheral neuropathy occurring at supplemental intakes 25 mg/day.

23. Taken together, the Panel indicated that the evidence suggested that symptoms could occur at doses of 50 mg/day B6. The reported large inter-individual differences in sensitivity to vitamin B6 toxicity was noted along with the large inter-individual variation in plasma PLP concentrations in response to vitamin B6 supplementation.

24. Overall the Panel concluded that “the evidence allows establishing with sufficient certainty that peripheral neuropathy may occur at supplemental vitamin B6 intakes of 50 mg/day in some individuals”.

Animal data

25. Evidence from animal studies is considered in section 3.5.1.2. Rats appear to be less sensitive to the effects of vitamin B6 with doses of 3000-6000 mg/kg bw/day being necessary to induce symptoms of peripheral neuropathy.

26. Beagle dogs have a urinary excretion of vitamin B6 that is similar to humans. and have been widely used to investigate vitamin B6 toxicity. Seven studies were available for the assessment. The Panel noted the absence of a control group in all studies, except Phillips et al., 1978. This study allowed the identification of a NOAEL and is described in the opinion as below.

27. In a study in Beagle dogs with a control group (Phillips et al., 1978), the toxicity of different oral doses of PN-HCl (0, 50 or 200 mg/kg bw per day) was tested (n=14 in total; n=4 for control group; n=5 for each treatment group; age range: 7-8 months) for 100-114 days (average: 107 days). Animals were randomly assigned to the three groups and were fed a nutritionally balanced commercially available diet. Two dogs were housed in each pen. PN-HCl was administered in gelatine capsules. The 'high dose' group initially received 250 mg/kg bw per day for a week, but as all dogs developed incoordination and ataxia, the dose was reduced to 200 mg/kg bw per day. Clinical examinations were carried out once per month and neurological assessments at biweekly intervals. Dogs in the 'high-dose' group lost weight within the first week of treatment. The weight was not recovered during the duration of the study. There was also an increase in heart rate in this group from on average 118 beats per minute pre-treatment to 160 beats per minute after 8 days of treatment which remained at this level until the end of the study. The signs that had been experienced by the dogs in the 'high-dose' group within the first week disappeared within another week after the dose had been reduced to 200 mg/kg bw per day and reappeared between 40 to 75 days after the start of the study with 100% of animals affected. Ataxic gait, muscular weakness and loss of balance were the first signs to appear. The neurological impairment increased in severity with time until they were so marked that dogs had difficulties in standing. Histological findings showed a pronounced loss of myelin and axons in the dorsal fasciculi throughout the entire length of the spinal cord and loss of myelin and nerve fibre degeneration in the dorsal sensory nerve roots. In the 'low-dose' group, signs of neurological disease did not develop, and they did not show lesions in the dorsal fasciculi. However, all five dogs in the group showed bilateral loss of myelin in the dorsal sensory nerve roots. No lesions were found in the control animals. The Panel considers that this study shows that supplemental vitamin B6 intake of 50 mg/kg bw per day in Beagle dogs for around 107 days leads to limited damage in the dorsal sensory nerve roots without the occurrence of symptoms of neurological disease. This provided evidence for a LOAEL of 50 mg/kg bw/day in Beagle dogs. The Panel also concludes that the studies in Beagle dogs suggest that high vitamin B6 intake damages afferent nerves mostly through axon degeneration, myelin breakdown

and vacuolisation of cytoplasm, with initial lesions mostly occurring in the dorsal root ganglia.

28. The potential mechanisms for vitamin B6 toxicity are described in section 3.5.1.3 but the causal mechanism remains unknown.

Other endpoints

29. The EFSA Panel also considered developmental toxicity which is discussed in section 3.5.2. The SCF had noted in 2000 that there was a lack of data on the neuronal toxicity of excess vitamin B6 intakes during development of the nervous system.

30. A number of case reports have been noted but studies in rats and monkeys have not shown teratogenicity. Section 3.5.2.1 describes the evidence retrieved through the systematic search covering congenital abnormalities (heart malformations and other malformations) concluding that there was no evidence of a positive relationship between vitamin B6 and congenital abnormalities in the dose range under review. Similarly, there was no evidence to suggest a positive relationship between B6 and growth restriction in utero or impaired fetal growth. Similarly, there was no evidence of developmental effects in animals. Overall, the Panel concluded that the available evidence did not suggest a relationship between high vitamin B6 intakes and outcomes indicative of developmental toxicity.

31. Other adverse health effects were discussed in section 3.5.3.1. These effects included photosensitisation and dermatological lesions, risk of hip fracture, impaired memorisation, anti-lactogenic effects and testicular toxicity. The panel concluded that “there is some evidence that vitamin B6 supplementation at a dose of 35-40 mg/day is associated with an increased risk of hip fracture. However, the evidence to date is insufficient to conclude on a causal relationship and a RP based on this observation cannot be used on its own. There is also an indication that vitamin B6 consumed at doses of 600 mg/day may suppress lactation, a level of intake that is beyond the RP originally used by the SCF (2000) to derive the UL. Evidence for a relationship of high vitamin B6 intakes with other outcomes is insufficient.

Hazard characterisation.

32. Section 3.6 discusses hazard characterisation. It was stated that experimental animal data show that vitamin B6 causes peripheral neuropathy in a dose related manner. A similar relationship has been shown in humans, and peripheral neuropathy is the critical effect for setting the UL for vitamin B6. The SCF (2000) had identified a RP of 100 mg/day based on peripheral neuropathy and mean vitamin B6 intakes in the human case control study by Dalton and Dalton (1987). Using the same study but a different observation, the Panel identified a lower RP than the SCF (2000), which is also supported by other available data. In the study by Dalton and Dalton (1987) neuropathy was reported in 48% of all women having taken vitamin B6 supplements 50 mg/day for at least 6 months. This percentage increased in a dose-dependent manner with higher vitamin B6 intakes. Based on the study by Dalton and Dalton (1987) and supported by other case reports (Dalton, 1985; Dalton and Dalton, 1987; Blackburn and Warren, 2017) and Member States' vigilance data, a RP of 50 mg/day can be identified. Taking all evidence together, the available data indicate that symptoms may occur at daily vitamin B6 intakes of 50 mg and below with a large interindividual variability. The value of 50 mg/day represents the lowest level of vitamin B6 intake that is associated with certainty with the development of neuropathy when consumed for more than 6 months, however smaller but unconfirmed B6 doses were also linked to this adverse effect. The panel could not identify a LOAEL or a NOAEL.

33. The sub-chronic study in Beagle dogs (Phillips et al., 1978) allowed the establishment of a LOAEL of 50 mg/kg bw per day.

Derivation of a TUL

34. The derivation of the UL is discussed in section 3.6.2. The Panel noted that since the assessment of the SCF (2000) no additional data had become available to revise the UL originally proposed by the SCF (2000). Therefore, the Panel proposed to apply a factor of 2 to account for the fact that there is an inverse relationship between dose and time to onset of symptoms of peripheral neuropathy. This factor covered the uncertainties as to whether the duration of exposure in the study by Dalton and Dalton (1987) was sufficiently long to cover this aspect. An additional UF of 2 was proposed to account for the limited available data. This covered the uncertainties as to the level of intake that would represent a LOAEL and the uncertainties as to whether the study by Dalton and Dalton (1987) was sufficiently representative and large to account for interindividual variability and adequately covered sensitive groups of the

population. The Panel noted that as the RP to which the UFs were applied is based on supplemental vitamin B6 intake, the UF of 4 would be sufficiently conservative to cover both dietary and supplemental vitamin B6 intake. Applying a UF of 4 to the RP of 50 mg/day identified from the study by Dalton and Dalton (1987), and supported by other available data, resulted in a UL of 12.5 mg/day for adults.

35. When using the LOAEL of 50 mg/kg bw per day derived from the sub-chronic study in Beagle dogs (Phillips et al., 1978) as a basis and applying an UF of 300, a UL of 0.17 mg/kg bw per day is derived, corresponding to 11.7 mg/day using a default body weight of 70 kg for adults. The UF of 300 is composed of the following: (a) a factor of 2 to account for interspecies variability in toxicokinetics; the default value of 4 suggested by the EFSA Scientific Committee (2012) for this purpose has been reduced by the Panel to 2, because of the similarities in vitamin B6 excretion between dogs and humans, (b) a default factor of 2.5 for inter-species variability in toxicodynamics, (c) a default factor of 10 to account for intra-human variability in toxicokinetics and toxicodynamics (default factors of 3.16 each), (d) a default factor of 2 to extrapolate from subchronic to chronic exposure, even though this default factor had been established for studies in rodents, and (e) a factor of 3 to account for the absence of a NOAEL

36. The Panel noted that the derivation of the UL from the study in humans leads to a similar UL as when the study in dogs is used as a basis. This increases the confidence in the resulting UL. The Panel proposes to establish the UL at the midpoint of these two ULs and round down. Therefore, based on the evidence in both humans and dogs, the Panel derives an UL of 12 mg/day for adults. The UL includes dietary and supplemental intake and covers all vitamin B6 vitamers.

37. The UL was considered to apply during pregnancy and lactation and was scaled allometrically (bw $^{0.75}$) for infants and children.

HBGVs from previous evaluations

38. As noted elsewhere (and see section 1.5 of the opinion) largely the same database has been used to set previous HBGVs. The limited database and methodological flaws in some of the studies were noted, with the work by Dalton being under particular scrutiny. The SCF (2000) derived a TUL of 25 mg/day based the UL on the case control study by Dalton and Dalton (1987) applying a UF of 4 to a RP of 100 mg/day. They stated that

“An upper level has been calculated by dividing the average intakes in the study of Dalton and Dalton (1987) of approximately 100 mg per day (the mean intake was 117 mg/day and the median was 100 mg/ day) by a factor of 2, because the intake corresponds to a possible effect level for long-term intake, and by a second factor of 2 to allow for deficiencies in the database. A larger uncertainty factor is considered not to be necessary, because the data of Dalton and Dalton (1987) were for a sub-group with high plasma concentrations, and because the resulting upper level of 25 mg per day has not been associated with adverse effects in any of the large number of published studies. This value is below the lowest doses associated with minor neurological effects following long-term intake and is 10- or 20-fold lower than doses associated with more severe adverse effects”.

39. The EVM used the Phillips study in dogs applying a UF of 300 (3 for LOAEL to NOAEL extrapolation, 10 for inter species variation, 10 for inter-individual variation) to the LOAEL of 50 mg/kg bw/day to derive a TUL of 10 mg/day. The EVM stated that

“In humans, a supplementary dose of 10 mg/day represents a clear SUL, with no adverse effects being anticipated over a lifetime’s exposure. Doses of 200 mg/day vitamin B6 or more taken for long periods are associated with reports of neuropathy in some human subjects. The effect of taking vitamin B6 at doses between 10 and 200 mg is unclear. The risk posed by such exposure in the short term may be negligible, but the available data do not allow identification of a dose or duration of exposure above the SUL that would be of negligible risk”.

40. The TUL proposed by EFSA uses some additional data to previous assessment, notably nutrivigilance and considered a number of additional endpoints. The Panel proposed applying a factor of 2 to the RP of 50 mg/day vitamin B6 to account for the fact that there is an inverse relationship between dose and time to onset of symptoms of peripheral neuropathy. This factor covered the uncertainties as to whether the duration of exposure in the study by Dalton and Dalton (1987) was sufficiently long to cover this aspect. An additional UF of 2 was proposed to account for the limited available data resulting in a proposed TUL of 12.5 mg/day..

Questions for the Committee

41. Do Members have any comments on:

a) The endpoint used to derive the proposed RP and UL

b) The key studies used

c) The UFs used

d) The other endpoints considered by the EFSA panel

e) Any other comments on this draft opinion or its annexes.

Secretariat

February 2023

Abbreviations

ADME	Absorption, Distribution, Metabolism and Excretion
EFSA	European Food Safety Authority
EU	European Union
EVM	Expert Group on Vitamins and Minerals
HBGV	Health Based Guidance Value
HCL	Hydrochlorate
LOAEL	Lowest Observed Adverse Effect Level
NDA	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NOAEL	No Observed Adverse Effect Level
PA	Pyridoxic acid

PL	aldehyde pyridoxal
PLP	pyridoxal 5’-phosphate
PM	amine pyridoxamine
PMP	pyridoxamine 5’-phosphate
PMS	Pre Menstrual Syndrome
PN	alcohol pyridoxine
PNP	pyridoxine 5’-phosphate
RBCs	Red blood cells
RP	Reference Point
SCF	Scientific Committee on Food (predecessor to the EFSA panels)
SUL	Safe Upper Level (term used by EVM and equivalent to TUL)
TUL	Tolerable Upper Level

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Annex A to TOX/2023/10

Link to consultation:

Public Consultation: (europa.eu)

Secretariat

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