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ANH INNOVATORS CLUB
SPECIAL BULLETIN

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Alliance for Natural Health
The Atrium, Curtis Road, Dorking, Surrey RH4 1XA, UK
e-mail: info@anhcampaign.org tel: +44 (0)1306 646600
www.anhcampaign.org

Reg. Office: Unit 5, Forge End, St Albans, Hertfordshire AL2 3EQ, United Kingdom. A Not-For-Profit Company Limited by Guarantee Reg No. 4438769.

EU Regulatory Overview

We are reaching a key time in company decision making when it comes to ensuring compliance of high-end, specialist foods/dietary supplements sold within the EU market as it is subjected to a series of EU Directives and Regulations applying to the sector. Of particular concern are a) food supplements containing vitamins, minerals and botanicals; b) herbal products that are potentially eligible under the simplified medicinal registration scheme offered by the Traditional Herbal Medicinal Products Directive, and; c) health claims under the Nutrition and Health Claims Regulation, including both claims that can benefit from transitional measures and implied claims contained in brand names.

Below we detail some key areas of EU regulation relating to food supplements, after which can be found (Section 5) a key list of urgent actions required by companies to help ensure compliance of particular food supplement products, ingredients and supporting marketing material and websites.

1. Food Supplements Directive (Directive 2002/46/EC) relating to vitamin and mineral food supplements sold or marketed within the EU

1.1 Background

- The Food Supplements Directive (FSD), as an EU Directive rather than a Regulation, is transposed into Statutory Instruments of each European Member State (presently 28). There can sometimes be slight differences in interpretation of the Directive in the Statutory Instruments in the different Member States.

- The FSD, and its related Statutory Instruments, aim to harmonise laws relating to food supplements for the purpose of facilitating free trade of food supplements within the European Union, while also protecting consumer health.

- Food supplements are defined under Article 2 of the Directive as any foodstuff "the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form", including capsules, tablets, powders, liquids, etc.

- The framework Directive came into force on 1 August 2003 (Article 15(a)), although derogations for products containing vitamin and mineral forms not included on the 'positive list' (Annex II) were given a four year transitional period. This derogation period expires on 31 December 2009 (Art 4(6)).

- The European Food Safety Authority (EFSA) is continuing to evaluate dossiers submitted under this derogation scheme and whilst significant numbers have been withdrawn, others have been subject to both positive and negative opinions (see: http://ec.europa.eu/food/food/labellingnutrition/supplements/food_supplements.pdf

- Although the Directive provides general guidelines over labelling and presentation of food supplements in terms of ingredients within products, the Directive currently only applies to vitamins and minerals.

- The Directive was originally intended to be applied subsequently to other groups of micronutrients used in food supplements, such as amino acids, essential fatty acids, fibre, botanicals, etc. (Recitals 6-8; Art 4(8)), however, the European Commission has for the time being put on hold the application of the Directive to ingredients other than vitamins and minerals, owing primarily to the difficulty in achieving consensus between Member States. Accordingly, until further notice, food supplement ingredients other than vitamins and minerals will not be harmonised across the EU an therefore will be subject to national rules, which may continue to vary considerably between Member States.

- The Directive will in the near future be amended to limit both minimum and maximum permitted levels (MPLs) of vitamins and minerals in food supplement products (which may also be the same levels set for fortified foods) across the EU (Article 5) (see section 2 below). There is a possibility that some Member States may allow higher levels for use domestically, with MPLs being applied only for trade between Member States, according to the principle of subsidiarity.

- The Judicial Review of the Directive commenced by the ANH, which culminated in a ruling from the European Court of Justice on 12 July 2005 (Joined Cases C-154/04 and C-155/04, *Alliance for Natural Health and others v UK*), provided important clarification and reduction in scope of the Directive, and, accordingly, reduced legal uncertainty.

1.2 Key Concerns

1. **Bans on specific vitamin and mineral forms from 1 January 2010.** Any vitamin or mineral form on the derogation list (http://ec.europa.eu/food/food/labellingnutrition/supplements/food_supplements.pdf) that has been given a negative opinion by the European Food Safety Authority (EFSA), has been withdrawn from the list or is neither on the derogation list nor the 'positive list' (Annex II of the Food Supplements Directive, including amendments to it) will be banned on 1 January 2010. The only exclusion is for natural sources of vitamins and minerals, as clarified in a statement from the European Commission in August 2007 (contact ANH for further details).

2. **Questionable scientific basis of EFSA negative opinions, at least** on 6 forms of vanadium and vitamin E tocotrienols issued by EFSA in February 2008 given that no exposure or dose level was stipulated—and that risk is clearly dose dependent. Given that safety is a key criterion for determination of eligibility to the 'Positive List', a particular nutrient or nutrient form cannot be regarded as generally unsafe, but rather it may become unsafe to particular population groups at a given dosage.

3. **Uncertainty over Directive scope** as to how or if the Directive will be applied to other nutrients (as proposed in Art 4(8)) or how Member States will choose to implement laws affecting these nutrients should EU harmonisation not proceed.

4. **EFSA guidance on botanicals** could lead some Member States to restrict or ban in food supplements botanicals which have been used safely both within and outside

the EU for many years (in some cases for hundreds or even thousands of years within the context of non-European traditional medicinal cultures e.g., Ayurveda, Traditional Chinese Medicine). For status on EFSA's evaluation of botanicals for use in food supplements, see http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178717026833.htm).

5. **Impact of EU medicines laws** regarding legal uncertainty about which food supplements may be considered 'clearly' food supplements, and which may not, as per the wording given in Recital 7 of amending Directive 2004/27/EC on Human Medicinal Products. This may give rise to unjustified medicinal classification of food supplements. The outcome of European Court of Justice case C-140/07 (*Hecht-Pharma GmbH v Staatliches Gewerbeaufsichtsamt Lüneburg*).

1.3 Note on botanicals in food supplements

1. **Botanicals are currently subject to EU General Food Law (EC Regulation No 178/2002/EC) and any additional national rules**, therefore compliance has to be checked via the relevant competent authorities in each of the Member States in which a product is sold. This often requires checks with the authorities responsible for both foods and human medicinal products. Please contact ANH should this information be required.

2. **EFSA risk assessments will increasingly become the key guidance for the establishment of national rules by Member States**. Given that EFSA is undertaking risk assessments for the use of botanicals in food supplements, it is important to stay abreast of developments in this area. Details can be found at: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620769656.htm. A Draft Guidance Document can be downloaded from: http://www.efsa.europa.eu:80/cs/BlobServer/DocumentSet/sc_draftguidance_botanicals_public_cons_update_en.pdf?ssbinary=true. Comprehensive comments relating to a consultation on this subject by EFSA (20 December 2007 – 15 February 2008) can be found at: http://www.efsa.europa.eu/EFSA/DocumentSet/botanicals_comments_consultation.xls?ssbinary=true

3. **Categorisation of risk by EFSA.** The central plank of EFSA's proposed general framework for assessing the safety of botanicals and botanical preparations used as ingredients in food supplements (see Draft Guidance document above) is to establish two categories:
    - Level A: Safety presumed, based on available knowledge;
    - Level B: Further testing and/or data required.

4. **Draft Compendia**. As part of EFSA's categorisation of risk, it has produced two draft compendia. Compendium 1 lists those herbs that may contain substances that are considered to be "toxic, addictive or psychotropic" and therefore "of concern". In relation to this category, the Draft Guidance states that: "presumption of safety can be applied only if there is convincing evidence of the absence of significant levels of these undesirable substances in the specific plant parts or preparations (either because initially absent in the source material, or excluded, or inactivated during processing). Compendium 2 lists those herbs that have been associated with previous food or medicinal use.

2. Proposal for EU harmonisation of Maximum Permitted Levels for vitamins and minerals

2.1 Background

- The principle of applying maximum levels (daily dosages) to food supplements is given in Recitals 13 and 15, as well as Article 5 of the Food Supplements Directive. The primary purpose for this measure is alleged to be consumer protection rather than facilitating the operation of a single (EU) market.

- In establishing 'maximum safe levels', which aim to ensure consumers are not at risk from excessive intakes (Recital 13), the Food Supplements Directive requires that due account is taken of Upper Safe Levels established through scientific risk assessment, dietary intakes from conventional foods and reference intake amounts (e.g, Recommended Daily Allowances or Reference Nutrient Intakes).

- The European Commission aims to release its proposal for actual maximum amounts (which will apply to daily dosages) in early 2009, and it may be around a year after this that the proposals are translated into law.

- The UK and Swedish governments, at least, are hopeful that subsidiarity might be achievable whereby Maximum Permitted Levels (MPLs) would be limited to food supplements being traded between Member States. Should subsidiarity be allowed, those Member States that uphold, based on opinions from their competent authorities, that safe levels for particular vitamins and minerals exceed those agreed for harmonisation as MPLs, will allow these higher levels for use within their national boundaries. This matter is presently under discussion between the European Commission, Member States, trade groups and other stakeholders and is by no means resolved at the time of writing.

2.2 Key Concerns

ANH has demonstrated significant scientific weaknesses in most of the methods presently under consideration by the European Commission for the determination of MPLs. These are summarised below:

1. **Nutrient groups vs nutrient forms**. The models under consideration fail to take into account variations in risk posed by different forms of nutrients (with exception of two forms of vitamin B3, namely nicotinic acid and niacinamide) and therefore risk assessments applying to a given nutrient group are based on the form of that nutrient group that is most hazardous to the most susceptible population group. This results in the application of excessively restrictive Upper Levels (ULs) to safer nutrient forms, which if applied in law, would result in a disproportionate impact. This problem can be resolved by ensuring, where there is differential risk between nutrient forms within a given nutrient group (e.g. synthetic beta-carotene vs dietary carotenoids; vitamin D2 vs vitamin D3; iron sulphate vs iron bisglycinate; L-ascorbic acid vs magnesium ascorbate), that individual risk assessments are applied to each nutrient form.

2. **Data from synthetic forms cannot necessarily be translated to natural forms**. Many studies used in risk assessments involve synthetic forms of nutrients, used either in isolation, or in limited combinations—often on diseased populations. They are not necessarily valid for natural forms of nutrients on healthy populations who seek benefits from supplementation (or fortification) e.g., risk assessments on synthetic beta-carotene (based on the CARET and ATBC trials involving smokers and asbestos workers) are not relevant to observational and epidemiological studies on dietary carotenoids among healthy populations.

3. **GLs should not be used as surrogates for ULs**. Scientifically-based UL values are few and far between. Guidance Levels (GLs) have often been used as surrogates for the UL but this is not scientifically acceptable given that they are such crude approximations to a true UL. If there are insufficient data to calculate a UL based on meaningful data, the MPL should await determination until such time that adequate data are available. Europeans have lived with a similar situation for decades in relation to RDAs; RDAs having only been determined for 6 minerals while 15 are listed on Annex I of the Food Supplements Directive.

4. **The margin between the RDA and UL cannot be assumed to be representative of risk**. One of the leading models under consideration by the European Commission (as proposed by the trade associations EHPM and ERNA) categorise risk on the basis of the margin between the RDA and the UL. The model assumes, generally correctly, that the risk of exceeding the UL is greatest when the margin between the RDA and the UL is narrowest. However, a second assumption that is intrinsic to the model is that exceeding the UL brings about an equivalent risk. This second assumption is clearly incorrect as it takes no account of either the nature, reversibility or severity of the risk for a given nutrient form, neither does it take into account the slope of the dose/response curve.

5. **Models need validation.** It is imperative that the outputs from any model (e.g., EHPM/ERNA or BfR models) are validated against those levels that are known to be beneficial or healthy in a normal diet. Many of the anomalies in model outputs result from the fact that the methods do not take into account variations between nutrient forms or the nature or severity of risk when the UL is exceeded. For example, BfR MPLs are compared below with food values (based on the USDA National Nutrient Database):

   - A 200 g sirloin steak gives you around 7.2 mg of zinc, over 3 times the BfR maximum level of zinc for food supplements
   - A single large raw carrot (70 g) typically contains 7.2 mg of beta-carotene (601 mcg Retinol Equivalents), around 3.6 times the BfR maximum level of beta-carotene for food supplements
   - One single (5 g) brazil nut typically contains 96 mcg of selenium, over 3 times the BfR maximum level for selenium for food supplements
   - One cup of raw french beans (180 g) provides about 346 mg magnesium, 3.5 mg zinc and 734 mcg folate—these values exceed the BfR MPLs for all three nutrients.

3. Nutrition and Health Claims Regulation (No 1924/2006) relating to all foods, food products and food supplements

3.1 Background

- The Nutrition and Health Claims Regulation (NHCR), as an EU Regulation, applies to all Member States and does not require transposition into the legislature of Member States via Statutory Instruments. The Regulation came into force on 1 July 2007 (Article 28).

- The Regulation applies to all foods and therefore food supplements, and seeks to harmonise all commercial nutrition and health claims made on labels and in advertising throughout the EU, allegedly to ensure the effective functioning of the internal market, whilst providing a high level of consumer protection.

- The Regulation means that all nutrition and health claims are disallowed, unless they are specifically approved by the European Food Safety Authority (EFSA). The only exception to this is that existing claims can continue to be used under transitional measures (Article 27).

- Health claims, being any claim that implies a health benefit, apply to any written or verbal claim, including any pictorial, graphic or symbolic representation.

- The NHCR offers two distinct pathways for companies wishing to make health claims:

    - Article 13 *generic* claims, applying to particular foods, or specific nutrients in a product or food supplement. Around 2000 claims submitted via competent authorities are presently being evaluated by EFSA, who will publish a list of approved claims in 2010. Only claims that are supported by human studies will be accepted. Progress of EFSA evaluations of these claims can be monitored via: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_article13.htm.

    - Article 14 disease-risk-reduction and childrens' health claims, which are supported by extensive data, including multiple clinical studies. These claims are generally product specific. The data requirements for such claims are so onerous that they are generally out of the reach of small to medium-sized enterprises (SMEs). Progress of EFSA evaluations of these claims can be monitored via: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_article14.htm.

- Some key transitional measures are:

    - Food supplements (or foods) on the market or labelled prior to 1 July 2007 that do not comply with the Regulation can continue to be sold until 31 July 2009 (Article 27 (1));

    - Products on sale before 1 January 2005 bearing brand names or trademarks that do not comply with the Regulation (e.g., implied, unapproved health claims) can continue to be used until 19 January 2022 (Article 27(2));

    - Nutrition claims made before 1 January 2005, that have been made under the proviso of Member States statutory instruments, can continue to be made until 19 January 2010 (Article 27(3));

    - Generic health claims that were already used prior to 1 July 2007 and that have been

accepted by Member State competent authorities can continue to be used under the responsibility of the 'food business operator' until EFSA publishes its list of approved generic (Article 13) health claims (Article 27(5) and (6));

3.2 Key Concerns

1. **Threat to freedom of speech** as the Regulation applies equally to both verbal and written, pictorial, graphic or symbolic statements or presentations. Unless 'authorised' by the Commission on the basis of EFSA approval, all suggestions or implications that a food or nutrient has particular characteristics or beneficial nutritional properties, or that a relationship exists between a food/nutrient and health, all claims are banned even if scientific evidence for such a claim exists.

2. **Disproportionate impact against small businesses**. The NHCR benefits large corporations in particular and has the potential to cripple SMEs, as Article 14 product-specific claims applications are excessively onerous and require evidence from randomised clinical trials (RCTs), which are prohibitively costly for the majority of smaller companies and not relevant for foods or food ingredients with many years, decades or even centuries of safe use, particularly where their benefit has been established via observational, epidemiological or clinical evidence.

3. **High level of consumer protection?** Nutrition and Health Claim regulations are intended to offer a high level of consumer protection, but since all products containing the same ingredients will be limited to the same generic claims, consumers will find it very difficult to distinguish between different products and make informed choices, leaving price as the key driver.

4. **The legal basis for requiring human studies for substantiation of Article 13 claims** is not made clear in the Regulation. Therefore, the ANH upholds that the legal basis for excluding health claims not supported by human studies is questionable. Claim applications were culled six months after the submission date by making provision of human evidence mandatory with no prior notification being provided to industry.

5. **The scientific basis for health claims is inadequately specified** as the Regulation indicates that claims should be substantiated by "generally accepted scientific data" (Recital 25 and Article 6). However, specific measures detailing the requirements for this substantiation do not appear to have been given.

6. **Have the principles of sound administration been ignored or inadequately followed?** In the opinion of ANH, interested parties have not been given the necessary level of guidance over the requirements for applications for health claims under Article 13, as per the measures of general application laid out in Articles 15 through to 18, leading to a lack of transparency and a shifting of 'goalposts' after the Article 13 dossier submission deadline.

4. Traditional Herbal Medicinal Products Directive (Directive 2004/24/EC)

4.1 Background

- The Traditional Herbal Medicinal Products Directive (THMPD) exists as a sub-Directive of the Human Medicinal Products Directive (2001/83/EC, amended by 2004/24/EC). This Directive essentially offers a simplified ('fast-track') medicinal licensing scheme for herbal medicinal products that are able to demonstrate, using a bibliographic review of safety data together with an expert report, 30 years continuous safe usage, of which at least 15 are within the EU (Article 16(c)1(c)).

- This simplified scheme avoids the need to demonstrate safety and efficacy, which are typically the most costly aspects of applying for a full medicinal licence (market authorization).

- Applications for a THMPD licence are made via particular Member States, with data being considered by the Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMEA), which has also been given responsibility to establish monographs for herbal substances (http://www.emea.europa.eu/htms/general/contacts/HMPC/HMPC.html). At the time of writing, 22 monographs are complete, and a total of between 200-300 are expected.

- Licenced THMPD products are intended for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment. This creates a major constraint since many traditional medicinal products are typically used in conjunction with advice by a practitioner, for minor but also for more serious ailments, including cancer, psychiatric diseases, infectious diseases (e.g., hepatitis, influenza), cardiovascular diseases or metabolic diseases such as diabetes, none of which would be acceptable by the licencing authority.

- The full provisions of THMPD come into force in April 2011. The provisions, however, provide particular obstacles for many SMEs in the natural health sector who are manufacturing and/or retailing traditional herbal products. There are a number of reasons for this:

    - Cost of compiling a dossier and applying for a licence. SMEs generally manufacture or sell a diverse range of products, each with relatively small turnover, as compared with large corporations, which are typically reliant on fewer products, each with high sales volumes. High costs for licencing therefore impact SMEs disproportionately compared with large corporations;

    - The requirement by the HMPC for high quality genotoxic data. For many herbal substances used in traditional cultures these data are not available, while in others they are viewed as being of insufficient quality by HMPC/EMEA. This requirement has been one of the major reasons for the small number of applications to the registration scheme (around 110 in total from 25 Member States, at the time of writing);

    - The requirement to meet pharmaceutical Good Manufacturing Practices

(GMPs), which considerably exceed the standards for food manufacture and are sometimes inappropriate for certain categories of ingredient or product (e.g., some botanicals). Additionally manufacturers are required to retain the services of a 'Qualified Person' to ensure compliance with pharmaceutical standards;

- Difficulty in compliance with the pharmaceutical criteria stipulated under the Directive, which, for example, require identification of marker compounds in order to meet stability requirements. While these criteria can be met in the case of single or two-herb combinations, they cannot generally be met in the case of poly-herbal products which are typical of many traditional medicinal cultures;

- Many traditional cultures utilise non-herbal products, including in particular ingredients of animal origin and minerals. These are presently disallowed by the Directive.

♦ The European Commission has published an important report entitled '*Report on the experience acquired as a result of the application of the provisions of Chapter 2a of Directive 2001/83/EC, as amended by Directive 2004/24/EC, on specific provisions applicable to traditional herbal medicinal product*' on 29 September 2008 (http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_09/comm_2008_584_en.pdf). The report recognises some of the difficulties that companies have had with the registration scheme, but indicates there is likely to be little future flexibility with regard to altering the provisions, with the primary exception of expanding the scope to include non-herbal substances. More hopeful, however, is the conclusion by the Commission that a new legal framework may be considered for particular traditional medical systems, e.g., Ayurveda, Traditional Chinese Medicine, anthroposophic medicine, etc.

4.2 Key Concerns

1. **Discrimination against non-European Herbal Traditions** by requiring at least 15 out of 30 years of usage within the EU, as the basis for proving long established, traditional usage. The basis for this requirement is the supposedly varying pharmavigilance standards in different regions, implying that standards outside of Europe may be lower than those within Europe. This provision seriously disadvantages Ayurveda, Traditional Chinese Medicine, South East Asian, Tibetan, Amazonian and southern African traditions, which are among the longest and most developed botanically-based healthcare traditions worldwide.

2. **Particular combinations of herbal products may be disallowed**. 'Traditional use' under the THMPD is based on use of an individual herb or specific combination of herbs. It therefore prevents use of new or innovative combinations that might be supported by emerging science.

3. **Products are subject to pharmaceutical criteria and GMPs**. Under the THMPD, manufacturers must meet pharmaceutical GMPs, including purity and stability criteria that are identical to those used in the case of conventional pharmaceuticals, under the provisions of the same base Directive (2001/83/EC). These criteria cannot be met in the case of many poly-herbal products owing to the complexity of mixtures, the masking of

known markers and, in other cases, the lack of standards for identification of markers.

4. **Traditional medicines are eligible for registration only if they are intended for minor ailments**, while traditional medical systems generally have developed to cater for the full range of ailments and diseases encountered in their indigenous environments. Accordingly, the registration scheme may be discriminatory against ethnic minorities within the EU who might wish to benefit from products associated with their traditional medical system. While food supplements are able to be sold legally within the EU containing ingredients that support the health (or reduce the disease risk) of, for example, cardiovascular or neurological systems, these are disallowed under the THMPD scheme.

5. **Excessive cost of accessing the THMPD regime**. The cost of meeting the data requirements for the THMPD, including the assembly of dossiers of bibliographic and expert evidence, as well as the requirements for genotoxicity data (which typically have to be commissioned as existing data are not available) is prohibitive for many SMEs.

6. **Herbal Products containing significant levels of vitamins and minerals will be prohibited** and allowed only if the action of those nutrients is considered 'ancillary' to that of the herbal ingredients.

7. **Herbal products containing non-herbal ingredients other than vitamins and minerals are currently disallowed**. However, the Directive may in the future be amended to allow such ingredients, although verifying their safety to the satisfaction of the HMPC is likely to be challenging and very expensive.

8. **Increased cost to consumer and restriction of freedom of choice** given that significant compliance costs will apply, which will be passed on to the end user, making the cost of products uneconomic for some and limiting their right to make their own health choice.

9. **Committee control**. Authorisations are controlled by the HMPC, which is weighted strongly towards drug pharmacologists/cognosists, as opposed to practicing medical herbalists and others with specific expertise on traditional medical practices.

10. **Impact on non-European herbal suppliers**. Many herbs potentially eligible under the THMPD scheme are produced by small-holder farmers and communities in non-EU countries. If products containing such herbs are disallowed as botanical-containing food supplements, and are also not able to be licenced under the THMPD scheme, these rural communities could be impacted very seriously.

5. Some key actions for compliance of food supplement products within the EU market

The following actions are applicable particularly to companies wishing to maintain compliance of food supplement products containing vitamins, minerals, botanicals and amino acids.

5.1 Compliance of food supplements containing vitamins and minerals

1. **Annex II of FSD positive list.** Check compliance of vitamin and mineral forms with those on Annex II of the FSD (http://www.anhcampaign.org/files/FSD_final-OJEC-2002.pdf) and any amendments to it, presently only Directive 2006/37/EC (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:094:0032:0033:EN:PDF) which provides a minor amendment to Annex II, most notably the addition of calcium-L-methylfolate (also known as 5-methyl hydroxyfolate) and ferrous bisglycinate.

2. **Derogated vitamins and mineral forms with positive opinions from EFSA**. Like those on Annex II, vitamin and mineral forms that have been subject to a positive opinion by EFSA can be used across the EU. The derogation list, which is updated regularly, can be accessed via: (http://ec.europa.eu/food/food/labellingnutrition/supplements/food_supplements.pdf) and positive opinions can be found by following the hyperlinked references to the opinions. Positive opinions by EFSA generally indicate an acceptable dosage range, so it is essential that these are met.

3. **Derogated vitamin and mineral forms with negative opinions from EFSA.** This group can no longer be used in any part of the EU. They can be identified via the hyperlinks to the EFSA opinions in the derogation list (http://ec.europa.eu/food/food/labellingnutrition/supplements/food_supplements.pdf). The only exemption for use of forms which have received a negative opinion, is for those that are natural components of a food, in which case the form is outside the scope of the FSD. This has been shown to be the case by the ANH following its submission of applications to the Annex II positive list in 2007. Vitamin E tocotrienols, for example, which have been subject to a negative opinion from EFSA, have been allowed for use by the European Commission if they are shown to be a component of a natural source of vitamins or minerals that has a long history of use as a conventional food.

4. **Derogated vitamin and mineral forms that have yet to be evaluated by EFSA**. These forms are readily identified on the derogation list vitamin and mineral forms (http://ec.europa.eu/food/food/labellingnutrition/supplements/food_supplements.pdf), and they are revealed as being neither withdrawn[1] nor subject to an opinion (they appear as normal black text without any asterisks). Such forms can continue to be used up until the expiry of the derogation period on 31 December 2009, unless

[1] See EFSA update (31 October 2007) at http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178656113040.htm, which explains the withdrawal of large numbers of sub-standard dossiers submitted by various UK stakeholders.

given a negative opinion by EFSA before this time. It is strongly recommended that decision-making is always based on the electronic version of the derogation list given its frequent updates; check the list regularly (e.g. monthly) to monitor the progress of evaluations. **Should any such vitamin and mineral form be of significant value to your business it may be important to submit additional data to EFSA in support of an existing dossier. Contact ANH for further details if relevant.**

5. **Annex II positive list is permanently open**. Should any company wish to apply to use a vitamin and mineral form that is neither listed on Annex II nor is it derogated, it can submit a dossier via a Member State for consideration by the European Commission and subsequent evaluation by EFSA. Given that the ANH case in the European Court of Justice (C-154/04) clarified and simplified the criteria necessary for an application to Annex II, the data requirements are not as onerous as thought previously. **Please contact ANH should further information or assistance with applications be required.**

5.2 Compliance of food supplements containing botanicals

1. Check current compliance in all Member States given influence of EFSA Draft Guidance Document on Member State competent authorities (see Section 1.3.1).

2. Keep abreast of EFSA risk assessment process (see Section 1.3.2).

3. Establish which botanicals within food supplement products sold in the EU are listed on:
   a) Draft Compendium 1
   b) Draft Compendium 2
   c) Neither
   [Contact ANH for provision of Draft Compendia, which are available as two Excel spreadsheet files, if required]

   There are particular concerns over the future marketability as food supplements of any botanicals that are present on Compendium 1 or neither Compendia. Contact the ANH for further information should this be the case.

5.3 Compliance of food supplements containing amino acids

1. Amino acids should be checked against the lists given in the Foods for Particular Nutritional Uses (PARNUTS) Directive (Directive 89/398/EEC as amended) (see European Commission site for further information: http://europa.eu/scadplus/leg/en/lvb/l21100.htm).

2. Of key importance is the amending Directive 2001/15/EC, and two subsequent amendments, namely Directives 2004/5/EC & 2006/34/EC. Between them these allow the following groups of nutrients in PARNUTS foods/supplements:

   - 116 vitamin and mineral substances
   - 28 amino acids
   - 3 carnitine substances
   - 4 choline substances

- Inositol
- Taurine
- 10 nucleotides

3. Any amino acid, or other PARNUTS ingredient, that is not present on any of these 'positive lists' much be checked by relevant Member State competent authorities for permissibility.

5.4 Compliance of health and nutrition claims

1. Ensure existing nutrition and health claims on all commercial presentations (ranging from product labelling to all marketing and promotional collateral) are compliant with the transitional measures listed under Article 27 of the NHCR (see Section 3.1).

2. Ensure data substantiating all claims is held on file by the company making the claim.

3. Given that EFSA will publish its approved list of generic (Article 13) claims in 2010, ensure that labels and packaging supplies are run down sufficiently for 2010 to allow production of new labels and packaging carrying compliant claims.

5.5 Compliance with nutrition/food/food supplement labelling requirements

1. Particular provisions for labelling are given in Directive 90/496/EEC and amending Acts, Directive 2003/120/EC and Regulation (EC) No 1882/2003.

2. Additional labelling requirements for food supplements are given in Article 6 of the FSD (Directive 2002.46/EC).

3. Check nutrition claims and conditions applying to them against the list of nutrition claims given in the Annex of the NHCR.

5.6 Compliance with EU General Food Law

1. Check that botanicals and other ingredients in food supplements, excluding vitamins and minerals which are subject to the FSD, are compliant with EU General Food Law (Regulation No 178/2002/EC) which attributes the primary legal responsibility for the safety of the products placed on the market to business operators.

2. Ensure that ingredients are not classified as 'novel foods' according to the Novel Foods Regulation (No. 258/97, as amended). This requires that all ingredients have had significant use prior to 15th May 1997, the date the Novel Foods Regulation came into force.

For further information about any of the above, or about the ANH, the ANH Innovators Club or ANH Consultancy Ltd, the latter of which provides confidential company-specific consultancy on all areas of EU regulatory compliance, please contact:

Meleni Aldridge
Development Manager
Alliance for Natural Health
The Atrium
Curtis Road, Dorking
Surrey RH4 1XA, United Kingdom
Tel: +44 (0)1306 646 550
Email: mel@anhcampaign.org

For further information see also the ANH website at www.anhcampaign.org