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Consultation on the revision of Commission Directive 91/321/EEC on infant Formulae and follow-on formulae (Working Document reference SANCO D4/HL/mm/D440180 Rev. 2)

Your letter of 4 February 2005

Dear Ms. Testori Coggi,

Thank you very much indeed for including ESPGHAN in the list of organisations that you contacted to request comments on this 2nd revision of the Draft Directive. We submit here some comments for your consideration.

Allow us to emphasize that we greatly support the general spirit and overall content of the Draft Directive. Please be assured of our full appreciation of the efforts of the European Commission to translate the conclusions of the report of the Scientific Committee on Food (SCF) of April 2003 into this important piece of legislation. Many aspects of this Directive will have a strong impact on the protection of health and well being of infants and young children throughout Europe.

We assume that the Commission may want to consider further modification of some details of the compositional requirements in light of ongoing discussions at the Codex Alimentarius level, in order to harmonise International and European standards wherever that may be appropriate and feasible. Thus, we refrain here from providing comments on compositional issues but offer to provide comments here as soon as the conclusions of Codex Alimentarius will become known. Rather, we focus here on 3 issues that are of major importance, i.e.

- the definition of follow-on formulae and the minimum age of introduction,
- the requirements for introduction of new or modified products into the market, and
- the requirements for introduction of new or modified claims.

Article 2 of the draft Directive provides definitions of Infant Formulae and Follow-on Formulae which fully agree with the definitions used by the Scientific Committee on

Food, current scientific knowledge and actual practice throughout Europe. Follow-on Formulae are defined here as formulae intended for use from the time when appropriate complementary feeding is introduced. In agreement with numerous paediatric organisations worldwide, we fully support this definition and strongly request that this definition should be used consistently throughout the Directive.

Therefore, we disagree with the parallel use of another, very different concept on Follow-on Formulae, such as outlined in Article 4, where the use of follow on formulae is generally recommended only for “infants aged over six months”, i. e. from the age of 7 months onwards. No justification or scientific reasoning is given for this alternative definition and its novel introduction into European legislation.

We should like to emphasize that this newly introduced age restriction for Follow-on Formulae is not supported by any scientific evidence, nor by the 2003 report of the Scientific Committee on Food. In fact, the recommendations and conclusions on Infant Formulae and Follow-on Formulae, including recommendations on compositional requirements, were based on the scientific evaluation of the concept on Follow-on Formulae as it is currently used throughout Europe, and on which most of the clinical evaluations of Follow-On Formulae have been based. Therefore, there is no basis to use the recommendations of the SCF on the composition of Follow-on Formulae for a different product category with a different indication. Thus, if the European Commission would in fact change the concept and definition of Follow-on Formulae as suggested in the revision 2 of this Draft Directive, which we do not support, it would be necessary that the Commission would

- a) offer a full justification for this change, and an exploration of its potential consequences and include this, at least in part, into the text of the legislation, and
- b) charge an independent scientific body, such as EFSA, to review the consequences for the compositional requirements of such newly defined Follow-on Formulae, and its scientific basis.

We assume that the concept of proposing the use of Follow-on Formulae generally only from the 7th month of life onwards may have resulted from a misinterpretation of the World Health Organisation’s (WHO) recommendation on full breastfeeding of infants for duration of 6 months. Needless to say, ESPGHAN wholeheartedly supports the promotion, protection and support of breast feeding and encourages breastfeeding of healthy infants for at least 6 months. However, we also recognize that the WHO recommendation on full breastfeeding of infants for the duration of 6 months is a population recommendation with a global scope, but it is not a recommendation for all individuals. Indeed, the WHO consultation concluded that some infants will benefit from introduction of complementary feeding prior to the 7th month of life and has recommended that the option of flexible introduction of complementary feeding be maintained to best meet the variability of requirements among infants. Therefore, this recommendation on a certain degree of flexibility needs to be reflected also in the European legislation.

We wish to emphasize that the scientific justification underpinning these WHO recommendations is based primarily on a possible reduction of infectious risks with ear-

lier cessation of full breastfeeding in populations with poor living conditions and high infectious disease prevalence, in particular under conditions where a safe and microbiologically pure source of drinking water is not available. These conditions do not apply for most European infant populations who fortunately enjoy high hygienic standards. Indeed, European infant populations the question of the optimal time of introducing complementary feeding to breastfed infants still remains controversial. Clearly, further scientific work is needed to resolve this issue, and in fact such research is currently being performed with support from the European Commission as part of DG Research's current 6th framework programme. The results of these current research activities will contribute to clarifying the optimal ranges of introducing complementary feeding under different circumstances.

It would appear inappropriate to introduce into legislation provisions which require major changes in the practice of infant feeding, while the scientific evaluation with EC-support is still ongoing and final conclusions cannot yet be drawn. Since the optimal age of introduction of complementary foods for European infants is not resolved at present, and any firm and restrictive decisions in legislation are not justified.

Furthermore, we wish to point out that there is no scientific basis for simply transferring the recommendations made for populations of breastfed babies to populations of formula fed babies. In fact, the Scientific Committee for Food has pointed out that there is no firm scientific evidence available to show that feeding infant formulae as the sole source of food for the first six months of life would be the optimal form of feeding non-breastfed infants.

The introduction of Follow-on Formulae should be linked to the time of introduction of complimentary feeding. However, the evidence available from recent studies do not provide conclusive evidence that postponing introduction of complementary foods to the age of seven months or later would generally greater health benefits for European infants. For example, Lanigan et al (2001) performed a systematic review of studies comparing the introduction of complementary foods at the ages of 4-6 months or 7 months, respectively. From over 400 published studies on this question that were identified, some 33 met specific inclusion criteria. Some 13 of these studies contained data that would support a recommendation for delaying the introduction of complementary foods until 6 months of age within the study population, whereas an equal number of another 13 of these studies did not support delaying the introduction of complementary foods until 6 months of age. The remaining seven were unable to provide evidence to support a change from the current WHO infant feeding recommendations which state that 'infants should be fed exclusively on breast milk from birth to 4-6 months of age'. None of the studies met all the methodological criteria. This review has shown that there is a lack of clear evidence to either support or refute a change to the current recommendations for the age of introduction of complementary foods to the breast milk or formula fed infant. The authors underline that whilst exclusive breast feeding for the first 6 months of life can support growth and development in some infants, sub-groups have been identified within certain populations who may require complementary feeding prior to this age (Lanigan JA, Bishop J, Kimber AC, Morgan J. Systematic review concerning the age of introduction of complementary foods to the healthy full-term infant. *Eur J Clin Nutr.* 2001 May;55(5):309-20.).

Other recent studies have addressed health effects of the time of introduction of specific food components, such as the introduction of gluten (a protein contained in cereals such as wheat and rye). A relationship between gluten exposure and later risk for diabetes was reported in genetically susceptible infants in Europe and in the USA. In one prospective birth cohort study, introduction of gluten-containing foods before the age 3 months was associated with significantly increased risk to develop islet autoantibody indicative of diabetes risk, whereas no difference was found for introduction at the ages of 4-6 or after 6 months (Ziegler et al 2003). Another birth cohort study was conducted from 1994 to 2002 and enrolled 1183 children at increased type 1 DM risk, with a mean follow-up of 4 years. From the results it appears that there is a critical time window of exposure to cereals in infancy outside which initial exposure increases diabetes risk in susceptible children (Norris et al 2003). Children initially exposed to cereals between the fourth through sixth month carried the lowest risk for developing autoantibodies, which persisted, after adjustment for HLA genotype, relative to earlier or later gluten introduction (Ziegler AG, Schmid S, Huber D, Hummel M, Bonifacio E. Early infant feeding and risk of developing type 1 diabetes-associated autoantibodies. *JAMA*. 2003;290(13):1721-8; Norris JM, Barriga K, Klingensmith G, Hoffman M, Eisenbarth GS, Erlich HA, Rewers M. Timing of initial cereal exposure in infancy and risk of islet autoimmunity. *JAMA*. 2003;290(13):1713-20.). These studies question whether delaying introduction of complementary feeds until the age of 7 months is always associated with optimal health outcomes.

Similar questions are raised by recent Scandinavian studies that investigated the relationship between the introduction of gluten into the infant diet and the later risk of celiac disease, an immunological intolerance to gluten. A population-based study of Swedish children, including 627 cases with celiac disease and 1254 healthy control children, studied the potential influence of dietary patterns in infancy on later disease risk. The risk of celiac disease was reduced in children if dietary gluten was introduced when they were still being breast-fed, as compared to later introduction after weaning from the breast [adjusted odds ratio (OR): 0.59; 95% CI: 0.42, 0.83]. This effect was even more pronounced in infants who continued to be breast-fed after dietary gluten was introduced (OR: 0.36; 95% CI: 0.26, 0.51). The authors conclude that gradual introduction of gluten-containing foods into the diet of infants while they are still being breast-fed reduces the risk of celiac disease in early childhood and probably also during the subsequent childhood period. (Ivarsson A, Hernell O, Stenlund H, Persson LA. Breast-feeding protects against celiac disease. *Am J Clin Nutr*. 2002 May;75(5):914-21.). Thus, Swedish paediatricians actively recommend the feeding of gluten containing complementary foods prior to the age of 6 months if the mother intends to stop breastfeeding before this age.

In view of the cited evidence, it is not justified to impose a strict age limit of at least 7 months for the introduction of Follow-on Formulae, and hence of complementary foods. Moreover, such a restriction might also result in nutritional disadvantages for some infants. The requirements of certain nutrients, such as protein or iron, change markedly with increasing infant age. The concept of successive use of Infant Formulae and Follow-on Formulae, which is well established in the EU, allows for a desirable stepwise adaptation of nutrient contents to the recipient infant's age. This well established concept is endangered by the proposed change in the definition of Follow-on Formulae.

Therefore, we request that the definition of Follow-on Formulae used in Article 2 should be used throughout the Directive, and any reference to a specific age be deleted.

2. Procedure for the introduction of new or modified products into the market

Article 4 specifies the conditions under which new or modified products may be introduced into the market. Infant Formulae containing ingredients that have never been used in the manufacture of infant formulae before can be placed on the market if the competent authority of the respective member state is simply notified by submission of a copy of the label. Not even this notification is required to put on the market Follow-on Formulae containing ingredients that have never been used before.

These conditions are by no means satisfactory, and indeed appear irresponsible. Infant Formulae differ markedly from other food products in that they present the sole source of nutrition during a critical period of rapid growth and development. Minor modifications of formulae can have major effects on infant health, and unfortunately many examples of untoward health effects induced by infant formulae have been documented (cf. Report of the Scientific Committee on Food, 2003). For example, in the past the introduction of certain modified infant formulae has led to

- reduced protein availability with impairment of growth,
- trace element deficiency with severe clinical disease,
- chloride deficiency with long-term neurological damage,
- thiamine deficiency with severe clinical disease, including neurological damage and several cases of infant death (observed in 2004 with a product manufactured in the EU; Fattal-Valevski A, Kesler A, Sela BA, Nitzan-Kaluski D, Rotstein M, Mesterman R, Toledano-Alhadeh H, Stolovitch C, Hoffmann C, Globus O, Eshel G. Outbreak of life-threatening thiamine deficiency in infants in Israel caused by a defective soy-based formula. *Pediatrics*. 2005 Feb;115(2):e233-8.)

Recent developments in formula innovation move from a focus on optimal nutrient provision towards a focus on functional effects in the infant, for example by addition of nucleotides, pre- and probiotics, gangliosides and other components. In such cases, safety considerations become even more complex and need to include some elements that previously were reserved only for pharmaceutical safety evaluation.

Therefore, there is unanimous agreement among scientific experts worldwide that the suitability and safety of new ingredients used in the production of Infant or Follow-on Formulae, and of Infant or Follow-on Formulae with a new or markedly modified composition, must be evaluated by an independent scientific authority “prior to introduction into the market”. This concept is put forward in recent and very clear recommendations issued by the Scientific Committee on Food, by ESPGHAN, by other paediatric authorities, and by the scientific evaluation of the Life Science

Research Organisation of the Institute of Medicine in the USA (Scientific Committee on Food. Report of the Scientific Committee on Food on the Revision of Essential Requirements of Infant Formulae and Follow-on Formulae (adopted on 4 April 2003). Brussels, European Commission, SCF/CS/NUT/IF/65 Final; Committee on Nutrition, European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN): Aggett PJ, Agostoni C, Goulet O, Hernell O, Koletzko B, Lafeber HL, Michaelsen KF, Rigo J, Weaver LT. The Nutritional and Safety Assessment of Breast Milk Substitutes and other dietary products for infants: A commentary by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2001;32:256-258; Koletzko B, Ashwell M, Beck B, Bronner A, Mathioudakis B. Characterisation of infant food modifications in the European Union. *Ann Nutr Metab* 2002;46:231-242; Gelardi RC, Mountford MK. Comments on LSRO report's recommendations on infant formula nutrient requirements. *J Nutr.* 1999 Jul;129(7):1390-2; Institute of Medicine. Committee on the evaluation of the addition of ingredients to infant formula. *Infant Formula: evaluating the safety of new ingredients.* Washington DC, The National Academic Press, 2004).

In agreement with these science based conclusions, adequate practices of scientific evaluation of modified formulae have been established all over the civilized world, for example by the US Food and Drug Administration, Health Canada, Australia and other countries. It would be irresponsible if the European Union would fall short of generally accepted science based safety standards.

A simple notification procedure, as proposed in the Draft Directive, will not provide sufficient protection for European infants from the serious health risks modifications of Infant Formulae could induce. One would expect that it is only a matter of time and chance until the next incident of adverse effects induced by a modified formula that had not been adequately tested will occur.

Therefore, ESPGHAN considers it essential that the scientific advice of the Scientific Committee on Food is followed and an authorisation procedure is introduced, with a structured review of the evidence to support the suitability for particular nutritional use and the safety of new and modified formulations, prior to the introduction of such products into the market. The current version of article 4 needs to be changed accordingly.

3. Introduction of new or modified claims.

Annex 4 lists criteria warranting a claim for Infant Formulae. Claims on the addition of optional ingredients are indicated (taurin, oligosaccharides, nucleotides), but the conditions warranting such claims are not stated. ESPGHAN finds it essential to define the minimum content of such additions and possible further conditions that must be fulfilled to warrant a claim. If such qualifications are missing, as is the case in the current draft, the consumer may be exposed to misleading claims, where the addition of optional ingredients in minimal amounts or under conditions that would not provide any reasonable probability for an expected benefit to the infant would allow for a label claim.

Furthermore, a health claim is proposed that relates to reduction of risks for allergies to milk proteins, but the proposed conditions warranting this claim are in clear contrast to the recommendations made in the report of the SCF. The SCF clearly indicated that the conditions for the claim proposed in the current version of 2.1 (a) have not relationship to the claim of a reduction of allergy risk; therefore, this section needs to be revised. Rather, the SCF concluded that clinical data showing a reduction of allergy risk and that are agreed upon by an independent competent scientific body would be an absolute prerequisite to warrant a health claim on reduction of allergy risk. This conclusion of the SCF needs to be reflected by the wording of the legislation.

ESPGHAN is also very concerned that no guidance is provided by the draft Directive on the process by which new or modified nutrition or health claims will be introduced. With respect to this matter, the SCF has concluded “that mechanisms and criteria should be developed for the communication not only of nutrient contents but possibly also of selected other effects of Infant Formulae or Follow-on Formulae if they have been demonstrated beyond doubt in vigorous studies with adequate scientific standards and the evidence has been accepted by independent scientific body review in such data”. ESPGHAN strongly recommends that this conclusion of the SCF be implemented in the text of the Directive. In the interest of European infants and their families, it is important that science based progress on infant feeding with clear demonstration of relevant benefits can be communicated to consumers who have to make choices between products, which will also serve to enhance the strive for innovations. However, vigorous scientific review is essential before such claims be allowed in order to protect misleading information, which unfortunately has occurred in the past.

We thank you very much indeed for considering our comments. We would be grateful if you could be kind enough as to make these comments also available to the EU member states and their delegations to the Standing Committee on Food.

Yours sincerely



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