# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

**Paper for information**

## COT review of risks arising from the infant diet and the development of atopic and autoimmune disease

### Introduction

1. The COT has been asked by the Scientific Advisory Committee on Nutrition (SACN) to provide advice on risks arising from the diet that are related to the development of atopic and autoimmune disease, in support of a review SACN are undertaking of UK Government recommendations on complementary and young child feeding.

2. A comprehensive review of the available published scientific literature has been commissioned by the Food Standards Agency and Imperial Consultants have been appointed to undertake the review of the evidence.

3. The purpose of this paper is to provide an update on progress with this work.

### Research progress update

4. The study is progressing well. Three separate systematic reviews of the published evidence are being undertaken:

- Systematic review A will explore the evidence relating to milk feeding and the child's future risk of developing allergic sensitisation, atopic disease, or autoimmune disease.

- Systematic review B will explore the evidence concerning the timing of introduction of specific allergenic foods into the infant diet during the first year of life and whether this influences the child's future risk of developing allergic sensitisation, atopic disease or autoimmune disease.

- Systematic review C will explore the evidence that exposure to or avoidance of specific dietary patterns, food groups or nutrients, during the infants' first year of life, during pregnancy or during lactation, influences the child's future risk of developing allergic sensitisation, atopic disease or autoimmune disease.

5. After extensive piloting and refinement of the search strategies, the searches were run on 25th July 2013 (final search strategies attached in Annex A)

6. A total number of 35,835 titles were sourced. However, after removing duplicate titles this number is reduced to 16,289. Title screening was undertaken

between February and April 2014, in duplicate by two independent assessors. Disputed titles or uncertainties were reviewed twice weekly. Following this, 1010 articles were found to be of relevance for either review A, B or C. A full breakdown of the eligible studies has been provided below. Note that some studies may be eligible for more than one review:-

- Review A: 531
    - Intervention trials: 61
    - Cohort studies: 328
    - Nested case control studies: 10
    - Case control studies:132

- Review B: 230
    - Intervention trials: 65
    - Cohort studies: 107
    - Nested case control studies: 7
    - Case control studies: 51

- Review C: 382
    - Intervention trials: 173
    - Cohort studies:165
    - Nested case control studies: 11
    - Case control studies: 33

7. Data extraction forms for all study types were developed and piloted. Data extraction began in May 2014 and is expected to complete by August 2014. The data analysis (including meta-analyses, subgroup analyses, critical narrative) is expected to take place during August and September 2014.

8. The Agency is expecting delivery of a draft final report in September 2014. The finding of the review (with a presentation from Imperial Consultants) is expected to be discussed by the COT on the 9 Dec 2014.

**Cows' milk protein hydrolysates and reduction of risk of developing allergic disease**

9. Members may recall that this review would not investigate protein hydrolysates and the risk of developing atopic and autoimmune disease. However since this time, a new formula containing cows' milk protein hydrolysates have been placed on the UK market and claims to reduce the risk of infants, developing allergic disease. The Department of Health has requested that the FSA assess whether this claim can be supported.

10. Directive 2006/141/EC specifies criteria that formulae containing protein hydrolysates must meet if they are to be allowed to be marketed as reducing the risk of developing allergy to milk proteins, however scientific evidence is required to support such claims.

11. There is a range of conflicting and contradictory evidence published on this subject, with EFSA recently producing a scientific opinion on the essential composition of infant and follow-on formulae[1] in which they concluded that:-

- *'the criteria given in Directive 2006/141/EC alone are not sufficient to predict the potential of a formula to reduce the risk of developing allergy to milk proteins. Clinical studies are necessary to demonstrate if and to what extent a particular formula reduces the risk of developing short- and long-term clinical manifestations of allergy in at-risk infants who are not exclusively breast fed.'*

12. The FSA had previously considered that this item would be discussed as part of an adhoc expert working group. However given the uncertainty in the evidence base the FSA has decided it is timely to more broadly review the scientific evidence on the consumption of cows' milk hydrolysed proteins and the reduction of risk of allergic disease and submit to COT for their consideration. The assessment made by COT can be used by the FSA to establish whether current and future claims made on such products placed on the UK market can be substantiated.

13. As a result of the synergies within the subject area and the broad search strategy employed by Imperial Consultants, all of the publications required for the cows' milk protein hydrolysate evidence review have been identified as part of the systematic review on infant feeding and development of atopic and autoimmune disease. The FSA therefore proposes to incorporate the protein hydrolysate review into the existing systematic review being undertaken by Imperial Consultants.

14. The following questions will be addressed by the evidence review:-

a) Does the use of either extensively or partially hydrolysed formula feeding influence children's future risk of developing atopic or autoimmune disease?

b) Does the extent of protein hydrolysis influence children's future risk of developing atopic or autoimmune disease? (i.e. extensively hydrolysed formula vs partially hydrolysed formula)

c) Does the type of protein hydrolysates used (i.e. casein or whey protein) influence children's future risk of developing atopic or autoimmune disease? Appropriate comparisons should be made.

15. This request will not impact on Imperial Consultants ability to deliver the outcomes of the overarching systematic review on infant feeding and development of atopic and autoimmune disease in the timelines required. It is expected that this review will be submitted to COT for their consideration in the Spring of 2015.

[1] EFSA Journal 2014;12(7):3760 [106 pp.]. Scientific Opinion on the essential composition of infant and follow-on formulae. doi:10.2903/j.efsa.2014.3760

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**Study protocols for literature review of evidence on risks arising from the infant diet and the development of atopic and autoimmune diseases**

**1. Information included within this Annex are:**

a. Review A: Milk feeding study protocol

b. Review B: Timing of allergenic food introduction study protocol

c. Review C: Maternal and infant diet study protocol

**Secretariat**