2nd meeting of the Joint SACN-COT Working Group on the timing of introduction of allergenic foods into the infant diet

17 March 2017, Skipton House, London

FINAL MINUTES- CLOSED session

Chair

Professor Mike Kelly, Independent Chair

Members

Dr Anthony Williams, retired SMCN chair
Professor Peter Aggett, SMCN member/SACN deputy chair
Dr Ken Ong, SMCN chair/SACN member
Professor Alan Boobis, COT Chair
Dr René Crevel, COT Member
Dr Paul Turner, external expert

Secretariat

Professor Louis Levy (PHE)
Rachel Elsom (PHE)
Alastair McArthur (PHE)
Paul Tossell (FSA)
Frances Hill (FSA)

Observers

Dr Adrienne Cullum

Chair’s welcome and introduction

1. Professor Mike Kelly welcomed Members to the meeting and introduced Paul Tossell, team leader of the Food Standards Agency’s Allergy and Intolerance Team, and Dr Adrienne Cullum, who will be joining Public Health England’s Nutrition Science team as team leader from the 18 April 2017.

2. The Chair asked Members for any change to declared conflict of interest. None was reported.
Agenda Item 1: Minutes of the previous meeting and Matters arising  
(SACN:COT/Allergenic/16/min01)

3. Members were invited to comment on the minutes of the previous meeting. The following were noted:

- **Paragraph 9** – amend text to clarify the form of egg introduced: ‘in the form which egg was introduced (e.g. pasteurised, baked etc.)’ to replace ‘type of egg’. It was noted that in all cases, eggs were hen’s eggs.

- **Paragraph 19** – amend text to the following: ‘concerns were expressed that since the discontinuation of funding for the Infant Feeding Survey, information has been lacking on: breastfeeding duration, the timing of introduction of complementary foods, supplementary vitamins use and breastfeeding rates once solid foods have been introduced.’

- **Paragraph 25** – delete the following text: ‘and the overall quality of the evidence.’

- **Paragraph 26** – amend text to clarify that data on pre-existing allergic status were available: ‘they further noted that participants’ pre-existing allergic status was not clear in each study’ to ‘they further noted that some of the participants’ pre-existing allergic status was not yet available in some of the studies.’

- **Paragraph 29** – amend sentence to the following: ‘they noted that EAT represented the best quality evidence to date, however, the study population was not representative of the general population.’

- **Paragraph 32** - amend sentence to the following: ‘they noted that the reference scenario and the alternative scenario do not necessarily equate to the intervention and the respective control group (e.g. the placebo group) in each study being considered.’

- **Paragraph 33** – add text for clarification: ‘Members discussed whether the reference scenario should be current policy or practice and agreed that the alternative scenario should be…’

- **Paragraph 34** – amend text to: ‘Members agreed it was important to expand the consideration of the reference scenarios to cover both current policy (i.e. exclusive breastfeeding to around six months) and current practice (e.g. 70% infants in the UK are on solids by 5 months of age) for both egg and peanut.’

- **Paragraph 37** – add text to give detail on current UK infant feeding policy: ‘(i.e. exclusive breastfeeding to around six months).’

- **Paragraph 39** – add reference to the COT statement on the review of the 1998 COT recommendations on peanut avoidance (2008)\(^1\) and expand the discussion on the EAT study findings: ‘the EAT study findings might indicate evidence for the harmful effect of delaying the introduction of peanut beyond age 12 months rather than providing support for ‘early’ introduction.’

- **Paragraph 40** – amend text to: ‘they stressed the importance of considering the quantity of peanut protein consumed and the duration and pattern of exposure required to produce the desired effect’.

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\(^1\) [https://cot.food.gov.uk/sites/default/files/cot/cotstatement200807peanut.pdf](https://cot.food.gov.uk/sites/default/files/cot/cotstatement200807peanut.pdf)
• **Paragraph 41** – amend text to: ‘it was noted that a strong recommendation needs to be made regarding the importance of population data collection on infant feeding behaviour in the absence of the Infant Feeding Survey. Without such data the impact of any change to recommendations would not be measurable at population level.’

• **Paragraph 42** - amend text to: ‘Members agreed that on the basis of the available evidence, it was not possible to determine whether either reference or alternative scenario is clearly preferable (Tier 0).’

• **Paragraph 43** - amend text to: ‘Members agreed that both BRAFO Tiers 1 and 2 should be considered.’

2. The minutes were agreed as a correct record of the meeting, subject to these amendments.

3. Members agreed that the minutes from the December 2016 meeting and all meeting papers from the March 2017 meeting should not be placed in the public domain until the joint group had concluded its discussions and the joint group’s statement had been published.

   **ACTION: Secretariat**

4. Professor Louis Levy reported that all actions from the previous meeting had been completed.

5. Members were invited to comment on proposed amendments to the Terms of Reference (ToR) for the joint group and agreed that the wording should be changed to the following:

   *In light of the work being undertaken as part of the SACN review on ‘Feeding in the First Year of Life’ and COT’s statement on timing of allergenic food introduction, to undertake a benefit:risk assessment on the timing of introduction of allergenic foods (hen’s egg and peanut) into the infant diet.*

   *Based on that benefit:risk assessment, to provide integrated advice to the UK health departments.*

   **ACTION: Secretariat**

**Agenda Item 2: Background on work to date (SACN:COT/Allergenic/17/01)**

6. The Chair invited Frances Hill to introduce the paper. She explained that the aim of the paper was to provide a summary of activity to date and that this would form the basis for the introduction of the joint group’s statement.

7. Members were invited to comment on the paper. Members requested that further information on the prevalence of allergy be included. They also requested information
be added to the introduction on intakes of egg and peanut in the UK (from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC)). They discussed a recent published paper by Palmer et al (2016)\textsuperscript{2} describing a randomised controlled trial (RCT) investigating the timing of introduction of hen’s egg. Members noted this had not been included in either the systematic review and meta-analysis by Imperial College London or the COT statement, since these preceded publication of the Palmer et al manuscript and the data in the report were not available prior to publication. Members were not aware of any key evidence that was due to be published imminently. Members noted that the sources of information for both the tables and figures in the document should be cited.

**ACTION:** Secretariat

8. Members raised concerns that in most of the studies considered, the comparison groups were not sufficiently representative of the reference and alternative scenarios being considered by the working group. In particular, in the non-intervention groups the introduction of solid foods often occurred much later than six months of age.

9. Members noted that the avoidance of allergenic foods in the non-intervention groups (for example, in the case of the LEAP study\textsuperscript{3}, the control group avoided peanuts for the first five years) might have exacerbated the likelihood of developing peanut allergy, therefore exaggerating any intervention benefit. Furthermore, such a period of protracted avoidance of peanut is not representative of current infant/child feeding habits in the UK\textsuperscript{4}.

10. Members stressed that the joint working group must base its conclusions on interpretation of objective measures and observations reported in the primary literature, rather than using the study authors’ interpretation of the data.

**Agenda Item 3: Secondary Analysis of LEAP and EAT\textsuperscript{5} data**

11. The Chair invited Dr Paul Turner to give a presentation on the ‘Introduction of allergens into the infant diet before six months of age’. Dr Turner reminded the group that he is a co-author on the Tan et al, 2016 paper\textsuperscript{6}.


12. Members made a number of observations during the presentation:

- since the joint group's first meeting in December 2016, further data on participants’ pre-existing allergic status in many studies had been made available in the public domain;
- in some of the studies, it was difficult to determine the amounts of allergen actually consumed at each age; the term “introduced” was often used to indicate commencement of consumption, but not necessarily successful consumption of a particular amount at a particular frequency;
- although some studies were conducted in high risk groups, the overall findings were still applicable to the general UK population. This interpretation had also been concluded by the COT;
- a recent secondary analysis had been published with respect to data from the LEAP study. Only 18% of the cohort were under six months of age at screening, and the secondary analysis concluded that the effect of avoiding peanut consumption appeared to be weaker in this subgroup; however, the original LEAP study authors have contested the methodology used for this secondary analysis. Furthermore, members commented that: the study was conducted in a high risk population and therefore might not be representative of the general UK population; there were low levels of exclusive breastfeeding with the majority of infants having consumed infant formula prior to the introduction of allergens; and, the comparator group avoided peanut protein for the first five years of life which is not representative of current practice in the UK.
- In contrast, the EAT study population was more relevant to the group’s discussions, specifically in trying to address the policy question regarding duration of exclusive breastfeeding and timing of introduction of solid foods into the infant diet. Members noted that the EAT study had been very successful in promoting sustained exclusive breastfeeding to six months, something which is also not representative of typical infant feeding behaviour in the UK; and
- members noted that study authors would have made decisions to facilitate analysis and interpretation of their data in order to draw conclusions and highlighted that there were alternative ways of analysing and interpreting the available data from these studies,

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7 Greenhawt et al. LEAPing Through the Looking Glass: Secondary Analysis of the Effect of Skin Test Size and Age of Introduction on Peanut Tolerance after Early Peanut Introduction. Allergy 2017… doi: 10.1111/all.13100

members agreed that there was not sufficient evidence to make a strong recommendation on the introduction of egg and peanut into the infant diet before six months of age.

13. Members thanked Dr Turner for his presentation and for the additional analyses he had presented. They discussed how to reflect unpublished analyses when considering the joint group’s statement, as these were not peer reviewed but had been produced to help the group in its discussions. Members agreed that they could reflect only published data in the joint statement, but acknowledged that these analyses had been useful to inform the group’s discussions.

**Agenda Item 4: Risk: Benefit on Evidence on the timing of introduction of peanut into the infant diet and influence on the risk of development of atopic outcomes and autoimmune disease (SACN:COT/Allergenic/17/02)**

14. The Chair invited Frances Hill to introduce the paper, which had been prepared to facilitate the group’s consideration of the evidence. She explained that the BRAFO approach had been used to help assess the available evidence and on the basis of this, provisional judgements on the data had been provided to stimulate discussion.

15. Members highlighted the limitations of the trial data; primarily, that while the available evidence addressed the alternative or intervention scenario, it did not adequately reflect the reference scenario. This was because the ‘control’ groups, which were different for each study, were not consistent with the reference scenario being considered by this group.

16. Members discussed whether the available evidence was sufficient to allow comparison of the introduction of peanut prior to six months of age, versus after six months of age. They concluded that that there was insufficient evidence to make a strong recommendation regarding the timing of introduction of peanut prior to six months of age.

17. Members agreed with the conclusions of the COT that the introduction of peanut prior to 12 months was likely to be beneficial. However, Members concluded that the evidence for a “window of opportunity” necessitating the introduction of peanut prior to six months of age was insufficient. Members agreed that the available data were not sufficiently clear to make a change to recommendations to introduce peanut before six months; however they stressed the evidence for the benefits of not delaying the introduction of peanuts once solids have been introduced into the infant diet and of its subsequent regular consumption.

18. Members concluded that some amendments were required to the paper SACN/COT/Allergenic/17/02 following the joint group’s discussions. The Secretariat agreed to make the amendments and reflect these changes in the draft statement. The Chair thanked the Food Standards Agency for leading the development of the paper.

**ACTION: Secretariat**
Agenda Item 5: Draft conclusions and recommendations for peanut

19. The Chair summarised the group’s discussions and asked Members to consider whether, based on the currently available evidence, recommendations on the timing of introduction of peanut into the infant diet should be changed. The group agreed that there were not sufficient data to make an unequivocal judgement that peanut should be introduced before six months of age to achieve a positive health outcome and that there was a lack of evidence for a window of opportunity.

20. Members again noted the issues with the reference scenario, as the comparator in the LEAP trial was later than six months (median age of introduction: 7.8 months). They stressed that the LEAP study delayed peanut introduction until five years of age in the control group which does not represent the reference scenario or current policy or practice. Members highlighted that there is evidence that introducing peanut between 6-12 months of age is beneficial. Members therefore recommended that advice should be strengthened to communicate that while peanut should not be introduced before around six months, it is important not to delay introduction beyond 12 months.

21. Members discussed how best to record the deliberations of this group. They concluded that they had been unable to progress fully with the BRAFO method given the limitations of the available evidence, but stressed that BRAFO had provided a very useful framework within which to consider the issue. They agreed that they should use the COT assessment of the evidence, as outlined in the 2016 COT Statement, as the basis for the joint group’s conclusions but added that terms such as ‘early’, ‘late’ and ‘delayed’ introduction needed to be defined more clearly, if possible.

22. Members agreed the following wording: ‘From around six months, complementary foods including peanut should be introduced into the infant’s diet in an age-appropriate form, where tolerated. Once introduced, infants should be exposed to peanut on a regular and ongoing basis that suits both the family and the individual child. The introduction of peanut should not be delayed beyond 12 months of age’.

23. This builds on the conclusions from the COT statement that: ‘from the evidence available early introduction of allergenic foods does not increase the risk of allergy or autoimmune disease. Indeed, the deliberate exclusion or delayed introduction of specific allergenic foods may increase the risk of allergy to the same foods’.

Agenda Item 6: Risk: Benefit on Evidence on the timing of introduction of egg into the infant diet and influence on the risk of development of atopic outcomes and autoimmune disease (SACN/COT/Allergenic/1703)

24. The Chair invited Frances Hill to introduce the paper, which had been prepared to facilitate the group’s consideration of the evidence. She explained that the BRAFO
approach had been used to help assess the available evidence and on the basis of
this, provisional judgements on the data had been provided to stimulate discussion.

25. Members discussed the evidence relating to the timing of introduction of hens’ egg
into the infant diet, and noted that the majority of studies had been included in the
original systematic review conducted by Imperial College London\(^9\). Three studies
had been published in full since publication of the systematic review and
accompanying COT statement: Palmer et al., 2016\(^10\), Tan et al., 2016\(^11\) and Natsume
et al., 2017\(^12\). The authors of the latter two studies provided sufficient data to Imperial
College London for Review B to allow their inclusion in both the systematic review
and accompanying COT statement.

26. Members were informed that data from only one study, Palmer et al (2016), were
missing from the systematic review. Members questioned whether the meta-analysis
and Trial Sequential Analysis (TSA) relating to timing of egg introduction into the
infant diet would be rerun in order to take account of the Palmer et al data, and were
informed that this would not change the overall GRADE score.

27. Members considered that there was limited evidence to support a health benefit of
erlier egg introduction (between 4-6 months) versus later egg introduction (after 6
months). However, as for peanut, the evidence for a “window of opportunity”
necessitating the introduction of egg prior to six months of age was insufficient.
Furthermore, members stressed that it would be difficult to identify which individuals
in the general population would benefit from this. Members discussed the differences
in the data on timing of peanut and egg introduction, noting that in clinical practice,
egg allergy often presents earlier than peanut allergy.

28. Members agreed that the evidence was not sufficiently robust to recommend a
change to the current policy on exclusive breastfeeding for around six months. They
stressed that it was important to keep public health messages on the introduction of
solid foods, including allergens, clear and consistent unless the evidence was
sufficiently strong to justify different messages. They highlighted that
recommendations for health care professionals may need to take into account

of Allergenic Food Introduction to the Infant Diet and Risk of Allergic or Autoimmune Disease: A
Systematic Review and Meta-analysis. Journal of the American Medical Association. 316(11:1181-
1192)

\(^10\) Palmer DJ, Sullivan TR, Gold MS, Prescott SL, Makrides M. (2016) Randomized controlled trial of
early regular egg intake to prevent egg allergy. J Allergy Clin Immunol. Aug 20. pii: S0091-
6749(16)30793-X. doi: 10.1016/j.jaci.2016.06.052. [Epub ahead of print]


\(^12\) Natsume O, Kabashima S, Nakazato J, Yamamoto-Hanada K, Narita M, Kondo M, Saito M, Kishino
step egg introduction for prevention of egg allergy in high-risk infants with eczema (PETIT): a
different clinical scenarios and that targeted advice may be appropriate for individuals
at a higher risk of hens egg allergy.

**Agenda Item 7: Draft conclusions and recommendations for egg**

29. Members noted that there was only limited evidence on the effect of introduction of
allergens between 4-6 months versus after six months, and as a result, the policy
question had not been adequately addressed. They considered there were good
quality data to support the introduction of hen’s egg before eight months of age.

30. Members concluded that, as with peanut, the introduction of egg should not be
delayed, but occur from around six months, at a time and in a manner to suit both the
family and the individual child, where tolerated. Members noted that once egg is
introduced into the infant diet, regular and ongoing consumption should be
maintained.

31. A Member suggested that the recommendation might be stated in weeks and not
months. Members advised that the current recommendation on the timing of
introduction of solid foods should remain as ‘around six months’ as opposed to
‘around 26 weeks’, because the latter gives spurious precision, while the former
better reflects the fluidity of each individual child’s development and readiness for
successful introduction of solids foods during complementary feeding.

32. Members concluded that some amendments were required to the paper
SACN/COT/Allergenic/17/03 to allow this information to be included within the draft
statement. The Secretariat agreed to make the amendments and to reflect these
changes in the draft statement. The Chair thanked the Food Standards Agency for
leading the development of the paper.

**ACTION:** Secretariat

33. Members noted that while the BRAFO approach had provided a useful framework to
help the group explore the issues, the group’s decisions were based on an expert
evaluation of the evidence. The BRAFO method was applied to a certain extent, as
reference or alternative scenarios were defined, however, the nature of the data
made applying the methodology in full difficult. Consequently, BRAFO was applied
without going into the finer detail, and this in combination with the COT and SACN
evaluations, had allowed clear conclusions for both peanut and egg to be reached.
Members discussed the tabulated data which had been compiled to assist the joint
group’s consideration of the evidence. They agreed that since this information would
be included in the draft statement, there was no need to retain the tables. In the light
of the agreed recommendations about peanut and hen’s egg that the working group
had crafted, it was felt that no further consideration of the data or reference scenarios
was helpful at this point.
Agenda Item 8: Next steps and Timings

34. The Chair summarised the outcomes from the group’s discussions. The Secretariat was asked to draft the Joint Statement and then to circulate this for agreement by correspondence. Members agreed that a further meeting of the group was not required and the Chair thanked Members for their contributions over the two meetings.

**ACTION: Secretariat**

35. Members highlighted the difficulties in monitoring the impact of infant feeding policy since the cancellation of the Infant Feeding Survey. They noted that the absence of any national data since 2010 had made the deliberations of the group more difficult and stressed the importance of having robust population data collection and monitoring systems in place.