Scientific Advisory Committee on Nutrition

Paper for information: Summary of responses to consultation

Agenda Item: 2

SUMMARY OF RESPONSES RECEIVED FROM SCIENTIFIC CONSULTATION ON THE IRON AND HEALTH DRAFT SACN REPORT.

Procedure

The Iron working group wrote to interested parties on the 17 June 2009 to alert them that the draft report on Iron and Health had been placed on their website. Comments on the science of the report were requested to be submitted by 23 September 2009.

Response

13 responses were received and are available, in full on the SACN website.

Responses were received from the following organisations and individuals:

1. Agriculture and Horticulture Development Board – representing BPEX and EPBLEX (successors of Meat and Livestock Commission in England)
2. British Nutrition Foundation (BNF)
3. Committee on Carcinogenicity
4. Committee on Toxicology
5. Dean, Jennifer
6. Food and Drink Federation (FDF)
7. Health Food Manufacturers' Association (HFMA)
8. McArdle, Professor Harry J, University of Aberdeen
9. MRC Human Nutrition Research
10. Northern Ireland Food Advisory Committee (NIFAC)
11. Quality Meat Scotland (QMS)
12. Rushton, Dr H, University of Portsmouth
13. Safe food
14. Scottish Food Advisory Committee (SFAC)
15. Vegetarian Society UK, Friends of the Earth, Sustain, and the Food for Life Partnership

Table 1- Overview of responses received to the Iron and Health draft report

	Comments	**Organisation/ Individual**	**Action agreed by Working Group**
General comments in support of report	In general, the document is very well written and includes all the important points for people working in the iron field.	Prof H McArdle	
	Welcome draft report and the emphasis on consumption of a healthy balanced diet containing a variety of foods containing iron, specifically advice on restricting the consumption of red and processed meat and the removal of the focus inhibitors and enhancers, which has sometimes been considered an issue for those wishing to follow a vegetarian or vegan diet. The recalculation of meat intakes from the NDNS is a much overdue piece of work that could have far reaching conclusions.	Vegetarian Society UK, Friends of the Earth, Sustain, & Food for Life Partnership	
	Report provides a valuable collation of the evidence on iron, which will be of use to nutritionists and others with interest in nutrition & health. Clarification about the role of enhancers and in particular inhibitors in western diets is very helpful. The modelling on iron and zinc intakes is also informative.	BNF	
	Overall, consider report very well written, giving an honest and impartial view on iron nutrition and is a valuable, comprehensive, and robust document. The report highlights issues/dilemmas associated with iron nutrition and iron status. Would encourage publication of the iron nutrition sections in a quality peer reviewed journal as well as on the website. NIFAC	NIFAC	
	Welcome report and generally support the conclusions and recommendations. This is a very comprehensive and up-to-date review of the ever evolving field of iron and health.	MCR-HNR	
	This comprehensive report is thorough and detailed.	SFAC	

General comments critical of report	Lacks clarity in defining main focus of report *(iron & health)* especially regarding colorectal cancer risks associated with red meat intake. Discussing these effects instead of risks associated with iron consumption alone could confuse reader. Many nutritional benefits associated with eating red meat have been left out hence report appears unbalanced & may lose credibility as an expert report.	QMS	
	Overall conclusions less clearly presented than in other SACN reports. This may limit use of report and could lead to misinterpretations of conclusions. The detailed bridge between what SACN believes its risk assessment shows (i.e. its conclusions) and the next stage, risk management, seems to be less transparent than in previous reports. Some conclusions & jumping off points for the next stage (risk management) are not articulated clearly enough & need to be more transparent.	BNF	
	Does not present an appropriate balance of the scientific evidence on iron & health. In particular, the focus on red & processed meat and the associated risk with colorectal cancer as presented by WCRF is out of proportion & context. The majority of associations between red/processed meat & colorectal cancer risk are weak and likely influenced by bias & confounding. Inclusion of this evidence would be misleading as significant errors & omissions have been identified that have been acknowledged by WCRF. Insufficient recognition given to difference between bioavailability of haem and non-haem. Fact that foods fortified with iron make little contribution to iron status is lost in detail of report. Nutritional importance of the variety of natural food sources of iron (e.g. red & processed meat) is not made apparent.	BPEX	
	Lacks balance in certain key areas, particularly in relation to evaluation of association between iron/red meat intake & colorectal cancer. Essential that focus of report clear.	SFAC	
	Do not believe that SACN's risk assessment has provided a sufficiently definitive steer in certain areas to warrant the conclusions that have been reached. Risk of misinterpretation where uncertainty or potential contradictions exist & may therefore be a hindrance rather than help to its audience, particularly those who develop nutrition policy. This review does not adequately comply with Agency's Science Checklist, particularly pt 19: *"Is it clear how the conclusion is reached based on the evidence presented to the committee?"*	FDF	

Table 2- Issues for discussion arising from responses received to the report

Subject	Comments	Organisation/ Individual	Actions agreed by working group
Biochemistry and metabolism	Report would read better if section on *Physiological requirements* preceded the section on *Biochemistry*.	J Dean	
	In introduction & overview of iron metabolism, report correctly identifies ceruloplasmin & hephaestin as ferroxidases involved in iron release from cells. However, omit to mention, in section on inherited diseases of iron metabolism, one of the major symptoms of aceruloplasminaemia, is iron overload in liver & brain, together with seizures & schizophrenic episodes (Harris et al, 1995; 1998).	Professor H McArdle	
Physiological requirements			
DRVs	UK RNI for females aged 19-50 years is considerably lower than others cited in table 3.2. No mention of these between country differences in the text which is inconsistent with para 106 which refers to differences in reference intakes for lactating women between countries.	HFMA	
	DRVs may be set too high, however not enough evidence available to say this is the case; but may be worth updating the DRVs to be sure this is a real medical problem rather than a statistical man made one!	NIFAC	
Pregnancy	UK should urgently consider revision and update of the DRVs for iron to include those for pregnancy and lactation. Although report acknowledges these issues, they remain largely unaddressed.	QMS	
	Should reexamine whether to recommend routine iron supplementation during pregnancy when at least 800 mg iron is lost & cannot easily be replaced. Routine supplementation recommended in USA. An FAO expert committee recommended routine supplementation (100 mg/d) in 2nd half of pregnancy although their levels seem excessive. Norwegians also support routine supplementation in 2nd half of pregnancy (Eskeland & Malterud, 1993) & suggest this protects mother's stores, another important area for consideration (Eskeland *et al*, 1997). Cochrane report considers more data needed (Haider & Bhutta, 2006). Agree, as there are some contradictory reports that may confound the data (Alwan, McArdle & Cade, submitted). Also considerations such as obesity in the mothers that can cause further complications (Pickard, 1986). Issue too important to ignore; to suggest we maintain the status quo is not the right way forward.	Professor H McArdle	

	Little attention paid to consideration of risks and benefits of iron supplementation during pregnancy (Bo et al, 2009) and to the effect of frequent pregnancies on maternal iron stores (e.g. King et al, 2003).	SFAC	
Measuring iron status	Paper enclosed for consideration: Rushton & Barth (2009) - *What is the evidence for gender differences in ferritin and haemoglobin?* Also enclosed manuscript of paper submitted to European Journal of Clinical Nutrition, which is currently being peer reviewed: Rushton et al, 2009 - *Recommended daily iron intakes are unable to maintain serum ferritin concentrations in women.*	Dr H Rushton	
Iron in the diet	Other rich sources of iron include dried fruits, molluscs, and fish paste to which iron oxides may be added as colourant; these foods should also be mentioned.	HFMA	
	Over last 50 years measurements of iron in a variety of matrices have shown lower concentrations using different analytical techniques. So is it possible that we are overestimating the overall iron content of foods; if so, this an issue that needs to be considered further.	NIFAC	
Models to predict bioavailability	Dainty *et al* (2003) model for predicting iron bioavailability from serum iron curves should be included in para 204.	MRC HNR	
Absorption/ Biovailability	Interpretation of the evidence of relative importance of haem iron compared with the larger contribution of less bioavailable non-haem iron does not come across clearly; this is potentially confusing & unhelpful & should be more transparent. Even small amounts of meat, below the amounts associated with colon cancer risk, potentially have the capacity to make a valuable contribution to iron status given the statements about superior bioavailability. But there is no comment that modest meat consumption is consistent with appropriate practice in meeting physiological requirements for iron (and zinc).	BNF	
Enhancers/ inhibitors	Enhancer of iron uptake has now been identified as glycerophosphocholine (Armah et al, 2008).	Professor H McArdle	
	Dietary advice in relation to enhancers of iron absorption should not be discarded as their overall effect may not be huge but could be beneficial for some individuals.	NIFAC	
Interactions with other micronutrients	Copper & iron are known to interact in their metabolism (McArdle *et al*, 2008); interaction now being unravelled at molecular level (Fosset *et al*, 2009). These interactions should be considered when making recommendations re iron intake. Although effects of enhancers/ inhibitors considered, effects of other micronutrients are not. Effect of reducing red meat intake on absorption of other micronutrients, e.g. zinc, is missing the point. The direct effect of, e.g. taking zinc supplements, on iron status or vice-versa, should also be reviewed.	Professor H McArdle	

	Important to provide further consideration of the interactions between iron & other micronutrients (e.g. Arruda et al, 2009), particularly in relation to supplements (de Oliveira et al, 2009).	SFAC	
Fortified foods	Report emphasises low & variable bioavailability of iron fortificants but how the balance of evidence is perceived by SACN is unclear as some of the statements seem inconsistent, e.g. para 667: '*evidence suggests that foods fortified with iron make little practical contribution to improving iron status'* vs para 668: '*no data to indicate that the bioavailability of dietary iron is a significant factor in the pathogenesis of anaemia and iron deficiency in the UK population'* vs para 274: *'only dietary factor consistently associated with iron status in observational studies is meat or haem iron'.* Is the conclusion that despite the low bioavailability of iron from cereal foods, SACN believes that there is sufficient absorbed so that there is no need any longer to promote modest red meat consumption as a means of achieving adequate iron intakes and status? Evidence is not provided to promote this view.	BNF	
	In disentangling associations between diet & achievement of adequate status, little distinction made between fortificant iron (discredited in paras 280 & 667) and haem iron.	BNF	
	Do not gain clear sense of value placed by SACN on fortified foods as source of iron. Report states '*evidence suggests foods fortified with iron make little practical contribution to improving iron status* (para 667) yet unsure how this conclusion reached as earlier para 257 claims '*there is limited evidence of a beneficial effect on iron status at a population level'.* These statements are conflicting.	FDF	
	People with additional iron needs (young women, toddlers) often more susceptible to poor health status as a result of prolonged low iron intakes. Therefore important that fortification does not stop as this may remove their main sources of iron.	NIFAC	
	Risk assessment & risk management of iron absorption from fortified foods & supplements will be essential, especially for toddlers in relation to iron supplementation & access to fortified foods.	NIFAC	
Supplements	Useful for SACN to comment on high iron levels in iron supplements prescribed for iron deficiency anaemia, e.g. 1 ferrous fumarate tablet contains 68 mg elemental iron, the dose is 3 tabs/day & treatment may last 6m. Tablets at this concentration also used to prevent anaemia (dose of 1 tablet/d). These levels are substantially above EVM guidance level.	HFMA	
	Ferric pyrophosphate should be added to the list of most common supplements (para 261).	MRC HNR	

Consequences of iron deficiency *Cognitive development*	Para 288 - another cause of iron deficiency anaemia is blood loss due to surgical interventions. An alternative to the hypothesis that iron deficiency can lead to poor cognitive development is the possibility that poor cognitive development and iron deficiency are both consequences of common factors including low family income & educational achievement, lack of breast feeding, poor feeding & low meat/fruit intake.	HFMA SFAC	
High iron intake/ high iron burden *Iron/Meat & cancer*	Suggest separate report on red meat & cancer is needed from relevant committees on Mutagenicity and Carcinogenicity. Although red meat consumption will impact on iron levels, the link between red meat & cancer is a distinct & separate issue. It has importance both as a public health issue & an economic issue. No unequivocal evidence of risk or absence of risk. Eating meat likely to correlate with many other lifestyle factors therefore all studies would be subject to considerable confounding. However impact of confounding should not be over stated as residual confounding is unlikely to entirely explain the observed increased risk. Any recommendations need to be framed in terms of biological & epidemiological limitations. Majority of studies indicate increased risk. Use of the word *'however' (since the evidence is based on prospective observational studies…)* in the conclusions of this section implies that basing the assessment on prospective observational data has limited the ability to interpret the data. This type of study can be one of the most informative. Helpful to state either that the data were limited but showed an effect or that the data were substantial but equivocal. Support conclusion that there is an association between red & processed meat and colorectal cancer but it is not known if it is causal. Even with residual uncertainties, risk appears small. Data needs to be separated and analysed to see exactly what causes the increased colorectal cancer risk. Factors that need further consideration include: is it the iron or meat that increases risk; types of meat (pig, cow, sheep); fat in the meat; cooking of the meat & anthropogenic amines; preservatives/processing agents added & their possible interactions . None of this is clear and hence the general recommendation that other scientific expert committees address this issue. The epidemiological data is insufficient to elucidate these important questions.	NIFAC COC COC COC COC NIFAC	

	This section addresses risks associated with red meat intake rather than iron *per se.* Reads as review of effects of meat consumption on colorectal cancer rather than a review of health consequences of iron. Would benefit from editing to provide improved clarity and a clear focus on the issue under consideration i.e. the effects of iron itself.	SFAC	
	The animal studies by Seril et al (2002; 2005) should be included as they show that a 2-fold increase in dietary iron dramatically increased colitis-associated colorectal tumour incidence, iron accumulation in colonic luminal contents, at colonic mucosal surface & in superficial epithelial cells.	MRC HNR	
	Alexander et al (2009) found *"the available epidemiological evidence does not appear to support an independent association between animal fat intake or animal protein intake and colorectal cancer".* Key et al (2009) showed colorectal cancer incidence higher in vegetarians than meat eaters (EPIC-Oxford). Their findings do not agree with WCRF findings or with whole EPIC cohort findings which both claimed higher intakes of red & processed meat intake associated with increased colorectal cancer risk. Failure to consider such evidence renders report somewhat unbalanced.	QMS	
	Excessive amount of text reexamines WCRF evidence (2007). IARC (Boyle et al, 2008) questioned rationale for designation of *convincing.* Number of criticisms about report (Truswell, 2009; Alexander et al, 2009). Extensive reference to the WCRF report unhelpful & misguided.	BPEX	
	A continual error throughout WCRF evidence is that processed meat categorised same as red meat. To have strong supportive evidence to suggest any reduction in red meat intake, studies would need to categorise red & processed meat separately.	QMS	
	BNF review on the hypothesis that high iron stores increase risk of CVD and cancer, which was commissioned by BPEX, suggested that this is not the case in healthy individuals (Kelly, 2002). The review identified that the proportion of non-haem iron (from fortified foods & supplements) that is unabsorbed by the gut will be greater than haem iron and therefore relevant to consider in this context.	BPEX	
	Paras 421, 434, 438: Should also refer to the new WHO World Cancer Report (2008) & their conclusion that: *'Preserved meat and red meat probably increase risk of colorectal cancer, but relative risks found so far are of the order of a 30% increase for very high versus very low intakes of red meat'.*	MRC HNR	

	Would welcome clarity on the evidence for the role of processing and overcooking in the putative link between CRC and red meat.	SFAC	
	Detailed reference to the various hypothetical mechanisms potentially responsible for the development of CRC is inappropriate as no causal link has been established.	BPEX	
	The various potential biological mechanisms to explain the association between meat & colorectal cancer are all plausible but none supported by robust evidence.	COC	
	The amount of evidence presented on cancer is disproportionate to that on cardiovascular disease.	BPEX	
Negative effects of iron supplements on growth	Para 468 - should add the 2006 systemic review of trials on effect of iron supplementation on physical growth in children (Sachdev et al, 2006) and emphasise their conclusion that: "*this review did not document a positive effect of iron supplementation on the physical growth of children. The identified predictors of heterogeneity should be considered as exploratory and requiring confirmation, not conclusive.*"	MRC HNR	
	Paras 468, 472, 489 – suggest using terms "iron replete infants and toddlers" instead of "children" as ages range between 4-24 m; the term "children" suggests older ages than this.	HFMA, COT	
	Any advice with regard to potential adverse effects of supplementation needs to be carefully worded so that people who are iron deficient are not deterred from taking supplements under medical supervision.	COT	
	Doses used in some studies much higher than intakes from foods or the RNI. Dose in the study by Dewey et al (2002) lower than that used in other studies but still reported reduced growth in iron replete children. Useful for report to comment on the doses used.	COT	
Other potential adverse effects of high exposures to iron	Paras 478-481: The mechanism involved in the link between haemochromatosis and diabetes mellitus is likely to involve direct tissue damage due to the deposition of iron in the liver and pancreas rather than a physiological effect due to high systemic levels of iron itself.	SFAC	
Effect of iron deficiency & excess on immunity and infection	HIV & TB are used as the only examples in this section. Section should be expanded as other agents have very complex means of sequestering iron and this may impact on other infections suffered in UK. An expanded section on infection virulence could usefully be included.	NIFAC	

	In para 505 – add emphasis here to WHO studies (Sazawal et al 2006; Tielsch et al, 2006) & subsequent WHO recommendation rather than leaving to para 513: *past 5 years have seen increasing concern over safety of current forms of oral supplemental & fortificant iron. Of particular high profile has been the work in Pemba (Zanzibar) showing that 12 m low dose supplemental ferrous sulphate in iron deficient children led to a significant increase in morbidity. On advice from the Data Safety Monitoring Board, the iron-containing arms of the trial were discontinued after approximately 20 months. The main reasoning for these observations is based around iron-induced exacerbation of infections such as malaria [Sazawal et al, 2006). Following this work the WHO identified optimal dose, duration and mode of supplemental iron delivery as key research questions. However, even in the absence of concomitant infection, questions have been raised over the safety of current forms of oral iron and, in 2004, the WHO and the FAO of the UN recommended future research in the development of iron tablets that can be administered less often, at less cost and with higher acceptability [WHO/FAO, 2006).* The conclusion in para 528 does not reflect para 513 re WHO 2006 guidelines for iron supplements in pre-school children, in particular the emphasis on distinguishing between iron deficient and iron replete. Effects of iron on emerging diseases such as H1N1 influenza should be considered. Agree with draft conclusions but wording unclear; could be improved by referring to the balance of evidence *(on balance there is no evidence to suggest that improving iron status in the UK would have any impact on infectious disease incidence or morbidity. Some evidence suggests that iron supplementation to improve iron status may have adverse effects in some subgroups of the population, e.g. those with HIV and children at risk of diarrhoea)*.	MRC HNR MRC HNR COT COT	
Dietary iron intakes & status of the UK population	Need to be clearer statements about role of iron fortified foods in the achievement of adequate iron intake in context of reference values. Low intakes of red/processed meat increase risk of negative iron balance in adults (Kelly, 2002) & predictor of low iron stores in children (Gibson & Ashwell, 2002). Meat intake positively associated with serum iron & Hb status in children under 24m (Morgan et al, 2002). Urge that relative importance of haem iron compared with less bioavailable non-haem iron made clearer. Report suggests that the 45% contribution to iron intake from cereals is more significant to iron intake/status than the lesser contribution from haem sources. Concerned that there is no comment to indicate that moderate intake of red & processed meat is appropriate practice in meeting physiological requirements for iron (& zinc). Need to highlight if there is an actual risk or merely a potential risk in relation to iron status.	BNF BPEX NIFAC	

Potential impact of reducing total red meat consumption	Para 652 (& 691) - Impact of reducing total red meat consumption on other aspects of public health will also depend on type of red meat being replaced with other foods; e.g. lean cuts of red meat are not high in salt, energy, total or saturated fat. If red meat replaced by lean meat then there will be little benefit to other aspects of public health as mentioned nutrients unlikely to change much & could even increase if, e.g., more cheese eaten instead. Wording of this para not very scientific & not well thought out. To assume that a reduction in total red meat could lead to reductions in intakes of salt, total energy, & saturated fat not underpinned by evidence. Therefore wrong to assume that such reductions would have significant public health benefits by contributing to a decrease in blood pressure, obesity & CVD. The available evidence presented in the report suggested no association between total iron intake or status & CVD. Para 652 - Fresh lean red meat contains virtually no salt & fat content of red meat has significantly reduced over the years due to improved farming, feeding, and preparation techniques. Why is zinc included as report is about iron? Meat & cereal products are good sources of zinc. Lowering meat will have a big effect on zinc status and may subsequently have an effect as the body is dependent on a regular supply of zinc as it has no zinc reserves. If red meat consumption was lowered would it mean that people who are in the EAR group may be at risk of falling into the LRNI group? Do not agree that reducing red & processed meat consumption would have little impact on the proportion of people with iron or zinc intakes below LRNI. Have grave concerns about the assumptions made in modelling exercise particularly the fact that the difference between haem & non-haem iron was not taken into account. Important role for meat as a source of zinc is understated in this evaluation & is therefore also misleading.	HFMA BPEX QMS NIFAC NIFAC BPEX	
Overall summary & conclusions	Agency clearly states that iron intake is not the primary driver for iron status. This should be emphasised in *Summary & conclusions* as well as it currently is in text. The summary highlights major concerns & issues. It does not emphasise uncertainties in the use of markers in as much detail as main body of the report. Due to the size of the report, people may only read summary. Para 658: need clearer definition for 'free iron' to avoid confusion with elemental iron.	NIFAC NIFAC NIFAC	

	Para 660: might be useful to clarify that the body has no mechanism for excretion of iron which in turn can create a risk of iron overload that can be difficult to rectify.	NIFAC	
	Para 661: Genetics and physiology will ultimately determine an individual's iron status and stores. This makes it almost impossible to predict iron absorption rates from one person to another as well as from one meal to another.	NIFAC	
	Para 667: requires further clarification; e.g. need to ensure last sentence is correct & correlates with info in table 9.3. Clarification also needed on impact of fortified foods when overall diet of an individual is poor, i.e. do fortified foods have a bigger impact or is it the body's ability to upregulate? Because fortified cereals contribute more iron to the diet than meats, the final sentence of this para is confusing & appears to conflict with evidence presented in table on p240 and also with para 680. Fortification needs to be balanced against red meat consumption in order to get a conclusive picture of the contribution of cereal fortification to dietary iron intake.	NIFAC	
	Para 668: as evidence emerges different messages in relation to iron may be required for different sectors of the population & certainly for developed and developing countries. This might usefully be highlighted in the summary.	NIFAC	
	Para 674 needs to be elucidated more clearly as it contains a lot of jargon that although explained in the text is excessively concentrated here.	NIFAC	
	Para 680 appears to contradict para 667. Would be helpful to know whether there are substantial differences between types of meat/breeds of cattle etc.	NIFAC	
	Evidence suggests that foods fortified with iron make little contribution to improving iron status. This is overlooked in this section which states that major dietary sources of iron in the diet are cereals which account for about half of iron intake for most of the population. This point needs to be clarified to ensure that the nutritional importance of natural food sources of iron such as red & processed meat is fully recognised to avoid further confusion.	BPEX	
Recommendations	Support recommendations but more detail would be helpful to readers.	BNF	
	Conventional advice is that meat/meat products & vegetables make a substantial contribution to dietary iron intakes (para 592). Continuation of this advice either has to be part of the recommendations of the report or clear evidence provided as to why it should change.	BNF	
	Should include recommendations on breast feeding & effect of delay between birth & cutting	NIFAC	

	umbilical cord.		
	Concerned that some of the recommendations do not appear to have convincing weight of evidence behind them & would not want to see policy changes as a result of this.	FDF	
Recommendation 1)	Should be widened to include emphasis on women in low income groups.	BNF	
	Health professionals are advised to be vigilant, and consider the use of iron supplements if required. As this could involve prescribing iron supplements, it would be relevant to have a scientific comment re the level of iron in prescribed tables in relation to EVM guidance.	HFMA	
	Recommendation to health professionals too vague. Needs to be supported by more practical advice that can be offered to vulnerable clients.	BPEX	
	States women of reproductive age at risk of iron deficiency; would be useful (particularly to health professionals who may only read recommendations) to highlight that is particularly the case for 15-18y & 35-49y as the prevalence of iron deficiency anaemia in these groups more than twice that of women 25-34y.	HFMA	
	The need for targeted messages and info for those who have enhanced requirements, e.g. children & teenage girls should be noted as an additional recommendation. Iron overload & iron depletion states need to be addressed.	NIFAC	
Recommendation 2	Stresses need for a healthy balanced diet with variety of iron containing foods & less emphasis on enhancers/inhibitors/fortified foods. However this does not sit well with current situation where almost half of dietary iron in the UK comes from 'staple' starchy foods that have added iron. More detailed advice, emerging from the risk assessment, would be welcomed by many.	BNF	
	Although support this recommendation, consider that there is insufficient justification for less emphasis on the use of iron fortified foods (especially given the current situation in the UK where almost half of adult iron intakes comes from fortified cereals/cereal products). Concerned that report could inadvertently imply that consumers should avoid iron fortified foods, if there is not sufficient evidence to make such a recommendation.	FDF	
	Support recommendation that healthy balanced diet important in helping people achieve adequate iron status but, in the case of school meals, to overlook the importance of particularly good sources of easily absorbed iron such as red/processed meat & dismiss the importance of inhibitors & enhancers of iron bioavailability, is a major oversight.	BPEX	

Recommendation 3	Terminology used needs to be clearly defined in relation to red & processed meat. Specifically, does processed meat refer to processed red meat only or is cooked poultry also intended.	NIFAC	
	Here & elsewhere, should be clear whether the weight is raw or cooked meat. Should also state that modest intakes can make a useful contribution to iron intake, which is justified from the evidence presented.	BNF	
	Recommendation to lower red meat intake does not seem justified, especially considering the clear need to improve iron status & the poor iron contributions from fortified foods.	QMS	
	Evidence concerning red meat & colorectal cancer based on epidemiological studies, confounding factors such as obesity or smoking may have influenced findings. Report draws attention to the limitations & methodological inconsistencies. However to still make a recommendation based on such fragile evidence does not seem logical or proportionate.	QMS	
	Recommendation that population consumption of red meat should be reduced does not appear to be justified given weakness of the epidemiological data, together with the many nutritional benefits of consuming red meat & fact that several sections of population have iron intakes below LRNIs & average intakes are already at/below level recommended by WCRF.	SFAC	
	Given the relatively high rate of iron deficiency in vulnerable groups such as toddlers, girls and women of reproductive age and those over 65, the recommendations should perhaps state clearly that the reduction of red meat in the diet is largely relevant for men only.	Safe Food	
	The haem iron contained in red & processed meat is known to have greater bioavailability than other (non-haem) sources & acts as an enhancer to absorption. For this to translate into a cautionary recommendation about red & processed meat assuming that lower consumption would 'probably' reduce the risk of CRC is confusing. Believe this recommendation would be misguided and open to misinterpretation.	BPEX	
	The advice to health professionals to be vigilant is too vague. Especially when combined with recommendation to lower red & processed meat as a 'precaution' even though it is stated that evidence is 'not conclusive'. This could lead to all sorts of confusion & mixed messages. Health professionals need to be provided with specific medical & dietary advice which they can interpret & deliver in an unambiguous way. This should give recognition to the nutritional importance of natural food sources of iron such as red & processed meat.	BPEX	
Research recommendations	With regard to meat and cancer, need to be greater efforts in the design of studies to better classify types of processed meat so that if dietary recommendations are required, they can be more precise and targeted.	BNF	

	Better markers for iron status need to be developed. Any useful marker needs to be sensitive and specific.	NIFAC	
	Until adequate markers of absorption are available claims on fortified foods will be difficult to substantiate. Once adequate markers of absorption are available possible areas of future research in this area could be: models to better understand how absorption takes place and what factors inhibit or enhance (including impacts of various food technologies); maximising the palatability and availability of iron simultaneously.	NIFAC	
	Studies have concluded that using iron intake to examine associations between iron and health can impact on validity of findings (Rickard et al, 2009). More research required to investigate an accurate means of assessing iron availability, in order to relate iron to health outcomes.	QMS	
	Research on role of iron fortification in maintaining *'normal'* iron status by preventing iron deficiency & the development of measures that enable bioavailability to be taken into account in human studies.BNF	BNF	
	Assumptions on which current reference values are based needs to be supported by further research. Concerned there is insufficient evidence to suggest changing current reference values despite the fact that these may be set too high. Also considerable difference between countries. Assumptions about iron absorption from foods on which these reference values are based differ. Development of measures that would enable bioavailability to be taken into account would greatly help our understanding. Improved data on the iron content of foods which make a major contribution to intake such as red & processed meat would also be helpful.	BPEX	

Table 3 – Risk management issues raised in responses

	Comments	**Organisation/Individual**	**Actions agreed by working group**
Report	Consider whether iron and health is an issue for the Agency to undertake further work on, or is it an area for the Department of Health. It is not fundamentally a nutrition issue provided there is access to sufficient available iron in the food supply and diet of most people. NIFAC	NIFAC	
Paragraph 661	Info developing in this area though not enough known at present. Agency is therefore not in a position to develop specific targets but it is important that it continues to monitor and take timely action on any research findings related to development of haemochromatosis in the population. This could inform approaches needed for different sections of the population; e.g. prevalence of haemochromatosis is higher in Republic of Ireland & regional differences in the prevalence of hereditary haemochromatosis require consideration. The Agency should monitor such patterns in association with Departments of Health. Consideration should be given as to whether the advice provided needs to be individually targeted or whether a public health approach can continue and be more appropriate?	NIFAC	

References

1. ALEXANDER D et al. Meta-analysis of animal fat or animal protein intake and colorectal cancer. *Am J Clin Nutr. 2009;* 89:1402-9.
2. ARMAH CN, SHARP P, MELLON FA, PARIAGH S, LUND E K, DAINTY JR, TEUCHER B & FAIRWEATHER-TAIT SJ. L-{alpha}-Glycerophosphocholine Contributes to Meat's Enhancement of Nonheme Iron Absorption. *J. Nutr.* 2008; 138, 873-877.
3. ARRUDA et al. Vitamin A deficiency increases hepcidin expression and oxidative stress in rat. *Nutrition*. 2009; 25(4):472-8.
4. BO S et al. Iron supplementation and gestational diabetes in midpregnancy. *Am J Obstet Gynecol*. 2009 201(2):158.e1-6.
5. BOYLE P et al. Diet, nutrition and cancer: public media and scientific confusion. *Ann Oncol.* 2008; 19:1665-1667.
6. DAINTY et al. Quantification of unlabelled non-haem iron absorption in human subjects: a pilot study. *Br J Nutr*, 2003. 90(3): p. 503-6.
7. DE OLIVEIRA K et al. *Cell Biochem Funct*. 2009 27(3):162-6.
8. DEWEY KG, DOMELLOF M, COHEN R et al. Iron supplementation affects growth and morbidity of breast fed infants: results of a randomized trial in Sweden and Honduras. *J Nutr.* 2002; 132:3249-55.
9. ESKELAND B & MALTERUD K. Iron supplementation in pregnancy: General practitioners'compliance with official recommendations',. *Scand J Prim Care. 1993;* 11, 263-266.
10. ESKELAND B, MALTERUD K, ULVIK RJ. & HUNSKAAR S. Iron supplementation in pregnancy: is less enough? A randomized, placebo controlled trial of low dose iron supplementation with and without heme iron. Acta Obstet Gynecol Scand. 1997; 76, 822-828.
11. FOSSET C, DANZEISEN R, GAMBLING L, MCGAW BA & MCARDLE HJ. Cu loading alters expression of non-IRE regulated, but not IRE regulated, Fe dependent proteins in HepG2 cells. *J Inorg Biochem. 2009;* 103, 709-716.
12. GIBSON S & ASHWELL M. The association between red and processed meat consumption and iron intakes and status among British adults. *Public Health Nutrition.* 2002; 6(4); 314-350.
13. HAIDER B & BHUTTA Z. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2006(4).
14. HARRIS ZL., KLOMP LW & GITLIN JD. Aceruloplasminemia: an inherited neurodegenerative disease with impairment of iron homeostasis. *Am J Clin Nutr. 1998;* 67, 972S-977S.
15. HARRIS ZL., TAKAHASHI Y, MIYAJIMA H, SERIZAWA M, MACGILLIVRAY RT & GITLIN JD. Aceruloplasminemia: molecular characterization of this disorder of iron metabolism. *Proc Natl Acad Sci U S A.* 1995*;* 92, 2539-2543.
16. KELLY C. Can excess iron increase the risk for coronary heart disease and cancer. *Nutrition Bulletin.* 2002.27; 165-179.
17. KEY TJ et al. Cancer incidence in vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford) *Am J Clin Nut. 2009;* **89**:1S-7S.
18. KING JC. *J Nutr*. 2003 133(5 Suppl 2):1732S-1736S.)
19. SACHDEV H, Gera T, and NESTEL P, Effect of iron supplementation on physical growth in children: systematic review of randomised controlled trials. *Public Health Nutr*, 2006. **9**(7): p. 904-20.
20. McARDLE HJ, ANDERSEN HS, JONES H & GAMBLIING L.Copper and iron transport across the placenta: regulation and interactions. *J Neuroendocrinol.* 2008; 20:427-431.
21. MORGAN J et al. Contribution of meat to iron status in young children under 24 months old. Sponsored by the Meat and Livestock Commission
22. PICKARD BM. Feeding children in the beginning – nutrition and pregnancy. 1986. 4:155-166.
23. RUSHTON H & BARTH JH. What is the evidence for gender differences in ferritin and haemoglobin? *Crit Rev Oncol/Hematol.* 2009 (in press).
24. SACHDEV H, GERA T & NESTEL P. Effect of iron supplementation on physical growth in children: systematic review of randomised controlled trials. *Public Health Nutr.* 2006. 9(7):904-20.
25. SAZAWAL, S., et al., Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial. *Lancet*. 2006; 367(9505): p. 133-43.
26. SERIL, D.N., et al., *Dietary iron supplementation enhances DSS-induced colitis and associated colorectal carcinoma development in mice. Dig Dis Sci*, 2002; **47**(6): p. 1266-78.
27. SERIL, D.N., et al., *Systemic iron supplementation replenishes iron stores without enhancing colon carcinogenesis in murine models of ulcerative colitis: comparison with iron-enriched diet. Dig Dis Sci*, 2005. **50**(4): p. 696-707.
28. TIELSCH JM et al. Effect of routinr prophylactic supplementation with iron and folic acid on preschool child mortality in southern Nepal: community-basedcluster-randomised, placebo-controlled trial. *Lancet.* 2006; 367(9505):144-152.
29. TRUSWELL AS. Problems with red meat in the WCRF2. *Am J Clin Nutr.* 2009; 89:1274-1275.
30. WHO, FAO (2006) Guidelines on Food Fortification with Micronutrients [LH Allen, B Benoist, O Dary and RF Hurrell, editors]. Geneva: World Health Organization and UN Food and Agricultural Organization.