European Food Safety Authority; Outcome of the Public consultation on the Draft Opinion of the Scientific Panel on Dietetic products, Nutrition, and Allergies (NDA) on Dietary Reference Values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol

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SCIENTIFIC REPORT OF EFSA

Outcome of the Public consultation on the Draft Opinion of the Scientific Panel on Dietetic Products, Nutrition, and Allergies (NDA) on Dietary Reference Values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, and cholesterol[1]

European Food Safety Authority[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

On 2 July 2009, the EFSA Panel on Dietetic products, Nutrition and Allergies (NDA) endorsed a draft Opinion on Dietary Reference Values for fats to be released for public consultation. This Scientific Report summarises the comments received through the public consultation and outlines how these were taken into account in the final opinion.

EFSA had received contributions from 40 interested parties (individuals, non-governmental organisations, industry organisations, academia and national assessment bodies).

The main comments which were received during the public consultation related to: the availability of more recent data, the nomenclature used, the use of a non-European food composition data base, the impact of genetic factors in modulating the absorption, metabolism and health effects of different fatty acids, the definition of "nutritionally adequate diet", the use of Dietary Reference Values in the labelling of foods, the translation of advice into food-based dietary guidelines, nutrient goals and recommendations, certain risk management issues, and to Dietary Reference Values of fats, individual fatty acids, and cholesterol.

All the public comments received that related to the remit of EFSA were assessed and the Opinion on Dietary Reference Values for fats has been revised taking relevant comments into consideration.

[1] On request from EFSA, Question No EFSA-Q-2009-00784, issued on 01 March 2010.

[2] Correspondence: NDA@efsa.europa.eu

[3] Acknowledgement: EFSA wishes to thank the members of the Working Group on Population Reference Intakes for the preparation of this EFSA scientific output: Carlo Agostoni, Jean-Louis Bresson, Jean-Michel Chardigny, Susan Fairweather-Tait, Albert Flynn, Ambroise Martin, Monika Neuhäuser-Berthold, Hildegard Przyrembel, John Joseph Strain, Inge Tetens, Daniel Tomé and EFSA's staff member Silvia Valtueña Martínez for the support provided to this EFSA scientific output.

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BACKGROUND

On 2 July 2009, the EFSA Panel on Dietetic products, Nutrition and Allergies (NDA) endorsed a draft Opinion on Dietary Reference Values for fats to be released for public consultation.

The scientific advice on nutrient intakes is important as the basis of Community action in the field of nutrition; for example such advice has in the past been used as the basis of nutrition labelling. The Scientific Committee for Food (SCF) report on nutrient and energy intakes for the European Community dates from 1993.

The European Commission has asked EFSA to review and if necessary update such advice to ensure that the Community action in the area of nutrition is underpinned by the latest scientific advice. To this end, EFSA has been requested to consider the existing Population Reference Intakes for nutrients and certain other dietary components.

Furthermore, and in order to communicate effectively on nutrition and on healthy diets to the public at large, it is generally more appropriate to express recommendations for the intake of individual nutrients or substances in food-based terms. To this end EFSA has also been asked by the European Commission to provide assistance on the translation of nutrient-based dietary recommendations for a healthy diet into food-based recommendations intended for the European population as a whole.

In line with EFSA's policy on openness and transparency and in order for EFSA to receive comments from the scientific community and stakeholders on its work, EFSA engages in public consultations on key issues. The work on Dietary Reference Values (DRVs) including food-based dietary guidelines is considered to be such an issue. Accordingly, the draft Opinion on DRVs for fats was released for public consultation for ten weeks (from 5 August until 15 October 2009) on the EFSA website[4]. Stakeholders were informed and invited to submit comments.

Together with other draft Opinions on DRVs, the draft Opinion on DRVs for fat was also discussed on a National Expert Meeting with Member States on Dietary Reference Values held in Barcelona on 7 and 8 September 2009.

EFSA has committed to publish the comments received during the public consultation as well as a short report on the outcome of the consultation, taking also into account comments received by Member States in the commenting period after the National Expert Meeting.

COMMENTS RECEIVED

At the end of the public consultation period in October 2009 had received contributions from 40 interested parties (individuals, non-governmental organisations, industry organisations, academia and national assessment bodies). All comments received were scrutinised by the NDA secretariat and subsequently compiled with reference to the contributor and the section of the draft Opinion to which the comment referred (see Appendix). Comments submitted formally on behalf of an organisation appear with the name of the organisation. The comments received by Member States during the National Expert Meeting are published in the minutes of that meeting on the EFSA website.

SCREENING AND EVALUATION OF COMMENTS RECEIVED

1. General comments

In general, the comments were constructive and aimed to help improving the draft Opinion. It was noted that several contributions copied or reiterated arguments brought forward already by other organisations.

[4] http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902045161.htm

Several comments pointed out that available or actualised data on e.g. intake were not used in the Opinion and that not the most recent recommendations of national authorities were quoted. Also, a general comment was to clarify the criteria used in the selection of literature on the health effects of dietary fats that was used in the preparation of the draft Opinion. Differences between DRVs, nutrient goals and recommendations and food-based dietary guidelines (and between the bases used for establishing them) were not generally acknowledged in the comments received. Clarification on the purpose of European DRVs and how these relate to national DRVs, to nutrient goals and recommendations, and to food-based dietary guidelines was requested.

2. Specific comments

The main issues addressed in the comments are summarised below.

Nomenclature: The Panel acknowledges the confusion caused by the use of different terms for the same type of dietary reference value and underlines the importance for the consistent use of such terms. Also, it was argued that the term "fats" comprises only solid fats as opposed to oils.

Non-European food composition data base: EFSA is asked why US instead of European data were used for the tables with fatty acid composition of some foods and fats and oils.

Genetic variability: EFSA is requested to consider the impact of genetic factors in modulating the absorption, metabolism and health effects of different fatty acids which might necessitate the setting of different dietary reference values for subjects with defined genetic backgrounds.

Definition of "nutritionally adequate diet": Several comments requested a definition of this term.

Labelling of foods: There was a request to take into account the impact of DRVs for fats on food labelling and communication of nutrition information to the consumer.

Food-based dietary guidelines: A comment requested EFSA to advise on recommended food group choices with respect to the content of fat and individual fatty acids to achieve a healthy eating pattern.

Risk management: EFSA was requested to advise on measures to inhibit or promote the consumption of foods with certain characteristics or to ban or support the use of constituents in foods considered to impair or enhance health.

Nutrient goals and recommendations: There was a request to provide, in addition to dietary reference values for energy, macro- and micronutrients, which are based on metabolic needs, markers of status, observed intakes in healthy populations, and/or valid indicators of health, recommendations on the quantitative nutrient composition of diets which are both feasible and suitable to maintain health.

Total fat: Some comments suggested that the proposed lower bound of the Recommended Intake Range (RI) (20 E%) may be too low for the following reasons: in most European countries fat intake is around 30 E%; replacement of fat by carbohydrate could have adverse effects on blood lipids and health; 20 E% fat may increase the likelihood of essential fatty acids deficiency, likewise of some vitamins, particularly in children. It is noted that the RI for children between 3 and 18 years of life is not mentioned in Section 6.1. It is also suggested that the impact of the position of individual fatty acids on the glycerol backbone on their absorption, metabolism and health effects should be taken into account in setting DRVs.

Saturated fatty acids (SFA): On the one hand, both recommendations for intake ranges (5 to 10 E%) and an Tolerable Upper Intake Level (UL) (10 E% or 12 E% in combination with TFA) are proposed. On the other hand, it was considered that a recommendation to keep SFA intake "as low as possible" is not a useful advice and perhaps not advisable, since replacement of SFA by carbohydrates does not appear to improve the ratio of total to HDL-cholesterol, and at appropriate levels of intake, SFA are

"essential". It was suggested that SFA are not a homogenous group of fatty acids with respect to their metabolism and their effects on blood lipids, and that this should be taken into account by establishing different DRVs for different SFA. It was also proposed that, when judging the effects of different nutrients on blood lipids, the ratio of total to HDL-cholesterol should be used instead of LDL-cholesterol concentrations since it is more predictive of the risk for cardiovascular diseases. An evaluation of the predictive strength of different biomarkers on disease outcomes (e.g. cardiovascular disease (CVD)) was suggested.

***Trans* fatty acids (TFA):** On the one hand, both recommendations for intake (0.5 to 1-2 E%) and an UL (1 E% or 12 E% in combination with SFA) are proposed. On the other hand, it was considered that a recommendation to keep TFA intake "as low as possible" is not a useful advice as cannot be easily converted to food label information. Elimination of TFA by eliminating some sources of TFA could have negative nutritional consequences on dietary patterns because TFA are not eaten as such but are natural constituents of many animal derived foods. The consumption of TFA has decreased in many European countries to presently low levels around 1 E% due to the restricted use of partially hydrogenated fats and oils in complex foods. The effects of TFA on biomarkers for risk of CVD and on CVD related outcomes differ according to the origin (i.e., from ruminant animals *vs* hydrogenation of fats and oils in technological processes). Therefore, DRVs or recommendations for TFA should be restricted to TFA industrially produced. Moreover, the consumption of TFA from ruminant animals is lower than that from "industrial" processes. Since conjugated linoleic acids (CLA) can contain *trans* double bonds, it should be considered as TFA.

***cis*-monounsaturated fatty acids (MUFA):** It was suggested that MUFA are indispensable in diets to fill gaps in energy expenditure and have by themselves physiological roles. Both Adequate Intake (AI) or RI and UL were proposed for MUFA. It was also suggested that different MUFA may have different physiological effects.

n-6 polyunsaturated fatty acids, specifically linoleic acid (LA): On the one hand, it was suggested that the proposed AI for LA is too low because, even if the AI is suitable to prevent LA deficiency, a role for LA in reducing the risk of CVD is observed seen only at intake levels of at least 6 E% or 5 to 8 E%. On the other hand, it was suggested to set an UL for LA because over-consumption of LA can lead to adverse effects, i.e., lipid peroxidation, increase in body fat and instability of atherosclerotic plaques as well as inhibition of desaturation of ALA.

Arachidonic acid (ARA): It was felt that the physiological roles of ARA are not well described, that several groups in the population can be considered at risk of ARA deficiency (e.g., vegans, infants and toddlers fed complementary food devoid of ARA) since LA intake has no influence on ARA levels, and that ARA synthesis in the human body may be too low to meet the requirements.

n-3 polyunsaturated acids, specifically α-linolenic acid (ALA): On the one hand, it was suggested that the proposed AI for ALA is too low because, even if the AI is suitable to prevent ALA deficiency, a role for ALA in reducing the risk of CVD has been observed at levels of intake 1 to 2 E%. This intake would also be appropriate to maintain a n-6/n-3 ratio below 5. The AI for ALA could include n-3 LCPUFA up to 10 % of the value.

Docosahexaenoic and eicosapentaenoic acids (DHA and EPA): The AI of 250 mg per day was considered to be too low and not optimal for the reduction of CVD risk, as beneficial effects have been observed with doses beyond 250 mg per day. Either an AI around 500 mg or two different AI, one for healthy subjects and one for secondary CDV prevention, were suggested.

A paragraph on the benefits of n-3 LCPUFA on mental health in adults and the elderly was considered to be missing by some stakeholders.

It was also noted that data on DHA accumulation in the brain in infants may have been incorrect.

There was a request to mention that besides fish there are other sources of DHA and EPA, to differentiate in the description of studies between fish/fish oil and other sources like single cell oils, and to mention the amounts of n-3 LCPUFA provided in the studies.

n-6/n-3 ratio: A reference value for the n-6/n-3 ratio in the diet was requested.

Conjugated linoleic acids (CLA): The comments received relate to the presence of CLA in human milk, to the lack of intake data, and to missing effects on lipid peroxidation.

Cholesterol: The comments received related to establishing DRVs (UL) and to a more extensive description of potential adverse effects of dietary cholesterol.

INCORPORATION OF THE COMMENTS IN THE OPINION

The EFSA NDA Working Group on Population Reference Intakes (PRI) was presented with the compilation of comments and discussed them at a dedicated meeting. Many of the comments were appropriate and aimed to enhance the scientific quality and clarity of the document. These comments were taken into account and the document was revised accordingly as follows:

General comments: Section 4 has been updated with the most recent recommendations for fats from national and international bodies, and Annexes 2 and 3 reporting intake data for dietary fats in different European countries have been updated and re-structured to accommodate most recently published intake data. The Opinion on principles for deriving and applying DRVs has been modified to clarify the differences between DRVs, nutrient goals and recommendations and food-based dietary guidelines, clearly stating that the task of the Panel will be limited to establishing DRVs for Europeans. Different sections in this Opinion have been modified to be consistent with the terminology and concept underlined in the final Opinion on Principles.

Nomenclature: Consistent with the scientific Opinion on Principles for deriving DRVs, which was amended based on the comments received during public consultation, the term "recommended intake range" has been replaced by "reference intake range". Also, consistent terminology as defined in the Opinion on principles has been used throughout the Opinion on fats. With regards to the terms "dietary lipids" vs "dietary fat", the Panel considers that both the terms "dietary fat" and "dietary lipids" include as main components triacylglycerols and phosphatidylcholine, and therefore no changes were introduced in the Opinion.

Non-European food composition data base: The Panel chose this database because of its completeness. The choice does not signify correctness of values which, moreover, can have wide ranges. The food items were chosen to demonstrate in exemplary fashion only the widely differing fatty acid patterns of some foods and not with the intention of providing a data reference base. No changes in the Opinion were considered necessary.

Genetic variability: The Panel considered this suggestion in the Opinion on Principles for deriving DRVs and will refer to the impact of genetic factors in modulating the absorption, metabolism and health effects of different nutrient (including fatty acids) (including this Opinion on DRVs for fat), where appropriate. However, the Panel considers that the present knowledge is insufficient to set specific DRVs for fats based on a particular genetic background.

Definition of "nutritionally adequate diet": "Nutritionally adequate diet" is a common expression to indicate food intake patterns that allow an adequate intake of all essential nutrients without the risk of an inadequate or excessive energy intake. The Panel considers that such diets are the goal of food-based dietary guidelines and fulfil the criteria set out in the Opinion on the development of foodbased dietary guidelines.

Labelling of foods: This comment was considered to be outside the terms of reference (ToR) for this Opinion. No changes were introduced in the text.

Food-based dietary guidelines: This request was considerd to be outside the ToR for this Opinion. On the one hand, EFSA has already provided guidance for developing food-based dietary guidelines; on the other, it is the task of managers in the field of public health and food safety. No changes were introduced in the text.

Risk management: This task is clearly out of the ToR and up to risk managers in the field of public health and food safety. No changes were introduced in the text.

Nutrient goals and recommendations: As clearly stated in the final version of the Opinion on Principles for deriving DRVs, the Panel considers that this request is outside the ToR. However, the Panel acknowledges that dietary reference values have to be converted into nutrient goals for the population and nutrient recommendations for individuals taking into account other considerations than pure scientific risk assessment (i.e., risk management). Also, the Panel has already provided guidelines on how to derive food-based dietary guidelines from DRVs and nutrient goals and recommendations.

Total fat: The Panel considers that, due to the inconsistent use of nomenclature for DRVs in the draft Opinion highlighted above, the term RI ("reference" intake range), may have been misinterpreted as a "recommended" intake range. The lower bound of the RI for total fat is not a recommended intake but a reference intake and the Panel has outlined that total fat intakes at this level, even if compatible with good health under certain circumstances, can be accompanied by too low intakes of some vitamins and/or energy in certain population subgroups, particularly children. The RI for children between 3 and 18 years of life is now mentioned in section 6.1 and Table 5 and it is the same as for adults (i.e., 20 to 35 E%). Finally, it is mentioned in the Opinion that different positions of different fatty acids in the glycerol backbone may have different health effects, but the data available is considered insufficient for setting different DRVs.

Saturated fatty acids (SFA): The Panel considers that intake recommendations or "target values" for consumption should be part of nutrient goals and recommendations and do not fulfil the criteria for the derivation of a DRV (see section above on nutrient goals and recommendations). This has been clearly stated in the final version of the Opinion. Also, the Panel does not consider SFA to be indispensable nutrients. They are, however, essential constituents of a diet as providers of energy and carriers of nutrients and they can, therefore, not be zero in a nutritionally adequate diet. Even if different SFA have different effects on blood lipids, the Panel considers that there are not sufficient data to set different DRVs for different SFA. The Panel considers that the ranking of the predictive strength of different biomarkers on disease risk is outside the ToR for this task.

***Trans* fatty acids (TFA):** The Panel considers that intake recommendations or "target values" for consumption should be part of nutrient goals and recommendations and do not fulfil the criteria for the derivation of a DRV (see section above on nutrient goals and recommendations). This has been clearly stated in the final version of the Opinion. The Panel refers to the definition of a "nutritionally adequate diet" above, which may contain some unavoidable amounts of TFA but considers that data at present are insufficient to derive an UL or an upper bound for a RI for TFA. Advice on the reduction of TFA in the diet by recommended food choices should be given in food based dietary guidelines. The Panel also considers that at present the available data are insufficient to derive different DRVs for TFA of different origin. Even if CLA are chemically TFA, the Panel decided to treat them separately from TFA with non-conjugated double bounds because specific physiological effects have been ascribed to CLA.

***cis*-monounsaturated fatty acids (MUFA):** The Panel notes that the available evidence does not allow attributing MUFA specific physiological effects that can be separated from the effects of replacing SFA (and TFA) or carbohydrates in the diet. Their role in the diet (e.g. effects of oleic acid on blood lipids when replacing carbohydrates, SFA and/or TFA), and the different physiological

effects different MUFA may have, should be taken into account when formulating nutrient goals and recommendations and food-based dietary guidelines. No changes have been introduced in the Opinion.

n-6 polyunsaturated fatty acids, specifically linoleic acid (LA): The Panel acknowledges that WHO recommends a LA intake of at least 6 E% for the prevention of CVD. However, the Panel considers that the intake recommendation by WHO is not equivalent to the AI as derived by the Panel and should be integrated into nutrient goals and recommendations and/or food-based dietary guidelines, as part of the association between LA (and other PUFA) intake and the reduction of CVD risk can likely be attributed to the substitution of SFA. Also, the Panel considers that the data available are insufficient to derive an UL for LA, and that the quoted negative effects of LA consumption should be dealt with in nutrient goals and recommendations and/or food-based dietary guidelines.

Arachidonic acid (ARA): ARA is mentioned in the Opinion as precursor of prostanoids and leukotrienes and comments are made on the ARA supply via food and endogenous synthesis. The Panel agrees that dietary LA has no influence on ARA levels but acknowledges that "low" levels of ARA are not equivalent to ARA deficiency and that even in subjects with demonstrated "low" ARA levels ARA deficiency symptoms have not been described. The Panel also considers that the data available do not permit to set a DRV (AR, PRI or AI, or UL) for ARA.

n-3 polyunsaturated acids, specifically α-linolenic acid (ALA): The AI value for ALA has not been based on data on the prevention of CVD and the Panel refers to the lack of an association between ALA intake and risk for fatal coronary heart disease or coronary heart disease events in a very recent meta-analysis of prospective cohort studies with intakes ranging from 1.4 to 2.5 g/day (Skeaff and Miller, 2009). The Panel prefers to propose separate AI for ALA and n-3 LCPUFA because of the unpredictable conversion rate of ALA to EPA/DHA. The Panel agrees that in nutrient-based guidelines a balance between LA and ALA should be part of the advice. Taking into account current consumption data in Europe this would mean to increase current ALA intakes.

Docosahexaenoic and eicosapentaenoic acids (DHA and EPA): The Panel has reconsidered the pertinent studies on the effects of n-3 LCPUFA on the risk of CVD and found the meta-analysis by Mozaffarian and Rimm (2006) particularly useful in setting an AI for DHA plus EPA, since daily doses for the effects were calculated and provided. That meta-analysis shows a significant threshold effect at intakes of 250 mg per day for cardiovascular mortality, whereas different doses (and time length) may be required for different mechanisms of action in order to obtain the effect, which may explain different findings in different studies depending on the background diet (DHA plus EPA level of intake) and risk level. The criticism on this meta-analysis relates to the graphic representation in which the number for the threshold might have been forced by the authors and was not real. Another problem is that observational and intervention studies are pooled, and that populations with very high baseline intakes are included, although an effort has been made to recalculate baseline risk in those cases. However, the Panel considers that this is the best available estimate to establish an AI for DHA and EPA on the basis of CVD risk in healthy populations, for which DRVs are meant.

A new section (5.12) on cognitive decline and dementia has been included in the Opinion.

More recent data on DHA accumulation in the brain in infants have been incorporated into the Opinion.

Other sources of DHA and EPA have been mentioned in the Opinion.

n-6/n-3 ratio: The Panel considered that setting a reference value for such a ratio cannot be done without consideration of the total amounts of the respective fatty acids in the diet or, vice versa, that it is preferable to consider the balance between n-6 and n-3 PUFA in nutrient goals and recommendations and food-based dietary guidelines taking into account their mutually inhibitory effects when one or the other is consumed in excess. No changes were considered necessary in the Opinion.

Conjugated linoleic acids (CLA): Information about the CLA content in human milk and a statement on the lack of intake data has been included in the Opinion. However, this information, or that on the effects of CLA on lipid peroxidation, does not change the conclusion that a DRV cannot be defined for CLA. No changes were considered necessary in the Opinion.

Cholesterol: Section 5.2.7 already clearly depicts the lipoprotein changes observed following defined intakes of cholesterol. Section 5.8.4 depicts the weak relationship between dietary cholesterol and CVD. No changes were considered necessary in the Opinion.

The Opinion was modified taking editorial comments into account where appropriate. Also, Annex 1 and Annex 2 reporting intake data for fats in different European countries have been updated and re-structured to accommodate most recently published intake data.

EFSA wishes to thank all stakeholders for their contribution.

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Mozaffarian D and Rimm EB, 2006. Fish intake, contaminants, and human health: evaluating the risks and the benefits. JAMA, 296, 1885-1899.

Skeaff CM and Miller J, 2009. Dietary fat and coronary heart disease: summary of evidence from prospective cohort and randomised controlled trials. Annals of Nutrition and Metabolism, 55, 173-201.

GLOSSARY / ABBREVIATIONS

AI	Adequate Intake
ALA	Alpha-Linolenic Acid
AR	Average Requirement
ARA	Arachidonic Acid
CLA	Conjugated Linoleic Acids
CVD	Cardiovascular Disease
DHA	Docosahexaenoic Acid
DRV	Dietary Reference Value
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic Acid
HDL	High Density Lipoprotein
LA	Linoleic Acid
LCPUFA	Long Chain Polyunsaturated Fatty Acids
MUFA	*Cis*-Monounsaturated Fatty Acids
PRI	Population Reference Intake
RI	Reference Intake ranges for macronutrients
SCF	Scientific Committee on Food
SFA	Saturated Fatty Acids
TFA	*Trans* Fatty Acids
ToR	Terms of Reference
UL	Tolerable Upper Intake Level

APPENDIX

COMMENTS RECEIVED ON THE DRAFT OPINION RELATED TO DIETARY REFERENCE VALUES FOR FATS DURING THE PUBLIC CONSULTATION PERIOD

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
AFSSA	1. Introduction	First of all, Afssa thanks Efsa for this huge and essential work for the definition of DRVs. This compilation of data and recommendations is a keystone element to support public health issues in European human nutrition. The contribution of national safety agencies may help Efsa and the NDA panel for the further discussions and amendments. 1. General remarks Our comments on this draft document are mainly based on Afssa current work on the update of fatty acids Nutritional Recommendations for the French population (Opinion in process). This work includes a thematic and extensive review of the literature on fatty acids. Collective expertise was used to define each value proposed as ANC for each fatty acid or group of fatty acids. Afssa work was undertaken by a large group of experts (almost 12), all specialized in the field of fatty acids, in order to integrate the best state of current knowledge. Our first general remark concerns the approach of this draft document: it directly focuses on pathologies on a case by case basis, but does not deal with nutritional requirements. Indeed, the nutritional requirements are not taken into account, which is not in line with the definition of dietary references (RDAs, DRVs, ANCs…). Hence, the draft document seems to include more pharmacological data than nutritional one. For example, the Nutritional Recommendations for the French population are defined as the intake allowing the nutritional requirements of almost every individual of the population (97.5%) to be covered. For the specific case of fatty acids, our framework considers 3 steps: - Identification of nutritional/physiological requirements - Identification of data allowing the modulation of these requirements according to physiopathological data (prevention objective) - Integration and synthesis of available physiological and physiopathological data to define the ANC Furthermore, we note that dietary recommendations were only established on the basis of human studies, and consequently, a large part of the available literature has not taken into account. Assuming that a lot of nutrition data have been obtained and are continuously being obtained in animal models, all types of studies (in vitro, animal models, clinical and epidemiological studies) have to be considered. If one only uses human studies, dietary references can only be established for few nutrients. In addition, some chapters are short, despite the accessibility of many studies on the subject (example cancers). So an extensive review of the literature is essential. The NDA panel includes only “diet related diseases” (Heart disease, Cancer, Obesity, Diabetes), though fatty acids are also implicated in other physiologic functions (cerebral function, ageing) and in other pathologies (for example: Age-Related Macular Degeneration). The fact that a nutrient is synthesized by the body cannot be interpreted as an absence of nutritional requirements and so does

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		not mean that it is not required in the diet. Hence the term "Nutrient is synthesized by the body" cannot be used to justify the absence of proposition of DVRs for cis-MUFA, SFA, cholesterol. In the same line, the absence of data, even for a nutrient for which the intakes have to be reduced (SFA) cannot lead to consider that no defined recommendations are needed. So, the general recommendation "should be as low as possible" is not appropriate. Although, some fatty acids are synthesized by the body, all of them have nutritional utility.
AFSSA	3. Dietary sources and intake data	2. Specific remarks Section 3.1 gives an interesting panorama of dietary sources and consumption data in European countries. However, these data have not to be considered as a basis for the definition of DRVs. They only give an idea of the current nutritional context.
AFSSA	6.1. Total fat	L 1839: "At the lowest observed intake of total fat (20%E) in european countries no over signs of deficiencies have been observed neither adverse effects on serum lipids". The status (nutritional requirements) in essential fatty acids is not any more covered with a total fat intake of 20 %. L 1841: « The panel proposes to set for adults a lower bound of the recommended intake range of 20E% and an upper bound of 35 E%." Regarding the recommendation of total fat, it rests on a non exhaustive review of literature. A total fat intake <30% probably leads to an increase of carbohydrates intakes (positive energy balance), which can be deleterious (impact of carbohydrates on metabolic syndrome). For a healthy population, a minimum of total fat intake of 30 % allows ensuring a minimum of essential PUFA. In addition, according to pathological data, there is no health benefit to reduce this intake below 30 %. Afssa has recommended fat intakes between 35 and 40 % of total energy intake for adults (male and female), considering an energy intake of 2000 kilocalories and an equilibrated energy balance.
AFSSA	6.2. Saturated fatty acids (SAT)	Another remark concerns SFA and MUFA which are always considered without differentiation into each group of fatty acids (example: a mixture of SFA). L 1867: "The panel recommends that SFA intake should be as low as possible within the context of a nutritionally adequate diet". Current available data allow making distinction among SFAs. So, we would like to point out that, according to recent studies, SFAs should not be considered any more as a homogeneous group. SFAs differ according to their structure, metabolism, cellular function and deleterious effects when their intakes are excessive. Their impact on lipids metabolism and probably on health are different, namely the atherogenic effect of lauric, myristic and palmitic acids at high intakes and the absence of deleterious effects of short and middle chain fatty acids and stearic acid. We also note that plasma cholesterol as cardiovascular risk marker is insufficient to incriminate SFA as a whole. Indeed, caproïc, caprylic, capric acids do not have a cholesterolemic effect when compared to lauric, myristic, and palmitic acids.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Moreover, if the SFAs recommendation is "as low as possible» and knowing that the third of phospholipids comes from SFAs we can wonder how the structure of membranes could be assured. Afssa working group proposes recommendations on SFA "atherogenic effect at high intakes", i.e lauric acid, myristic acid and palmitic acid (= 8 %E) and an upper limit for total TFA (= 12 %E). We note that the effect of total fat on insulin-sensitivity is a matter of debate. However, only 2 studies are quoted in the draft document, the methodology of one of which might be discussed (small sample; experimental conditions not realistic).
AFSSA	6.3. Cis-monounsaturated fatty acids (Cis-MUFA)	L1876: "The panel therefore proposes not to set any DRV for cis-MUFA" Afssa considers that MUFA should not be considered any more as a heterogeneous group. Available data on cardiovascular risks allow setting a recommendation for oleic acid of 15-20 %, the value of 20 % be considered as an upper limit.
AFSSA	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	L 1896: "The panel proposes to set an AI for linoleic acid of 4%E" We agree with the recommendation for linoleic acid but we note that it doesn't refer to an upper intake level. There is some inconsistency between the summary and the conclusion on CV risk as the effect of linoleic acid is not even mentioned. The pooled study by Jakobsen et al (2009) could have been quoted. L 1910: "The panel proposes to set an AI for alpha-linolenic acid of 0,5%E" We propose to set an ANC for alpha-linolenic acid of 1%E. This value has been defined according to : (1) observational epidemiologic studies in cardiovascular field (2) the necessity to cover PUFA requirements in terms of cardiovascular prevention, (3) the aim to maintain a LA/ALA ratio<5. Moreover, we note that no intervention study is taken into account for the definition of the value for alpha-linolenic acid. L 1925: "The panel proposes to set an AI of 250 mg for EPA plus DHA based on considerations of cardiovascular health" Afssa proposes an ANC of 500mg for EPA+DHA considering specifically cardiovascular prevention. This recommendation is in line with literature and other international recommendation (ISSFAL).

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
AFSSA	6.5. Trans fatty acids (TFA)	L 1943: "The available evidence indicates that TFA from ruminant sources have similar adverse effects on blood lipids and lipoproteins to those from industrial sources » This sentence should be put into perspective of some recent clinical and epidemiological studies. (Afssa, 2009; Chardigny JM. et al.,2008; Jakobsen MU. et al., 2008; Motard-Bélanger A. et al., 2008) We can observe that conjugated linoleic acid is not treated in this part thought they are also TFA. We will send you the full review of our opinion on the update of ANCs on fatty acids as soon as it will be completed and signed by the Afssa Executive Director. We are also available for further discussions with the NDA panel members, including further interview of the chair of the Afssa Working Group. References : Afssa (2009) Opinion of the French Agency for Food Safety regarding the estimation of trans fatty acids intake in the French population Chardigny JM, Destaillats F, Malpuech-Brugère C, Moulin J, Bauman DE, Lock AL, Barbano DM, Mensink RP, Bezelgues JB, Chaumont P, Combe N, Cristiani I, Joffre F, German JB, Dionisi F, Boirie Y, Sébédio JL (2008) Do trans fatty acids from industrially produced sources and from natural sources have the same effect on cardiovascular disease risk factors in healthy subjects? Results of the trans Fatty Acids Collaboration (TRANSFACT) study. Am J Clin Nutr 87: 558-66. Jakobsen MU, Overvad K, Dyerberg J and Heitmann BL (2008) Intake of ruminant trans fatty acids and risk of coronary heart disease. Int J Epidemiol 37: 173-82 Motard-Bélanger A, Charest A, Grenier G, Paquin P, Chouinard Y, Lemieux S, Couture P, Lamarche B (2008) Study of the effect of trans fatty acids from ruminants on blood lipids and other risk factors for cardiovascular disease. Am J Clin Nutr 87: 593-9.
Anthill	Conclusions and recommendations	The last 4-5 years people have started to eat quite opposite to todays reccomendations regarding carbohydrates, saturated fats and n6-fats. The results is amazing. People who have suffered from chronical diseases, ordinary dieseses, overweight and an overall bad health are now getting much better. I have for the last 3,5 years daily read stunning experiences form former sick people who now are healthier than they"ve been in a long time. The major changes in their diets have been these. 1. Carbohydrate restriction, wich lower blood glucose and insulin levels wich also lower inflammation. 2. More saturated fatty acids as a replacement for the carbohydrate energy. 3. Less omega-6 fatty acid from margarins an vegetable oils, to stop the inflammation process and to get a better balance between n3 and n6. This way to eat has been adapted also by a lot of proffessionals and now they"ve also noticed the benefits of it. Every well done study in the past have the same conclusion also. Better blood glucose, blood pressure and blood lipids profile for diets with less carbohydrates and more fats.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		In order to get as healthy as a man can be, you have to eat the way a man are supposed to eat.
Arbeitskreis Omega-3 e. V.	Conclusions and recommendations	Line number 2026-2035 Kommentar des Arbeitskreis Omega-3 e. V. Nach Meinung des Arbeitskreis Omega-3 e. V. – einer Initiative von Wissenschaft und Wirtschaft – ist der vorgeschlagene AI von 250 mg EPA/DHA für Erwachsene zu niedrig angesetzt. Nach Ansicht des Wissenschaftlichen Beirats des Arbeitskreis Omega-3 e. V. rechtferti-gen die Ergebnisse wissenschaftlicher Forschung eine höhere Zufuhr-empfehlung von mehr als 300 mg EPA/DHA pro Tag [1] sowie eine zusätzliche tägliche Zufuhr von 200 mg DHA während Schwanger-schaft und Stillzeit [2]. Zahlreiche Fachorganisationen wie die ISSFAL, SACN und AHA [3-5] haben daher ihre Empfehlungen eben¬falls höher angesetzt (450-500 mg EPA/DHA pro Tag). Dies ist hin¬sichtlich der von der FDA als GRAS angesehenen Zufuhrmenge von bis zu 3 g EPA/DHA pro Tag gut zu rechtfertigen [6]. Der Arbeitskreis Omega-3 e. V. empfiehlt daher dringend, als AI für Erwachsene und junge Menschen im Alter von 2 bis 18 Jahren eine Menge von mehr als 300 mg EPA/DHA pro Tag festzulegen und für Schwangere und Stillende eine zusätzliche tägliche Zufuhrmenge von 200 mg DHA. Literatur: [1] Harris WS, Mozaffarian D, Lefevre M, Toner ChD, Colombo J, Cunnane St C, Holden JM, Klurfeld DM, Morris MC, Whelan J (2009): Towards establishing dietary reference intakes for eicosapentaenoic and docosahexaenoic acids. J Nutr 139: 804S-819S [2] Koletzko B, Lien E, Agostoni C, Böhles H, Campoy C, Cetin I, Decsi T, Dudenhausen JW, Dupont C, Forsyth S, Hoesli I, Holzgreve W, Lapillonne A, Putet G, Secher NJ, Symonds M, Szajewska H, Willats P, Uauy R; World Association of Perinatal Medicins Dietary Guidelines Working Group (2008): The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations. J Perinat Med 36: 548-549 [3] ISSFAL (2004): Recommendations for intake of polyunsaturated fatty acids in healthy adults. URL: http://www.issfal.org.uk/Welcome/PolicyStatement3.asp (cited 24.08.09) [4] UK Scientific Advisory Committee on Nutrition (2004): URL: http://www.sacn.gov.uk/pdfs/fics_sacn_advice_fish.pdf (cited 07.07.09) [5] American Heart Association (2006): Diet and lifestyle recommendations Revision 2006. A statement from the American Heart Association Nutrition Committee. Circulation 114: 82-96 [6] Department of Health and Human Services, US Food and Drug Administration (1997): Substances Affirmed as Generally Recognized as Safe: Menhaden Oil. Fed Regist. 62: 30751-7 05. Oktober 2009

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Arbeitskreis Omega-3 e. V. – Der wissenschaftliche Beirat – Dr. Ing. David Bahri Prof. Dr. Michael Hamm Prof. Dr. Heinrich Kasper Prof. Dr. Hans-Ulrich Klör Dipl. oec. troph. Dirk Neuberger Prof. Dr. Volker Richter Priv. Doz. Dr. Peter Singer Prof. Dr. Ursel Wahrburg
Association de la transformation laitière française	1. Introduction	Additional references on our comments made on the summary (part 3 of 3) Stender S, Astrup A, Dyerberg J (2008) Ruminant and industrially produced trans fatty acids: health aspects. Food Nutr Res. 2008;52. doi: 10.3402/fnr.v52i0.1651.
Association de la transformation laitière française	1. Introduction	Additional references on the comments made about the summary (part 2 of 3) Jakobsen MU, Overvad K, Dyerberg J, Heitmann BL (2007) Intake of ruminant trans fatty acids and risk of coronary heart disease. Int J Epidemiol Feb;37(1):173-82. Kelly FD, Sinclair AJ, Mann NJ, Turner AH, Abedin L, Li D (2001) A stearic acid-rich diet improves thrombogenic and atherogenic risk factor profiles in healthy males. Eur J Clin Nutr Feb;55(2):88-96. Kennedy ET, Shanthy AB, Powell R (1999) Dietary-fat intake in the US population. J Am Coll Nutr 18(3):207–212 Krauss RM (2001) Dietary and genetic effects on LDL heterogeneity. World Rev Nutr Diet 89:12-22 Lecerf JM (2009) Fatty acis and cardiovascular disease. Nutrition Reviews 67:273-283. Lewis C, Park Y, Dexter P, Yetley E (1992) Nutrient intakes and body weights of persons consuming high and moderate levels of added sugars. J Am Diet Assoc 92(6):708–713 Melanson EL, Astrup A, Donahoo WT (2009) The relationship between dietary fat and fatty acid intake and body weight, diabetes, and the metabolic syndrome. Ann Nutr Metab 55(1-3):229-43. Mensink RP, Zock PL, Kester A, Katan MB (2003) Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol ratio and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. Am. J. Clin. Nutr. 77, 1146-1155. Mente A, de Koning L, Shannon HS, Anand SS (2009) A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. Arch Intern Med 169:659-669. Mozaffarian D (2005) Effects of dietary fats versus carbohydrates on coronary heart disease: a review of the evidence. Current Atherosclerosis Report 7 (6): 435-445 Mozaffarian D, Aro A, Willett WC (2009) Health effects of trans-fatty acids: experimental and observational evidence. Eur J Clin Nutr May;63 Suppl 2:S5-21

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Mozaffarian D, Rimm EB, Herrington DM (2004) Dietary fats, carbohydrate, and progression of coronary atherosclerosis in postmenopausal women. Am J Clin Nutr 80:1175–1184. Nakamura Y, Okamura T, Tamaki S, Kadowaki T, Hayakawa T, Kita Y, Okayama A, Ueshima H (2004) NIPPON DATA80 Research Group. Egg consumption, serum cholesterol, and cause-specific and all-cause mortality: the National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged, 1980 (NIPPON DATA80). Am J Clin Nutr Jul;80(1):58-63. Nicklas TA, Webber LS, Koschak ML, Berenson GS (1992) Nutrient adequacy of low fat intakes for children: the Bogalusa Heart Study. Pediatrics 89(2):221–228 Peitzsch RM, McLaughlin S (1993) Binding of acylated peptides and fatty acids to phospholipid vesicles: pertinence to myristoylated proteins. Biochemistry Oct 5;32(39):10436-43. Ravnskov U (1998) The questionable role of saturated and polyunsaturated fatty acids in cardiovascular disease. J Clin Epidemiol Jun;51(6):461-4; discussion 465 Rioux V, Galat A, Jan G, Vinci F, D"Andrea S, Legrand P (2002) Exogenous myristic acid acylates proteins in cultured rat hepatocytes.J Nutr Biochem Feb;13(2):66-74. Rioux V, Legrand P (2007) Saturated fatty acids: simple molecular structures with complex cellular functions. Curr Opin Clin Nutr Metab Care 10(6):752-8 Salter AM, Mangiapane EH, Bennett AJ, Bruce JS, Billett MA, Anderton KL, Marenah CB, Lawson N, White DA (1998) The effect of different dietary fatty acids on lipoprotein metabolism: concentration-dependent effects of diets enriched in oleic, myristic, palmitic and stearic acids. Br J Nutr. 1998 Feb;79(2):195-202 Sengupta S, Muir JG, Gibson PR (2006) Does butyrate protect from colorectal cancer ? J Gastroenterol Hepatol Jan;21(1 Pt 2):209-18.
Association de la transformation laitière française	1. Introduction	Additional references on the comments made about the summary (part 1 of 2) AFSSA (Agence Française de Sécurité Sanitaire des Aliments) (2001) Apports nutritionnels conseillés pour la population Française. Paris, Lavoisier Tec et Doc AFSSA (Agence Française de Sécurité Sanitaire des Aliments) (2009) Avis de l'Agence française de sécurité sanitaire des aliments sur l'estimation des apports en acides gras trans de la population française (Request 2007-SA-220) Ailhaud G, Guesnet P, Cunnane SC (2008) An emerging risk factor for obesity: does disequilibrium of polyunsaturated fatty acid metabolism contribute to excessive adipose tissue development? Br J Nutr Sep;100(3):461-70. Ailhaud G, Massiera F, Weill P, Legrand P, Alessandri JM, Guesnet P (2006) Temporal changes in dietary fats: role of n-6 polyunsaturated fatty acids in excessive adipose tissue development and relationship to obesity. Prog Lipid Res. May;45(3):203-36. Billett MA, Bruce JS, White DA, Bennett AJ, Salter AM (2000) Interactive effects of dietary cholesterol and different saturated fatty acids on lipoprotein metabolism in the hamster. Br J Nutr Oct;84(4):439-47. Borgese N, Aggujaro D, Carrera P, Pietrini G, Bassetti M (1996) A role for N-myristoylation in protein targeting: NADH-cytochrome b5 reductase requires myristic acid for association with outer mitochondrial but not ER

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		membranes. J Cell Biol Dec;135(6 Pt 1):1501-13 Casey PJ (1995) Protein lipidation in cell signaling. Science Apr 14;268(5208):221-5. Dabadie H, Peuchant E, Bernard M, LeRuyet P, Mendy F (2005) Moderate intake of myristic acid in sn-2 position has beneficial lipidic effects and enhances DHA of cholesteryl esters in an interventional study. J Nutr Biochem. 2005 Jun;16(6):375-82 Donnelly JE, Sullivan DK, Smith BK, Jacobsen DJ, Washburn RA, Johnson SL, Hill JO, Mayo MS, Spaeth KR, Gibson C (2008) Alteration of dietary fat intake to prevent weight gain: Jayhawk Observed Eating Trial. Obesity 16(1):107-12. Elmadfa I, Kornsteiner M (2009) Dietary fat intake - a global perspective. Ann Nutr Metab 54(suppl): 8-14 German JB and Dillard CJ (2004) Saturated fats:What dietary intake? Am J Clin Nutr 80:550-559 Gibney M, Sigman-Grant M, Stanton JL, Keast DR (1995) Consumption of sugars. Am J Clin Nutr 62(1 suppl):178S–194S Gibson SA (1997) Non-milk extrinsic sugars in the diets of pre-school children: association with intakes of micronutrients, energy, fat and NSP. Br J Nutr 78(3):367–378 Griel AE, Kris-Etherton PM (2006) Beyond saturated fat: the importance of the dietary fatty acid profile on cardiovascular disease. Nutr Rev May;64(5 Pt 1):257-62. Hackett A (1993) National and community food policies for dental health in the UK. In: Rugg-Gunn AJ, ed. Nutrition and Dental Health. Oxford, United Kingdom: Oxford University Press; 1993:410–451 Hashim SA, Arteaga A, Van Itallie TB (1960) Effect of a saturated medium-chain triglyceride on serum-lipids in man. Lancet. 1960 May 21;1(7134):1105-8. Harvey-Berino J (1999) Calorie restriction is more effective for obesity treatment than dietary fat restriction. Ann Behav Med Spring;21(1):35-9 Howard BV, Van Horn L, Hsia J, Manson JE, Stefanick ML (2006) Low-fat dietary pattern and risk of cardiovascular disease: theWomen"s Health Initiative Randomized Controlled Dietary Modification Trial. JAMA Feb 8;295(6):655-66. Hu FB, Stampfer MJ, Rimm EB, Manson JE, Ascherio A, Colditz GA, Rosner BA, Spiegelman D, Speizer FE, Sacks FM, Hennekens CH, Willett WC (1999) A prospective study of egg consumption and risk of cardiovascular disease in men and women. JAMA Apr 21;281(15):1387-94.
Association de la transformation laitière française	1. Introduction	Comments on background and summary : The criteria to make conclusions should be consistent throughout the document. The summary should be consistent for all fats and in accordance with the information in the document. Lines 42+81+84+95+104 It is not clear how the evidence is graded. In the summary and also further on in the document words such as the following are used: “there is evidence“ (line 42), “negative (beneficial) relationship“ (line 81), “also evidence“ (line 84), “no consistent evidence“ (line 95) and “no convincing evidence” (line 104).

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Line 44 In the context of obesity, calorie restriction is more effective for obesity treatment than dietary fat restriction. Indeed, dietary fat restriction did not prove to be superior to calorie restriction, thus strengthening the public health message that calories do count (Harvey-Berino, 1999; Donelly et al., 2008; Melanson et al., 2009) Line 48 The 20 E% does not seem representative of the European fat intake. Indeed, according to Annex 1b of this draft opinion mean intakes are almost all above 30 E%. The population with very low intake is obviously a specific population (elderly men in Portugal). This confirms that the 20 E% as the lower bound of the intake range is not adapted for the general population. Line 50 The value of 20 E% is not appropriate as it is not representative of the lowest intake in Europe. According to AFSSA (2001), the balance of fatty acid intake (especially PUFA) is more difficult to achieve below 30 E%. Besides, consumption of a low-fat diet (defined as containing 20% of energy from fat) was shown to induce atherogenic dyslipidemia (German and Dillard, 2004; Volek et al., 2009). There are other negative effects of too low fat intake. As mentioned in this report (lines 1068-1070) "Very low fat diets tend to increase the risk of an insufficient intake of PUFA, can impair the absorption of fat-soluble vitamins and be associated with insufficiency of other essential nutrients like zinc and B vitamins". Studies have also suggested that interventions to lower dietary fat content and different fat compositions lead to a compensatory increase in sucrose content. There has been a concern that dietary recommendations aimed at achieving a low saturated-fat diet might lead to inappropriately increased sugar intake (Gibney et al., 1995) and some studies suggest that an inverse relationship exists between the intake of fat and simple sugars (Gibson, 1997; Lewis et al., 1992; Hackett, 1993). Other studies show that children with an intake of <30% of energy from fat consumed more carbohydrates (mainly sucrose) than those children whose diets contained >40% of energy from fat (Nicklas et al., 1992; Kennedy et al., 1999). Recent advice to consume low-fat, high-carbohydrate diets to reduce serum LDL cholesterol levels can also result in reduced HDL levels and increased levels of triglycerides, small dense LDL and insulin, which have been shown to increase the risk of coronary heart disease (Krauss, 2001; Volek et al., 2008). Reducing total fat intake can lead to increased intake of carbohydrates. A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005) and can lead to a high synthesis of palmitic acid. Recent studies show that a lower fat-diet but rich in carbohydrates stimulated saturated fatty acids (SFA) synthesis - especially palmitate - at high rates (Wilke et al., 2009). Line 55 The recommendation for total fat intake between 3 years and adult is missing.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Association de la transformation laitière française	1. Introduction	Line 59 It should be clear what is meant by expressions like "a mixture of SFA" and also if this mixture is nutritionally relevant. A meta-analysis of 60 controlled trials on effects of dietary fatty acids and carbohydrates on the ration of serum total to HDL-cholesterol and on serum lipids by Mensink et al. (2003) showed no significant change when carbohydrates constituting 1% of energy were replaced iso-energetically with saturated fat. For individual SFA, the predicted ratio was significantly lower for lauric acid when replaced by carbohydrates constituting 1% of energy while no significant predicted changes were observed for palmitic, myristic or stearic acid, respectively. The researchers states that total:HDL cholesterol is a more sensitive and specific risk predictor than total cholesterol and concludes that isoenergetic replacement of SFAs with carbohydrates does not improve the serum total:HDL cholesterol. All natural fats contain both SFA, which do not change this ratio, and unsaturated fatty acids, which lower it. As a result, even the replacement of dairy fat and tropical fats with carbohydrates will increase the ration of total to HDL cholesterol. Jakobsen et al. (2009) showed that for a 5% lower energy intake from SFAs and a concomitant higher intake from carbohydrates, there was a significant direct association between carbohydrate and coronary events (hazard ratio: 1.07, 95% CI: 1.01-1.14). Lines 59-60 To reflect lines 1238-1240 of this scientific opinion, following information should be concluded in the summary: "There is a positive, dose-dependent relationship between the intake of a mixture of SFA and serum LDL and HDL cholesterol concentrations, when compared to carbohydrates. As a consequence, the total to HDL cholesterol ratio does not change." Line 66 It should be clear what the scientific evidence is for making the recommendation of a SFA intake "as low as possible". The 2009 Joint FAO/WHO Expert Consultation on "Fats and Fatty Acids in Human Nutrition" sets dietary recommendations for total fat at 20-35 E% (acceptable macronutrient distribution range) compared to the population nutrient intake goal of 15-30 E% mentioned in the 2003 WHO report (Elmadfa and Kornsteiner, 2009). For children from 2 to 18 years, the recommendation for the total dietary fat intake is 30-40 E% depending on activity (Uauy and Dangour, 2009). Lines 67 and 145 It should be clear what is meant by a "nutritionally adequate diet". A definition cannot be found in the text.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Association de la transformation laitière française	1. Introduction	Those comments are about the summary Line 67 This recommendation does not reflect the recent scientific evidences about SFA. The evidence of the role of SFA in CHD is not conclusive (Mente et al., 2009). Studies provide only inconclusive evidence of the effects of modification of total, saturated, monounsaturated, polyunsaturated on cardiovascular morbidity and mortality (Howard et al., 2006; Ravnskov 1998; Mente et al., 2009; German & Dillard, 2004; Volk, 2007). Moreover, some studies show that in some case a greater saturated fat intake is associated with less progression of coronary atherosclerosis, whereas carbohydrate intake is associated with a greater progression (Mozaffarian et al., 2004; Griel et al., 2006). Besides, the Women Health Initiative (WHI) study indicates that the decrease of fat intake (leading to an intake of 9.5% SFA) did not significantly reduce the risk of stroke, coronary heart disease, or cerebro-vascular disease in postmenopausal women (Howard et al., 2006). In addition, a recommendation of "as low as possible" would not be achievable in normal life with a normal diet and would result in strict and impossible guidelines to follow. Moreover, this recommendation "as low as possible" is not relevant due to recent scientific results showing the real effect of SFA on health - especially on cardiovascular health (Skeaff and Miller, 2009; He et al., 2007; Mozaffarian, 2005, Hooper et al., 2001 and 2002) (for details see comments lines 1627-1644). A low intake of SFA could lead to an excessive consumption of MUFA and PUFA, which could represent health hazards, especially with regard to intake of n-6 fatty acids (Lecerf, 2009; Ailhaud, 2006). SFA have different physiological functions depending on their chain length. Thus, SFA should not be evaluated as one single group (Sengupta 2006, Hashim, 1960; Tsuji, 2001; Yu et al., 1995; Kelly, 2001; Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Casey, 1995; Rioux, 2002; Peitzsch, 1993; Borgese, 1996; Dabadie, 2005). As a conclusion, a lot of scientific data shows that saturated fat has no negative effect but rather positive effects. It would therefore be unreasonable to consider all SFA as just one single group that would have negative impact on health. The different physiological functions of SFA should be taken into account in order to evaluate the nutritional reference values. Line 86 However, nutritional recommendation should not stress n-6 PUFA over consumption but promote instead a good balance between n-3 PUFA and n-6 PUFA intake. The relative intake of n-6 to n-3 PUFA is indeed clearly emerging as a new factor in the development of adipose tissue (Ailhaud et al., 2008) Line 97 There has been evidence on negative effects on health of excessive intakes of n-6 PUFA and lipid peroxidation (Elmadfa and Kornsteiner, 2009). It could also contribute to excessive adipose tissue development (Ailhaud, 2006; Lecerf, 2009). Therefore, an upper limit should be considered in order to protect consumer health. Line 128

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		The recommendation should take into account the ratio of n-3/n-6 PUFA as this would give a better idea of what should be considered as a balanced diet. Besides, the relative intake of n-6 to n-3 PUFA is clearly emerging as a new factor in the development of adipose tissue (Ailhaud et al., 2008). An optimal intake with a ratio of n-3/n-6 PUFA should also be fixed by EFSA, like it is the case in all the national and international recommendations. In order to determine this ratio, a conversion factor can be applied to LC PUFAs (LA to ARA, and ALA to EPA and DHA). For adults, this leads to an optimal n-6 PUFA: n-3 PUFA of 5:1.
Association de la transformation laitière française	1. Introduction	Those comments are on the summary Lines 129-141 If the limited data suggest that the effects of ruminant and industrial TFA on blood lipid profiles are similar when consumed in similar quantities, it is important to mention that very few people consume the high levels of ruminant TFA used in these studies and that observational studies do not support adverse CHD effects of ruminant TFA in amounts actually consumed (Mozaffarian et al., 2009). This is reinforced by the recent WHO scientific update on TFA (Uauy et al., 2009). Similarly, the recent AFSSA on TFA report states that TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at a low level (0,5 to 0,9% of the total energy intake) (AFSSA, 2009). The EFSA recommendation concerning the dietary reference value for TFA should therefore deal only with industrially derived TFA. TFA from natural origin should not be included. Line 145 Total TFA should be replaced by TFA from industrial origin. Line 146 It is irrelevant to compare industrial and natural trans fatty acids (TFA) when consumed in equivalent amounts. Stender et al. (2008) showed that the amount of TFA in industrial fat can be as high as 60% whereas the content of natural TFA in for instance milk fat is approximately 4%. In the WHO scientific update on trans fatty acids Uauy et al. (2009) summarises that evidence from observational studies in which estimated TFA consumption from industrial and ruminant sources of TFA has been distinguished and from studies in which specific TFAs have been measured utilizing biomarkers generally do not support an adverse effect of ruminant TFA, in the low amounts usually consumed, on risk of CHD. The intake of ruminant TFA is low in most populations and to date there is no conclusive evidence supporting an association with CHD risks in the amounts usually consumed. In contrast, TFA produced by partial hydrogenation of fats and oils should be considered industrial food additives having no demonstrable health benefits and clear risks to human health. A recent analysis from Denmark, a country with a relatively high intake of dairy products, showed no associations between absolute or energy-adjusted ruminant TFA intakes and CHD in an 18-year follow-up study of 3686 Danes, aged 30–71 years, without previous CHD at baseline (Jakobsen et al., 2007).

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Lines 156-158 Eggs are also a significant source of dietary cholesterol. They provide almost half of the dietary cholesterol in a western diet (Vorster et al., 1992). However, it is important to add that dietary cholesterol has very little influence on plasma cholesterol values which are regulated by numerous genetic and nutritional factors through cholesterol absorption or synthesis. Besides, there is no strong evidence that dietary cholesterol is related to CHD or stroke (Hu et al. 1999; Nakamura et al., 2004)
Association de la transformation laitière française	2. Categories, structure and function	Line 394 Protein myristoylation is only one way to regulate enzyme activity. Protein palmitoylation should be mentioned as well since it is one of the most frequent post-translational modifications found on proteins (Bijlmakers and March, 2003). Line 396 The role of the position of fatty acids on the triglyceride backbone should be addressed. Addition of following paragraphs: The first key step governing the bioavailability and metabolic impact of dietary lipids is their digestion. Therefore, fats with the same fatty acid composition might differ in their metabolic impact, due to difference in triglyceride composition. Gastric lipase acts preferentially on fatty acids esterified at the sn-3 position, while pancreatic lipase has a preference for the sn-1 and sn-3 positions. In the chylomicrons, 75% of all fatty acids located at the sn-2 in dietary triacyl-glycerols are maintained at this sn-2 position in the triacyl-glycerols of chylomicrons (Michalski, 2009; Armand, 2007). Especially for babies, C16:0 at the sn-2 position instead of sn-1 or sn-3 position is beneficial. It has been shown in a study with preterm infants (>35 weeks of gestation) that both palmitic acid and calcium absorption are improved and are comparable to infants who were breast-fed when an infant formula was used having 74% of the C16:0 at the sn2 position compared to an infant formula with the same amount of C16:0 but only 28% was positioned at sn2 (Lucas et al., 1997). Furthermore, for formula fed infants it has been shown that palmitic acid at sn-2 (instead of palmitic acid at sn-1 and sn-3) results in a significant increase in whole body bone mineral content and density, softer stool and less stool soap fatty acids (Kennedy et al., 1999b). Line 414 Saturated fats are essential for cell membranes. In our brain, the two dominant fatty acids are palmitic acid and steraric acid (both around 20-25%) (Carver et al., 2001). Classification of saturated fatty acids (SFA) only from a biochemical point of view is no longer relevant (Lecerf, 2009). SFA must be considered individually according to their chain length because they all have different effects. Short-chain and medium-chain SFA are metabolised differently than long-chain SFA. Metabolism of SFA should be included in this scientific opinion. Lines 423-424 The human body can synthesise substantial amounts of SFA. During a low fat / high carbohydrate diet up to 45% of the VLDL

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		triglycerides can be newly synthesized. The preferentially formed fatty acid by mammalian fatty acid synthase is palmitate (C16:0) (Cooper Hudgins et al., 1996). Recent studies show that a lower fat-diet but rich in carbohydrates stimulated saturated fatty acid synthesis (especially palmitate) at high rates (Wilke et al., 2009).
Association de la transformation laitière française	2. Categories, structure and function	Line 461 "The conversion of linoleic acid is very limited": what is limited? For children: Olegard and Svennerholm (1971) found no differences in plasma and erythrocyte phoshoglyceride AA of 3-month-old infants who either had been fed breast milk or were bottle fed with a milk formula with only traces of AA. This implies that LA is readily converted to AA in young infants. Line 475 Goyens et al. (2006) does not give conversion rates of 8-12%. It rather states that "After the low-LA diet, the percentage of dietary ALA incorporated into the ALA plasma phospholipid compartment was significantly increased by 4% compared with the control diet (P 0.012). In contrast, consumption of the high-ALA diet significantly decreased the incorporation by 8% and 12% compared with the control diet (P 0.001) and the low-LA diet (P 0.001), respectively." Lines 483-486 This paragraph should be extended and would fit better at line 441. Lines 487-492 Add this paragraph: Vaccenic acid (the predominant TFA from ruminants) is converted into rumenic acid (cis-9, trans-11 CLA). Endogenous synthesis from vaccenic acid (trans-11 18:1; VA), the major biohydrogenation intermediate produced in the rumen, is the predominant source of cis-9, trans-11 CLA in milk fat (Lock et al. 2004). Some animal studies show that vaccenic acid could have a beneficial effect on plasma triglycerides, LDL cholesterol and inflammation (Wang et al., 2008). Line 492 Add to the following sentence "TFA do not serve any vital functions" this: "in the present state of scientific data". If there are scientific publications attesting the absence of vital function of TFA, those references should be specified and added. Lines 494-495 Replace with following sentence: "CLA is a generic term for a group of..." The use of term "natural PUFA" is confusing here as it suggests that CLA is not from natural origin. Cis-9, trans-11 CLA (rumenic acid) is from natural origin as it comes from bioconversion of trans-vaccenic acid through the action of ¿9 desaturases (Lock et al. 2004). By contrast, trans-10, cis-12 CLA is mainly produced by industrial processing. Line 497 The different types of cholesterol transporters should be explained within this scientific draft opinion (HDL, VLDL…)

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		Line 502 Cholesterol is not "also" synthesised by the body but "mainly" synthesised by the body. Moreover, this endogenous production is regulated by the dietary intakes in healthy subjects. Line 503 Cholesterol also plays an important role in "lipid raft" mechanisms for protein sorting at various stages of the secretory and endocytic pathways (van Meer and Sprong, 2004). Cholesterol is involved in the synthesis of vitamin D, in cell membranes construction, and participates to the digestion process with the creation of specific acids (AFSSA, 2001). Line 508 Phytosterols should be covered in this scientific draft opinion as EFSA recently released a scientific opinion on this topic.
Association de la transformation laitière française	2. Categories, structure and function	Lines 414-424 As for PUFA, additional information about structure and functions of SFA should be added. SFA are components of reserve triglycerides, glycerophospholipids and sphingolipids (membrane structure, myeline…). SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions. They have to be classified regarding their chain length: - Structure and function of short and medium-chain fatty acids : Short and medium-chain SFA have a specific metabolism. As reported by Bach and Babayan (1982), triglycerides made of C6:0, C8:0, C10:0 and C12:0 (MCTs) have unique physical, chemical, and structural characteristics and their modifications (structured lipids) make special lipids tools for solving certain medical problems. They are indeed hydrolyzed both faster and more completely than long-chain triglycerides (LCTs). The products of this hydrolysis are absorbed as fast as glucose. MCTs are oxidized rapidly in the organism and they have a very low tendency to deposit as body fat. As reported by Sengupta et al. (2006), short-chain butyric acid is likely to have a protective function against colon cancer (inhibition of tumour proliferation, apoptosis induction). Short and medium-chain SFA have a hypocholesterolemic effect at physiological dose. This effect of diets high in C8:0 and C10:0 was shown in humans by Hashim (1960). Mediumchain SFA have also a beneficial role in adiposis. The human study of Tsuji et al. (2001) suggests weight loss with a diet high in medium-chain fatty acids. C6:0, C8:0 and C10:0 have a role in weight reduction, reduced fat deposition, decrease of VLDL production, hypocholesterolemic effect and antiviral role (Rioux et al., 2007; Legrand, 2008; Neyts et al., 2000). - Structure and function of long-chain fatty acids : Long-chain SFA are converted, in part, by ¿9-desaturation in monounsaturated fatty acids, but with significantly different effectiveness, increasing with the length of the chain. Stearic acid is the best substrate of ¿9-desaturase; and its conversion to oleic acid is important (Legrand, 2002; Legrand, 200;, Kritchevsky, 1988). The long-chain stearic acid has no negative effects on cholesterol level (Yu et al.; 1995) and, as presented by Kelly (2001), it has a beneficial effect on thrombogenic and atherogenic risk factors in males.

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		Myristic acid has a positive action through an increase of HDL-cholesterol when consume at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000). Some SFA regulate specifically the activity of proteins by acylation (myristoylation, palmitoylation). Some studies show that, for example, myristic acid plays a key role through its ability to acylate proteins, a reaction which is called N-terminal myristoylation. Various examples of important cellular regulations where the intervention of myristic acid is proven have been described (Casey, 1995; Rioux, 2002; Peitzsch, 1993; Borgese, 1996). Myristic acid also has a function in the biosynthesis of EPA and DHA (Dabadie et al., 2005; Rioux et al., 2005) and of sphyngolipids (Beauchamp et al., 2007). C20:0, C22:0, C24:0 have a role in nervous structure (myelinisation) (Bourre et al., 1976a and b). Line 430 No information is given to what extent humans can synthesise MUFA. Line 441 The role of n-3/n-6 PUFA ratio should be addressed. Because n-3 and n-6 PUFA are metabolised to LCPUFA by the same enzyme system, excess dietary LA (n-6) may decrease the formation of DHA (LCPUFA n-3) from LNA. In addition, AA (LCPUFA n-6) formation is lower when excess (n-3) LNA is provided (Uauy and Castillo, 2003). Both n-3 and n-6 LCPUFA are needed. However, inWestern diets with ample n-6 PUFA, the balance between tissue n-3 and n-6 LCPUFA might be sub-optimal (Lands, 2008).
Association de la transformation laitière française	3. Dietary sources and intake data	Line 572 The 18:1 TFA profiles of ruminant fat and hydrogenated vegetable oils show considerable overlap for many isomers. However, in contrast to ruminant fat non-palm-based-vegetable cooking oil can contain considerable amounts (0.4-2.7%) of C18:2 trans-cis, cis-trans and trans-trans, and C18:3 trans (up to 2.7%) (Tang, 2002). Partially hydrogenated vegetable oils can contain 1–65% of TFA, of which isomers of elaidic acid (trans-9 and trans-10 18:1) are the two most common isomers. On the other hand, dairy products contain smaller amounts of TFA (1–8% of total fatty acids in milk fat), and the main isomer is vaccenic acid (trans-11 18:1). Humans can utilize vaccenic acid, in the endogenous synthesis of rumenic acid (cis-9, trans-11 18:2), a fatty acid that may not have a negative effect on biomarkers of CVD risk. These two sources of TFA differ in their TFA isomer distribution and contribution to dietary intake, and, as a consequence, they also may have different biological effects (Chardigny et al., 2008) Lines 574 and 579 The actual content of TFA in wt% of total fatty acids in animal fat and industrial fat should be included in the table 4. The concentration of industrial hydrogenated TFA may be as high as 60%, whereas the maximum content of natural TFA in ruminant fat is about 6% (Stender et al., 2008). This information should also be included in the text in connection of the table 4. Line 583 In humans the conversion rate of trans-vaccenic acid to rumenic acid is around 19% (Turpeinen et al., 2002) to 20% (Lock et

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		al., 2005). Line 593 In France, more recent data than Volatier (2000) and Deschamp (2005) is available. The INCA 2 study, for example, is more recent and could be used for this paragraph and the annexes (AFSSA, 2009b). Line 605 The presented data are not representative of the whole population but rather for a specific target group of the population (elderly in Portugal for example). Besides, some methods (like FFQ) are not accurate. Line 618 Data for the lowest intake in Portugal are not representative as it concerns the elderly population which is not an average but an extreme level. Besides, data are not very accurate as it is FFQ method. Line 627 In France, according to the INCA 2 study, the SFA intake is more around 15% than 17% (AFSSA, 2009b). Line 669 For those countries where separate intake data for industrial TFA and natural TFA are available, those should be provided (Craig-Schmidt, 2006; Jakobsen, 2007). Lines 676-678 The available data shows that total TFA intake has decreased close to WHO recommendation of 1 E%. This is due to reformulation of food products containing TFA originating from partially hydrogenated vegetable fats and oils. In the same report, WHO also mentions that most TFA are contributed by industrially hardened oils and that to promote cardiovascular health, diets should provide a very low intake of TFA from hydrogenated oils and fats (Uauy et al., 2009). Lines 681-682 Leave out “including … from other sources”. Replace by (after line 684): In most European countries with a high TFA intake (>2.5 g/d), the major part of the TFA was from industrial sources (Craig-Schmidt, 2006). Line 690 “In adults, average intakes range from nearly 200 mg/day to 655 mg/day”. This is not an average intake (replace “average” by “extreme range”): 655 mg/day concerns only one study for adult men.

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Association de la transformation laitière française	3. Dietary sources and intake data	Lines 509-519 Why are a US database used and a European database reference not required? Dietary databases indeed exist in Europe, for example, CIQUAL 2008 in France. European intake data should be given, where possible. No distinction is made between short-chain, medium-chain and long-chain SFA (see table in comments to line 530). Lines 513 The purpose of including table 2 is not clear. The selection of fats does not cover the major food groups in the diet. Other animal fats, such as tallow, fish fat and vegetable oils and margarine as well as shortenings for industrial processing should be included in table 2. Isomers of trans 18:1 should also be included in the table. Lines 514 In table 2 the ratio n-6/n-3 PUFA should be added as this is relevant information for the fatty acid balance of fats and oils. Lines 520-529 The Dutch NEVO table for fatty fish provides following data: total fat (g) 23.8, SFA 5.6, MUFA 10.5 PUFA 5.1 (high SFA fish (g total fat/g SFA) = Mackerel (30.7, 7.4); Eel (35, 8.7); Herring (14, 3.3); Salmon (14.2, 3.7)). These numbers differ quite a lot from the fatty fish data given in table 3. The basis for the selection of animal-derived food products is not entirely clear as, for example, eggs are missing. Besides, it is inconsistent to choose on one side only lean meat but on the other side present only standard butter and full fat milk. Semi-skimmed milk should be used instead as it is the most consumed type of milk in Europe. In France, for example, 73% of the milk consumed is semi-skimmed milk (data from CNIEL, Centre National Interprofessionnel de l"Economie Laitière, 2007). Line 523 Several dietary databases exist in Europe, for example, CIQUAL 2008 in France. Why was US data used? Line 530 The main characteristic of milk fat is the variety of fatty acids it contains: more than 400 different fatty acids. Milk fat contains typically around 65-70% SFA and 30-35% unsaturated fatty acids. Amongst saturated fatty acids in milk fat, there are typically around 10-13% short- and medium-chain SFA and typically around 50-55% long-chain SFA, including palmitic (min. 20 – max. 32%), myristic (min. 8 – max. 15%) and stearic acid (min. 6 – max. 13%). Milk fat is also relatively rich in the short-chain SFA C4:0 (butyric acid, min. 7 – max. 14%). Line 532 The lauric acid content in milk fat is more than 10-fold lower than that of coconut oil and palm kernel oil. Therefore, milk fat can - compared to these fats - not be called lauric acid rich (see table 2).

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		Lines 538-539 For example, dairy fat contains a substantial amount of oleic acid (Legrand, 2008). In the French population, dairy products are also the first contributor of MUFA according to the INCA 2 study (AFSSA, 2009b) Line 551 Appreciable amounts of ALA can also be found in animal and dairy fat. In France, for example, dairy products are the first contributor to ALA intake according the SUVIMAX adult consumption survey (SUVIMAX is a French survey done between 1994 and 2002 on 13 000 people) (Astorg et al., 2004) Line 568 There should not be a focus only on C18:1. Ruminant trans fats may contain up to 20% C16:1 (Stender et al., 2008) which shows that profiles of ruminant TFA and industrially produced TFA differ quite substantially (Mendis et al., 2008; Shingfield et al., 2008; IDF Bulletin 377, 2002). Lines 569-570 The TFA content of margarine and fat spreads may vary, depending on the proportion of partially hydrogenated oils used. However, recent analyses have shown that products with high levels of industrially produced TFA are still available on the market (Stender et al., 2008). The range of TFA content in wt% of total fatty acids of those products should be added.

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Association de la transformation laitière française	4. Overview of dietary reference values and recommendations	Line 693 It is not clear on which criteria the chosen dietary guidelines were selected. Line 705 It is important to mention that some national recommendations in Europe such as in France take into account the different effects of TFA according to their sources (natural or industrial) (AFSSA, 2009a). Lines 749-756 The 2009 Joint FAO/WHO Expert Consultation on "Fats and Fatty Acids in Human Nutrition" sets dietary recommendations for total fat at 20-35 E% (acceptable macronutrient distribution range) compared to the population nutrient intake goal of 15-30 E% mentioned in the 2003 WHO report (Elmadfa and Kornsteiner, 2009). For children from 2 to 18 years, the recommendation for the total dietary fat intake is 30-40 E% depending on activity (Uauy and Dangour, 2009). Lines 771-775 Different SFA should be considered independently as there is evidence to indicate that certain SFA might have a beneficial role. Recent data show that the different SFA in milk fat have different effects on health. Several studies show that short-chain and medium-chain SFA do not have a negative impact on the blood lipid profile. They are easily digested and metabolised differently in the body compared to longer chain fatty acids. Certain long-chain SFA such as stearic acid act neutral on the cholesterol level. Myristic acid has various physiological roles in the body such as protein metabolism and the synthesis of n-3 long-chain fatty acids (Lecerf 2009, Legrand 2008, Rioux and Legrand 2007). Lines 776-779 Only the newest guideline available should be used. The Health Council of the Netherlands has published updated dietary reference intakes for fats and fatty acids for the Netherlands in 2006. It is stated there that "The average intake of saturated fatty acids in the diet needs to be cut from 13 to 14 per cent of energy intake to less than 10 per cent." Therefore, the dietary reference value for SFA for adults is < 10 E%. A mentioning of "as low as possible" cannot be found in the summary of the Dutch guidelines. Line 780 The 2009 Joint FAO/WHO Expert Consultation on "Fats and Fatty Acids in Human Nutrition" confirms that the intake of SFA should not exceed a maximum level of 10 E% (Elmadfa and Kornsteiner, 2009). Lines 918-921 Within the Nordic Nutrition Recommendations (2004), a maximum intake of 10 E% of SFA plus TFA is given. It is also mentioned that the intake of TFA from hydrogenated oils should be as "low as possible" (table 1).

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Association de la transformation laitière française	4. Overview of dietary reference values and recommendations	Lines 930-933 In 2005, AFSSA has done a review of studies on the metabolism and toxicity of TFA and their impact on health. They concluded that consumption of total TFA above 2% of total energy intake resulted in a significantly increased risk of CVD. At that time, they did not really distinguish the origin – natural or industrial - of TFA. New data concerning TFA content of food, population intakes as well as new scientific results from epidemiological and clinical studies have conducted AFSSA to reassess its previous conclusions (AFSSA, 2009a). AFSSA considers that: - The estimated average intake of TFA in the French population (around 1%) is lower than the threshold of 2% of the total energy intake. This is true for adults as well as for children independently of age and sex. The intake is lower than in 2005. - It is necessary to pursue the improvement of the food composition tables with regard to TFA. The contribution of different types of food to TFA intake should be considered in more detail, in particular the cheapest priced products, discount products, catering and small-scale ("artisanal") products etc. which are insufficiently known at this moment. - Considering the total TFA intake, the origin of the TFA, natural or industrial, should be taken into account. Concerning TFA of natural origin; consumption levels in the French population (0.5-0.9% of the total energy intake) are lower than levels identified as not posing a risk of CVD (1.5% of the total energy intake); TFA from industrial origin that are present in foods only have a technological function. Thus, AFSSA encourages the efforts to reduce the use of industrial TFA in human food, in order to reduce the risk of exposure. As a conclusion, the recommendation is to decrease TFA intake only concerns industrial TFA. Lines 934-937 Only the newest guideline available should be used. The Health Council of the Netherlands has published updated dietary reference intakes for fats and fatty acids for the Netherlands in 2006. It is stated there that “mono trans fatty acid intake needs to be brought down from 1 to 2 per cent to less than 1 per cent.” Table 6 (line 2915) has to be updated accordingly with the dietary reference value of TFA for adults < 1 E% (instead of “as low as possible”). There only the values for EPA and DHA refer to the 2006 Dutch guidelines. Line 938 The 2009 Joint FAO/WHO Expert Consultation on “Fats and Fatty Acids in Human Nutrition” confirms that the UL for TFA from ruminants and industrially produced sources should be <1% E. This recommendation is done with the focus on industrial trans fat being reduced to 0.5 E%. Ruminant trans fat intake was not recommended to be lowered because the average intake is at approximately 0.5 E% (Elmadfa and Kornsteiner, 2009). Line 939 The Nutritional Recommendations for the French Population (AFSSA, 2001) indicate that the limitation of exogenous cholesterol does not seem to be justified for the general population, as dietary cholesterol has only very limited impact on blood cholesterol. Line 944

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		The Nutritional Recommendations for the French Population (AFSSA, 2001) indicate that for older children and adolescents it does not seem reasonable to recommend fat intake below 30 E%. Line 969 The French recommendations for SFA intake for children are 8 to 12 E% (AFSSA, 2001). Line 1032 The French recommendations for cholesterol intake for children after 3 years of age are 300 mg/day (AFSSA, 2001). Line 1035 The recent AFSSA report should be taken into account for the overview of dietary recommendations in the table (AFSSA, 2009a). Thus, a distinction between natural and industrial TFA should be made. The WHO recommendation also concerns only TFA from industrial origin. This should be specified here (WHO, 2003).
Association de la transformation laitière française	5.1. Dietary requirements	Line 1050 In purpose of defining dietary guidelines for nutrients such as fat, a transparent and systematic review of the scientific data has to be performed. In the present scientific overview "5.1 Dietary requirements", the method used for selecting scientific data is not presented. Line 1067 As mentioned in lines 614-616 "In adults average total fat intakes ranged from less than 30 E% to 47 E%. About 43% of the reported average data were between 30 and 35 E%; 13% were 40 E% or higher". This average value (in addition to lower and upper end) is also important as it shows that for adults the fat intake is over 30% in more than 50% of the average data reported. Line 1068-1070 This sentence should also be in the summary. Lines 1072-1073 "Such low fat intakes are highly unlikely in European countries": If very low fat intakes are very unlikely in Europe, the lowest recommended fat intake should not include this kind of low consumption as it is not representative. Under 30 E% of fat consumption, a balanced intake of the different fatty acid is indeed hard to achieve (AFSSA, 2001). Lines 1072-1074 Please provide references for this statement. It seems important to take into account that reducing total fat intake can lead to an increase in carbohydrate intake. A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005) and can lead to a high synthesis of palmitic acid. Recent studies show that a lower fat-diet but rich in carbohydrates stimulated saturated fatty acid synthesis - especially palmitate - at high rates

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		(Wilke et al., 2009). Line 1118 In lines 1109-1112 a clear example is given that diets containing less than 30 E% from fat can have negative effects on weight and vitamin intake. Only in the STRIP Trial evidence is provided that 25-30% has no negative effect on growth and neurological development. Furthermore, none of the studies presented found negative effects of higher fat intake (>35%) compared to lower fat intakes. Why than come to 25% as appropriate (line 1118) and in the table "Summary of DRVs for fats" (line 2055) to an RI of 20-35% for >4 year olds? It appears more prudent to advise a level of 30-40%. Line 1121 Previous studies have suggested that interventions to lower dietary fat content and improved fat quality lead to a compensatory increase in sucrose content. There has been a concern that dietary recommendations aimed at achieving a low saturated fat diet might lead to inappropriately increased sugar intake (Gibney et al., 1995) and some studies suggest that an inverse relationship exists between the intake of fat and simple sugars (Gibson, 1997; Lewis et al., 1992; Hackett, 1993). Other studies show that children with an intake of <30% of energy from fat consumed more carbohydrates (mainly sucrose) than those children whose diets contained >40% of energy from fat (Nicklas et al., 1992; Kennedy et al., 1999a). Moreover, restriction of fat in children is questionable (Olson, 2000). There is no evidence that low-fat diets in childhood will prevent atherosclerosis in adulthood. The claim that low-fat diets are safe in childhood is based on observations over a too short time to establish safety. If growth and development of children are not changed with low-fat diets, the proof of long-term safety is not substantiated. Lines 1139-1142 Editorial comment: "A LA intake of less … the form of LA." is also taken from Hansen et al., 1963. The reference should be cited after that sentence.

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Association de la transformation laitière française	5.10. Cancer	Line 1778 It should be added that it concerns TFA from industrial origin as the author indicate that ”a high serum level of trans monounsaturated fatty acids, presumably reflecting a high intake of industrially processed foods, is probably one factor contributing to increased risk of invasive breast cancer in women.” Line 1780 It is not “associated” as there is “limited evidence” (WCRF/AICR, 2007) Line 1781 There are only “limited-suggestive evidence” and no association (WCRF/AICR, 2007). Line 1785 The WCRF/AICR Expert Report “Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective” (five years of work driven by an independent panel of 21 world renowned scientists) is the most recent and complete synthesis of the available scientific data on this topic. It would be pertinent to refer to this report systematically. For example, WCRF judged that: There is “limited evidence-no conclusion” to support a link between fats and oils or fatty acids composition and breast cancer risk, whatever the menopausal status. There is “limited evidence-suggestive” that butter increases lung cancer risk There is limited-suggestive evidence that foods containing animal fats increases colorectal cancer risk (not any word about olive oil) A new study from China suggests that increasing the intake of n-3 fatty acids, and decreasing intakes of n-6, could reduce the risk of colorectal cancer. The highest dietary ratio of n/3-n-6 was associated with a 95 per cent increase in the risk of women developing colorectal cancer, according to results of a study with 73.242 Chinese women participating in the Shanghai Women"s Health Study (Murff et al., 2009).

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Association de la transformation laitière française	5.2. Serum lipids and lipoproteins	Line 1223 In purpose of defining dietary guidelines for nutrients such as fat, a transparent and systematic review of the scientific data has to be performed. In the present scientific overview "5.2 Serum lipids and lipoproteins" the method used for selecting scientific data is not presented. Lines 1223-1228 The relevance of lipoprotein markers should be mentioned and discussed in relation to their relevance for hard endpoints. A randomized clinical trial (RCT) that shows a statistically significant benefit in disease mortality rather than a benefit for a surrogate endpoint is the pinnacle of evidence–based medicine. However, this is not always feasible. Cholesterol markers have been used as surrogate endpoints to study the effect of dietary fat in RCTs - especially as a marker for CVD risk. For many years, the only biomarkers of CHD risk recognized by health authorities have been total cholesterol and LDL cholesterol. Recently, the Expert Panel of the WHO Scientific Update on trans fatty acids pronounced the ratio of total cholesterol to HDL cholesterol as the "best single lipid predictor of CHD risk" (Uauy et al., 2009). Extensive research has changed the simplistic view of atherosclerosis (the major underlying cause for CHD (Das, 2007)) as a disorder of pathological lipid deposition to a more complex concept of an ongoing inflammatory response (Stoll and Bendszus, 2006). Therefore, effects on inflammatory markers are often included in newer RCTs. Lines 1231-1234 No references are provided for this statement. Lines 1229-1236 The conclusion of 5.2.1 is missing. According to EDA interpretation, these results show that at low intake of SFA (<10 E%) decreasing total fat intakes worsen the lipid profile leading to higher atherosclerosis risk (increases the total/HDL cholesterol ratio and TG, decreases serum concentrations of HDL cholesterol) (See also Mensink et al., 2003). The decrease of fat intake in men to 28% or 24% at stable body weight, leads to a decrease of LDL cholesterol but also to an decrease of HDL cholesterol, an increase of TG and LDL small and dense) (Lefebvre et al., 2005; Wood, 2006; Dreon, 1999).
Association de la transformation laitière française	5.2. Serum lipids and lipoproteins	Line 1237 Not only long-chain, but also medium-chain and short-chain fatty acids should be discussed for disease risk. Short and medium-chain fatty acids are not transported via the chylomicron system, and are not linked to changes is lipoprotein profiles. This is also relevant for paragraphs 5.8 and 6.2. Their effects on CAD and cholesterol have not been a dietary issue (German and Dillard, 2004). There is some evidence that short and medium-chain fatty acids have antiviral and antitumor activity (German and Dillard, 2004). SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions (Parodi, 2009). Short and medium-chain SFA have a hypocholesterolemic effect at physiological dose (this effect of diets high in C8 and C10 was shown in humans by Hashim (1960). In a recent meta-analysis, the effects of the individual SFA on the serum lipoprotein profile have been estimated (Mensik et al.,

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		2003). Iso-energetic replacement of carbohydrates with lauric, myristic and palmitic acids all resulted in increased total, LDL and HDL cholesterol concentrations. But as the cholesterol-raising effects of lauric acid were proportionally higher on HDL than on LDL cholesterol, replacement of carbohydrates by lauric acid resulted in a significantly lower total / HDL cholesterol ratio (The ratio of total to HDL cholesterol is a more powerful predictor of CHD risk than either total or LDL cholesterol levels (Stampfer et al., 1991)), which suggests a decrease in atherosclerotic risk. Stearic acid had the smallest effect on HDL cholesterol but lowered total and LDL cholesterol, and thus also decreased the total / HDL cholesterol ratio. Palmitic acid is the only fatty acids which increased the total / HDL cholesterol ratio (Mensink et al., 2003), fact confirmed in other studies (Salter et al., 1998; Billet MA, 2000). Stearic acid decreases LDL cholesterol, similar effect that oleic acid (Mensink, 2005). No differences between the effects of the different SFA on fasting serum triacylglycerol concentrations were detected (Mensink, 2003) (see especially figure 3 of this study). Myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol when consume at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Dabadie, 2005; Tholstrup et al., 1994 and 2003b). Negative effects of myristic acid that have been described were only the result of massive doses that are well above the usual consumption (Staiger K et al., 2006). Lines 1238-1241 The term "mixture" used here leads to an oversimplification and does not indicate which SFA are concerned. EFSA should indicate what the SFA involved are. Besides, SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions. Doses, population and references should also be indicated to support this statement. Line 1251 The analysis of sub fractions in subjects given low carbohydrate diets with either higher or lower content of SFA shows that the saturated fat intake results in an increase in the larger buoyant LDL rather than the smaller LDL particles. The small, dense LDL particles have been associated with increased risk of CVD, whereas large LDL particles have not (Krauss, 2006). Mozaffarian et al. (2004) also show that in postmenopausal women with relatively low total fat intake, a greater saturated fat intake is associated with less progression of coronary atherosclerosis. The proposed hypothesis is that a decrease in fat intake leads to worsen the lipid profile: decrease of HDL cholesterol, increase of TG and B-phenotype of LDL (small and dense LDL) (Dreon et al., 1998; Dreon et al., 1999; Krauss et al., 2006; Lefebvre et al., 2005).
Association de la transformation laitière française	5.2. Serum lipids and lipoproteins	Line 1314 However, the intake of ruminant TFA is low in most populations. In the French diet, for example, the natural TFA intake ranges from 0.5-0.9% of the total energy intake (AFSSA, 2009a). This amount is far lower than the 3.7% tested in the Motard-Bélanger study (2008). The French intake values have been established by a consumption survey, INCA2 (2006-2007), on more than 4000 persons (AFSSA, 2009b). Lines 1326-1327

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		"The intervention studies do not provide evidence that a mixture of CLA isomers, cis-9, trans-11 CLA, or trans-10, cis-12 CLA have an impact on the serum lipoprotein profile." However, as explained in this scientific opinion on line 1319-1321 some studies are showing that cis-9, trans-11 is more favourable as compared with trans-10, cis-12 CLA on lipoprotein profile. The conclusion should be also that more studies are needed on purified CLA isomers. Line 1340 Kratz also conducted a systematic review on animal and human (intervention and observational) studies. Based on the results of these studies, the author found that an increase in dietary cholesterol intake resulted in only a minimal increase in the total/HDL cholesterol ratio, as most subjects can effectively adapt to higher levels of cholesterol intakes (Kratz, 2005). Lines 1342-1344 "Under iso-energetic conditions, the most favourable lipoprotein profile to lower atherosclerotic risk is achieved when a mixture of SFA and TFA is replaced by a mixture of oleic acid, linoleic acid and fish fatty acids. These effects are dosedependent". Those sentences should be removed from the scientific draft opinion: "mixture" does not mean anything and as shown in our previous comments it is not possible to consider SFA as a whole in terms of structure, metabolism and cellular functions. The same remark can be made for TFA: the difference should be made between industrial or natural TFA. The intake of ruminant TFA is indeed low in most populations. In the French diet, for example, the natural TFA intake ranges from 0.5-0.9% of the total energy intake (AFSSA, 2009a). This amount is far lower than the 3.7% tested in the Motard-Bélanger study (2008). The French intake values have been established by a consumption survey, INCA2 (2006-2007), on more than 4000 persons (AFSSA, 2009b). Lines 1341-1346 The effect of stearic acid is neutral (Yu et al., 1995). The effects are also dose dependant. Myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol when consumed at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000). Consumption of naturally occurring TFA at levels found in regular diets does not contribute to elevated risk of cardiovascular disease (see the European Parliament study, 2008).

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Association de la transformation laitière française	5.2. Serum lipids and lipoproteins	Lines 1253-1254 Cis-MUFA had similar effects on serum total cholesterol concentrations as carbohydrates in Hegsted et al. (1965). Thus, many researchers compared the effects on MUFA, in particular oleic acid, and carbohydrates on the distribution of cholesterol over the different lipoproteins (Grundy, 1986; Mensink and Katan, 1987). From these studies it appeared that effects of oleic acid and carbohydrates are indeed similar on total cholesterol concentrations, but that oleic acid increased HDL cholesterol and lowered VLDL cholesterol and triacylglycerol concentrations (Thijssen and Mensink, 2005). Line 1266 Please provide reference for this statement Lines 1281-1282 Remove: "like diets containing mixtures of SFA". This sentence is not relevant in this part about TFA. Besides, the term "mixture" is not precise and does not mean anything about which fatty acids are concerned. Line 1284 Clarke (2009) is not an intervention study. It is just a simulation. Lines 1294-1296 Please provide reference for this statement. Lines 1297-1298 "In most of the human intervention studies reviewed above, the effects of trans-MUFA from hydrogenated vegetable oils were assessed". This sentence should be the introduction of the paragraph as there are two parts here, one about industrially produced TFA, the other one about ruminant TFA, starting line 1298. Lines 1298-1299 Extreme high intakes of ruminant TFA (3.7 E% or 5 E%) indeed appear to have adverse effects on blood lipid profiles. However, these high levels of ruminant TFA cannot be reached with a normal diet. The habitual intake of ruminant TFA is far below this amount (Craig-Schmidt, 2006; Willett and Mozaffarian, 2008). On the other hand, ingesting 20-40g (> 5 E%) industrially produced TFA is not at all unrealistic (Stender et al., 2008). Why is this not mentioned? Line 1301 "3.7% of energy from TF" This high percentage does not reflect the usual intake in European countries. In France, TFA intake from natural origin represent only 0.5-0.9% of the total energy intake (AFSSA, 2009a). Line 1307 The European Parliament study on TFA (2008) aimed at providing background information to Members of the European

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		Parliament on TFA. The report highlighted the fact that although there was considerable scientific evidence showing a causative link between intake of industrially produced TFA and cardiovascular disease, scientific studies also revealed that consumption of naturally occurring TFA at levels found in regular diets do not contribute to elevated risk of cardiovascular disease. Therefore the authors mentioned that it is important to make a clear distinction between naturally occurring and industrially produced TFA when developing possible guidelines for action to reduce the intake of TFA. Any legal restrictions should be limited to industrially produced TFA. Line 1309 Remove "like diets containing mixtures of SFA". This sentence is not relevant in this part about TFA. Besides, the term "mixture" is not precise and does not mean anything about which fatty acids are concerned. Line 1311 "Consumption of diets containing trans-MUFA also…" "Also" has to be removed as TFA and some SFA do not have the same effects on HDL cholesterol. Lines 1312-1314 "The available evidence indicates that TFA from ruminant sources have similar adverse effects on blood lipids and lipoproteins to those from industrial sources". This is true only at very high levels of TFA intake, corresponding to diets with 3.7% of energy from TFA - indeed 9 litres of semi-skimmed milk, 4 kg of yoghurt or 800g of camembert cheese – as the average content of TFA in milk fat is 5.39% of total fatty acids (AFSSA, 2005).
Association de la transformation laitière française	5.3. Haemostatic function	Line 1362 If the studies are far from consistent, those sentences should be reformulated. Suggestion: "Although C12:0 to C16:0 SFA have been suspected to increase factor VII levels as compared to stearic acid (C18:0), the studies were far from consistent and no conclusion can be made. Moreover, in one study, post-prandial increases in activity of factor VII were less after consumption of meals rich in SFA, especially stearic acid, than after a consumption of meals enriched with unsaturated fatty acids (Thijssen and Mensink, 2005; Tholstrup et al., 2003a)." Line 1364 Relative to oleic acid, and unlike to n-6 PUFA, either medium-chain SFA or lauric or myristic or palmitic acids did not affect collagen-induced whole blood aggregation. Furthermore, ADP-induced platelet aggregation was not changed by medium-chain saturated fatty acids or myristic acid (Thijssen and Mensink, 2005; Temme et al., 1998). Line 1375 According to the Thijssen and Mensik (2005), thromboxanes (TX) and prostaglandins (PG), two eicosanoids, play an important

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		role in the haemostatic balance. Both types of eicosanoids are synthesised from the C20 fatty acids, arachidonic acid (C20:4n-6) and EPA (C20:5n-3), after release from membrane phospholipids. Eicosanoids of the n-2 series, such as TXA2, are synthesized from the n-6 arachidonic acid in platelets, while prostaglandins I2 (PGI2) is synthesised in the vascular endothelium. TXA2 is a potent vasoconstrictor and a stimulus for platelet aggregation, whereas PGI2 has opposite effects. Eicosanoids of the n-3 series such as TXA3 and PGI3 are principal metabolites of the n-3 fatty acid EPA. TXA3 is less active than TXA2, meaning than the vasoconstrictor effects due to n-6 fatty acids is higher than the ones induced by the n-3 fatty acids. The anti-aggregation effects of PGI3 and PGI2 are however comparable. Furthermore, n-6 PUFA increased urinary 11-dehydro-TXB2 excretion compared with saturated and monounsaturated fatty acids, which seemed to reflect an ADP-induced platelet aggregation (Lahoz et al., 1997; Thijssen and Mensik, 2005). Increased ADP-induced platelet aggregation is associated with increased atherosclerotic risk (Elwood et al., 1991; Thijssen and Mensik, 2005).
Association de la transformation laitière française	5.4. Inflammation and immne function	Line 1422 Additional information: A randomized, controlled, 3-diet, 3-period crossover study was published in 2007 in the American Journal of Clinical Nutrition (Zhao et al., 2007). Hypercholesterolemic subjects (n=23) were assigned to 3 experimental diets: a diet high in ALA (6.5 E%), a diet high in LA (12.6 E%), and an average American diet for 6 weeks. Results showed that increased intakes of dietary ALA elicited anti-inflammatory effects by inhibiting pro-inflammatory cytokine production (IL-6, IL-1ß and TNF-a) in cultured PBMCs (Peripheral Blood Mononuclear Cells). Changes in PBMC ALA and EPA were associated with beneficial changes in TNF-a release. ALA could thus have some effects of reduction in the production of inflammatory cytokines. Line 1426 This line correctly reports that TFA from hydrogenated sources (not ruminant sources) have been linked to adverse effects on inflammatory profile in epidemiological studies. Why is this not mentioned in the overall summary (line 129-146)? Lines 1434-1439 While it is mentioned in the conclusion that no consistent picture has emerged on effects on n-6 PUFA, no references are provided for that in part 5.4.1.
Association de la transformation laitière française	5.7. Body weight control and energy balance	Lines 1583-1593 Profound quantitative and qualitative changes have taken place in the last four decades in the Western industrialised world, particularly the rising intake of n-6 and declining intake of n-3 PUFA. A recent review (Ailhaud et al., 2008) suggests that this imbalance in PUFA intake is an emerging risk factor contributing in addition to long-term net positive energy balance. The authors propose that several aspects of unbalanced PUFA metabolism conspire to stimulate fat cell formation and to increase the prevalence of overweight and obesity such as low n-3 PUFA intake, overestimation of linoleic acid requirement and significant increase in the LA:LNA ratio. Thus, nutritional recommendation should not stress the n-6 PUFA over consumption, and promote instead a good equilibration between n-3 PUFA and n-6 PUFA.

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		Line 1618 It is important to add in the conclusion that based on some recent studies, nutritional recommendation on n-6 PUFA intake should not promote their over consumption but rather a good balance between n-3 PUFA and n-6 PUFA (Ailhaud et al., 2008).
Association de la transformation laitière française	5.8. Cardiovascular disease	Line 1626 General comment on this part about "Cardiovascular disease: the analysis on the effect of lipids on cardiovascular disease is quite poor compared to the analysis made on serum lipids and lipoproteins made in part 5.2. For example there is almost no data on stroke, which is actually a part of cardiovascular diseases and should be considered. Ecological studies suggest that saturated fat (mostly animal fat) is inversely associated with stroke. Some studies suggest that high intake of PUFA could have a negative effect on oxidation process and inflammatory mechanism involved in the stability of the plaque (Thies et al., 2003). Epidemiological studies show that saturated fat is either associated to a significant decreased risk of stroke (Framingham Study – ischemic stroke, Gilman, 1997; Nurses' Health study – hemorrhagic stroke, Iso, 2001; Japanese cohort of 4500 subjects - hemorrhagic stroke, Iso, 2003) or no related to the risk of stroke (Health professional Study, He, 2003) Line 1632 What are the selection criteria for selecting only those four studies? Line 1628 Concerning total fat, a reduction in fat intake is frequently construed as a recommendation in cardiovascular disease prevention. However, the question is now increasingly subject to debate (Mozaffarian et al., 2004). Line 1644 Howard et al. (2006) also shows that no benefit was observed in terms of coronary disease, cardiovascular or cerebrovascular disease with the decrease of fat intake and decrease of SFA to 9.5%. On the contrary, for some women with cardiovascular history, there was an increase of their cardiovascular disease risk linked to a decrease of lipids and SFA intake.
Association de la transformation laitière française	5.8. Cardiovascular disease	Line 1716 The words "of SFA" should be deleted as not all SFA have the same effects. TFA should be replaced by "industrial TFA". All research (either epidemiological or interventional studies) tends to show that in healthy people diets low in SFA were unsuccessful in reducing the incidence of cardiovascular disease. In this context, the recommendation "as low as possible" has neither scientific value nor scientific justification. Line 1720 The genetic aspect should be included in this scientific draft opinion. There is a wide inter-individual variability in the response to dietary changes since genetic polymorphisms modulate the effects of nutrients. In terms of cardiovascular diseases,

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		polymorphisms at multiple genes have been associated with differential effects in terms of lipid metabolism. Many examples can be given. A habitually low saturated fat diet is associated with a beneficial lipoprotein profile only among homozygotes of the APOC3 promoter 455T-625T polymorphism. (25% of the population) (Brown S et al., 2003). Another example of a well-documented nutrigenetic interaction is that of the apoAI gene which is a major structural and functional component of HDL cholesterol. A significant interaction between this polymorphism and PUFA intake in determining plasma HDL cholesterol concentration has been demonstrated in women in the Framingham Study. In carriers of the A allele, higher PUFA intakes (>8 E%) were shown to be associated with higher HDL cholesterol, whereas in G/G homozygotes, the opposite effect was observed (Lovegrove and Gitau, 2008). The concept of gene-environment interactions modulating common disease risk factors is now well founded and should be taken into consideration for more individually targeted approaches to disease prevention and therapy (Ordovas, 2009).
Association de la transformation laitière française	5.8. Cardiovascular disease	Lines 1627-1644 (last part of our comments on those lines) In conclusion, the results of the studies described above tend to show that dietary intervention in healthy people of diets low in total fat or SFA were unsuccessful or provided insufficient evidence in reducing the incidence of cardiovascular disease (for more details, see also Ravnskov, 1998; Ramsden et al., 2009). It also appears that in coronary heart disease, the overconsumption of n-6 PUFA must not be encouraged since it can increase plaque instability (Lecerf, 2009). A recent systematic review of 146 prospective cohort studies and 43 RCTs from Europe, the US and Asia, investigating dietary factors related to CHD carried out by Mente et al. (2009) found insufficient evidence of an association between intake of total fat, SFA, PUFA, milk, meat and eggs and risk of CHD, but found protective associations for intakes of MUFA, fish, n-3 fatty acids, folate, whole grains, vitamins E and C, beta carotene, alcohol, fruit and fibre. A harmful association was found for TFA and foods with a high glycemic index. One of the conclusions stated "it is unlikely that modifying the intake of a few nutrients or foods would substantially influence coronary outcomes." In a review paper from Parodi (2009), 24 reports of 11 cohorts were the only prospective cohort studies found which evaluated the association between SFA and risk of CHD. Among these, 4 studies found a significantly positive association between SFA intake and risk of CHD, 3 found no association and 2 found a negative association. Overall, these results are inconsistent and do not provide convincing evidence of an association between SFA and risk of CHD. The evidence extracted by Gibson et al. (2009) from 12 major prospective cohort studies involving more than 280.000 subjects does not consistently demonstrate a direct relationship between the intake of dairy foods and increased risk of CVD (CHD, IHD or myocardial infarct), even though it is recognized that dairy fat is a contributor of saturated fat intake and excess saturated fat intakes has been associated with a higher incidence of CVD. The authors noted that "the studies available for examining the effect of dairy food consumption on CHD are too varied in design, quality and dietary assessment methodology to evaluate the nature of the relationship." From a meta-analysis of 15 cohort studies carried out by Elwood et al. (2008), the relative risk of stroke or heart disease in subjects with high milk or dairy consumption was 0.84 and 0.79 respectively, relative to the risk in those with low consumption.

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Association de la transformation laitière française	5.8. Cardiovascular disease	Lines 1627-1644 (Part 2) Elmadfa and Kornsteiner (2009) stated that "The meta-analysis by Skeaff and Miller (2009) demonstrated that the relative risk of CHD death in the highest (14–18 E%) category of SFA consumption was not significantly different from that in the lowest (7–11 E%) category. High compared with low SFA consumption was not significantly related with diverse risk factors of CHD events." Skeaff and Miller (2009) carried out a very recent and exhaustive review of cohort studies and controlled trials of dietary fats and CHD mortality or morbidity (search in the Cochrane Library, Cochrane reviews, article databases, systematic reviews, meta-analysis, etc.). 28 individual cohort studies were selected, in which there were about 6,600 CHD deaths amongst 280,000 participants during approximately 3.7 million person-years of follow-up. The authors state on p. 191: "According to the classic 'diet-heart' hypothesis, high intake of SFAs and cholesterol and low intake of PUFAs increase serum cholesterol levels and risk of CHD. However, few within-population studies have been able to demonstrate consistent associations with any specific dietary lipids, with the exception of trans fats and n-3 fatty acids. The available evidence from cohort and randomized controlled trials is unsatisfactory and unreliable to make judgment about and substantiate the effects of dietary fat on risk of CHD." Continuing further it is mentioned that "Furthermore, the evidence from cohort studies of dietary intake of fats and CHD is mostly unreliable (with few exceptions) because most studies have ignored the effects of measurement error and regression dilution bias." According to the results of this study - Total fat: . Intake of total fat was not significantly associated with CHD mortality, with a RR for highest compared with the lowest category of 0.94 (95% CI of 0.74-1.18, p=0.583); . Intake of total fat was also unrelated to CHD events (RR 0.93, 95% CI 0.84-1.03, p=0.177); . No significant association of total fat intake with CHD mortality (RR 1.06, 95% CI 0.88-1.28, p=0.517) or CHD events (RR 1.02, 95% CI 0.98-1.05, p=0.404) per 5% total energy increment in total fat intake ; . Overall, the mean or median total fat intake in all cohort studies varied from 27-47% total energy. - SFA: . Intake of SFA was not significantly associated with CHD mortality (RR 1.14, 95% CI 0.82-1.60, p=0.431) for highest compared to lowest category of SFA intake . SFA intake was not significantly associated with CHD events (RR 0.93, 95% CI 0.83-1.05, p=0.269 for high vs. low category) . No significant association of SFA intake with CHD death (RR 1.11, 95% CI 0.75-1.65, p=0.593) per 5% total energy increment in SFA intake . Overall, the mean or median SFA intake in all cohort studies varied from 9-20% total energy. - MUFA: No significant association with CHD mortality / CHD deaths or CHD events - PUFA: . Intake of PUFA was strongly significantly associated with CHD mortality with a RR 1.25, 95% CI 1.06-1.47, p=0.009) for highest compared to lowest category . High compared with low PUFA intake was not associated with CHD events (RR 0.97, 95% CI 0.74-1.27, p=0.825) for highest

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		compared to lowest category . Significant lower risk of CHD events (RR 0.84, 95% CI 0.70-1.00, p=0.049) per 5% total energy increment in PUFA intake, but not with CHD mortality. Moreover, the results of this review showed that the RR of fatal CHD was not reduced by either low-fat diets or diets with a high polyunsaturated to saturated fat ratio (P/S ratio).
Association de la transformation laitière française	5.8. Cardiovascular disease	Lines 1645-1694 (first part of our comments on those lines) Two other clinical trials of dietary supplementation with n-3 fatty acids exist: the DART and Lyon Heart studies, which are both secondary prevention trials. The DART study (Burr et al., 1989; Burr et al., 2007) was conducted in 2003 men after myocardial infarction, with 3 treatment arms: reduction of SFA intake to 30% energy with a P/S ration of 1:0, an increase of fatty fish (200-400 g/week), or an increase in cereal fibres to 18g/d. Advice to modify fat intake did not confer any obvious benefit, perhaps partly because it entailed greater changes in dietary habits and was therefore inadequately followed. Indeed, the advice about dietary fat did not achieve the expected differences in intakes, partly because of incomplete compliance with the advice and partly because of spontaneous changes in the control group. After 2 years, total fat accounted for 31.4% and 35.2% in the fat-advice and the non-fat advice groups respectively, and the corresponding mean P/S ratio were 0.8 and 0.4, although patients had regularly nutritional recommendations and advice given by a professionals of dietetics. However, the fish advice was associated with a 29% reduction in overall mortality, and this result was unaffected by adjusting variables at baseline. The Lyon Heart study (de Lorgeril et al., 1994; Renaud et al., 1994; de Lorgeril et al., 1999) was a randomized secondary prevention trial aimed at testing whether a Mediterranean type diet may reduce the rate of recurrence after a first myocardial infarction. The intervention diet was rich in a-linolenic acid (0.8% versus 0.3% in the control group) and provided around 30 E% from fat, 8 E% from SFA (12% in the control group), 13 E% from MUFA (10% in the control group) and <4 E% from linoleic acid (n-6 LA) (>5% in the control group). The study lasted over a 5-year period and was conducted on 302 patients, compared to 303 control patients. There was also an additional follow-up after the 5 initial years for 46 months. The recurrent myocardial infarction, all cardiovascular events, and cardiac and total death were significantly decreased by > 70% in the group consuming the Mediterranean diet. These protective effects were not related to serum concentrations of total, LDL or HDL cholesterol. With regard to any association between the plasma concentration of major fatty acids and recurrence, only 18:3 n-3 and 22:6 n-3 tended to be inversely associated with recurrence of outcomes (p=0,11 and p=0,16 respectively) for myocardial infarction and cardiovascular deaths (no significance for other outcomes as heart failure, stroke, pulmonary or peripheral embolism, angina, thrombophlebitis).

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Association de la transformation laitière française	5.8. Cardiovascular disease	Lines 1645-1694 (secont and last part of our comments on those lines) Skeaff and Miller (2009) conducted a very recent and exhaustive review of cohort studies and controlled trials of dietary fats and CHD mortality or morbidity (search in the Cochrane Library, Cochrane reviews, article databases, systematic reviews, meta-analysis, etc.). Results found that: - ALA: No association with intake of ALA and CHD death (RR 0.84, 95% CI 0.53-1.31, p=0.439) or CHD events (RR 1.05, 95% CI 0.78-1.42, p=0.730) for highest compared to lowest category of intake - LC PUFA: . For cohort studies on n-3 LC PUFA, there were about 5,361 deaths amongst 256,000 participants during 4 million person-years of follow-up. . Intake of n-3 LC PUFA or fish consumption were strongly associated with CHD mortality (RR 0.82, 95% Cl 0.71-0.94, p=0.006) for the highest compared with lowest category. . Intake of n-3 LC PUFA was not associated with decreased risk of CHD events, non fatal CHD, total myocardial infarction, sudden cardiac death. . For meta-analysis of randomized controlled trials of n-3 LC PUFA or fish and CHD, there were about 1,300 CHD deaths amongst 37,000 participants during 140,000 person-years of follow-up. Depending on the inclusion or exclusion of DART . 2 study, risk ratios of the different parameters were totally changed (either a reduction or a non significance), limiting the interpretation.
Association de la transformation laitière française	5.8. Cardiovascular disease	Lines 1695-1700 Non-conjugated polyunsaturated TFA should be addressed in relation to disease risk. There is evidence that polyunsaturated TFA (trans 18:2) could pose a higher risk for ischemic heart disease and sudden cardiac death and CHD than monounsaturated TFA (trans 18:1) (Lemaitre et al., 2006; Baylin et al., 2003) These polyunsaturated TFA are from industrial sources, and can only be found in trace levels in ruminant fats. The WHO experts come to a different conclusion. They do make a difference between ruminant and industrially produced TFA: "The current growing body of evidence from controlled trials and observational studies indicates that TFA consumption from partially hydrogenated oils adversely affects multiple cardiovascular risk factors and contributes significantly to increased risk of CHD events. Although ruminant TFAs cannot be removed entirely from the diet, their intake is low in most populations and to date there is no conclusive evidence supporting an association with CHD risks in the amounts usually consumed. In contrast, TFA produced by partial hydrogenation of fats and oils should be considered industrial food additives having no demonstrable health benefits and clear risks to human health. The WHO Scientific Update on TFA concludes that restaurants and food manufacturers should avoid using industrially derived TFA in food products and that governments should take steps to support alternative fats or oils for TFA replacement. The evidence on the effects of TFA and disease outcomes strongly supports the need to remove PHVO from the human food supply." (Uauy et al.,

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		2009). The limited data suggest that the experimental effects of ruminant and industrial TFA are similar when consumed in similar quantities, but very few persons consume such high levels of ruminant TFA, and observational studies do not support adverse CHD effects of ruminant TFA in amounts actually consumed (Mozaffarian et al., 2009). AFSSA concluded it its recent report that TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at very low level (0.5-0.9% of the total energy intake) (AFSSA, 2009a). Lines 1701-1712 Incidence of nonfatal and fatal CHD and stroke corresponding to the daily egg consumption was determined in 37,851 men and 80,082 women in 2 large prospective cohort studies (the Health Professionals Study and the Nurses Health study). Results showed no evidence for an overall significant association between egg consumption and risk of CHD and stroke, after adjustments for age, smoking and other potential CHD risk factors. The authors found a significant association between egg consumption and CHD and stroke in only a subgroup of diabetic patients (thus with abnormalities in lipid metabolism). Kratz also conducted a systematic review on animal and human (intervention and observational) studies. A large number of observational studies (Honolulu Heart Study, the Puerto-Rico Heart Health Program, the Lipid Research Clinics Prevalence Follow-up Study, the Nurses Health Study, the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study and the Hawaii Cardiovascular Study) did not find any relationship between the intake of dietary cholesterol and the risk of CHD. Moreover, some other studies which primarily found a potential positive link between cholesterol intakes and CHD noted that the results were no longer significant after adjustments for consumption of vegetable, proteins and fibres, since they usually go hand in hand in individual diets (Kratz, 2005).
Association de la transformation laitière française	6.1. Total fat	Line 1831 As mentioned in this scientific draft opinion (lines 1068-1070), “Very low fat diets tend to increase the risk of an insufficient intake of PUFA, can impair the absorption of fat-soluble vitamins and be associated with insufficiency of other essential nutrients like zinc and B vitamins”. Line 1840 The 20 E% does not seem representative of the European fat intake. Indeed according to Annex 1b of this draft opinion means intakes are almost all above 30 E%. The population with very lower intake is obviously a specific population (elderly men in Portugal). This confirms that the 20 E% as the lower bound of the intake range is not appropriate for the general population. Line 1843 The value of 20 E% is not appropriate: it is not representative of the low intake in Europe and according to AFSSA (2001) below 30 E% the balance of fatty acid intake (especially PUFA) is more difficult to achieve because of the composition of the usual food products. Besides, a growing body of evidence (observational, experimental, clinical trials and meta-analysis) indicates that the traditional diet – CHD paradigm (reduction of total and saturated fats and increase of carbohydrates) is inadequate.

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		Firstly, no positive relation in prospective cohorts and randomized trials between total fat reduction and incidence of CHD has been found. Secondly, reducing total fat leads to increase carbohydrates (Skeaff and Miller, 2009; Mozaffarian 2005; Elmadfa and Kornsteiner, 2009; Hooper et al., 2001 and 2002; Gordon et al., 1981). A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005). Line 1847 The recommendation for total fat intake between 3 years and adult is missing.
Association de la transformation laitière française	6.2. Saturated fatty acids (SAT)	Line 1851 It should be clear what is meant with expressions like "a mixture of SFA" and also if this mixture is nutritionally relevant. In order to determine dietary reference values for nutrients, it is important to be aware of that no biochemical measurement in the human body can represent the effect of various nutrients. It is thus of greatest importance to examine the direct relationship between consumption of the food item/nutrient and the risk of disease. In the second paragraph of 6.2, the main discussion is made on SFA and LDL cholesterol and not cardiovascular disease. According toWHO, the ratio of total and HDL cholesterol is a more reliable biomarker. Lines 1851-1852 This sentence does not represent the conclusion of the scientific opinion on line 1238-1240 where it is stated that "There is a positive, dose-dependent relationship between the intake of a mixture of SFA and serum LDL and HDL cholesterol concentrations, when compared to carbohydrates. As a consequence, the total to HDL cholesterol ratio does not change". Line 1855 However, Mozaffarian (2004) shows that in some case a greater saturated fat intake is associated with less progression of coronary atherosclerosis, whereas carbohydrate intake is associated with a greater progression. Besides, the Women Health Initiative (WHI) study indicates that no benefit was observed in terms of coronary disease, cardiovascular or cerebro-vascular disease with the decrease of fat intake and 9.5% SFA (Howard, 2006).
Association de la transformation laitière française	6.2. Saturated fatty acids (SAT)	Line 1858 The only link between SFA and health concerns total blood cholesterol (LDL and HDL). However, and contrary to carbohydrates which only increase the LDL cholesterol, SFA increase both HDL and LDL. Moreover, not all SFA but only a few have impacts on cholesterol so on this matter SFA cannot be considered as a whole. Only lauric, myristic and palmitic acids are known to increase total cholesterol, while short and medium-chain fatty acids are neutral (Mensink 2005 and 2003; Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Dabadie, 2005; Tholstrup et al., 1994 and 2003b; Hashim, 1960; Parodi, 2009). In a recent meta-analysis, the effects of individual SFA on the serum lipoprotein profile have been estimated (Mensik et al., 2003). Iso-energetic replacement of carbohydrates with lauric, myristic and palmitic acids all resulted in increased total, LDL and HDL cholesterol concentrations. But as the cholesterol-raising effects of lauric acid were proportionally higher on HDL than on LDL cholesterol, replacement of carbohydrates by lauric acid resulted in a significantly lower total

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		/ HDL cholesterol ratio, which suggests a decrease in atherosclerotic risk. Stearic acid had the smallest effect on HDL cholesterol but lowered total and LDL cholesterol, and thus also decreased the total / HDL cholesterol ratio. Palmitic acid is the only fatty acid which increased the total / HDL cholesterol ratio (Mensink, 2003), a fact confirmed in other studies (Salter et al., 1998; Billet MA, 2000). No differences between the effects of the different SFA on fasting serum triacylglycerol concentrations were detected (Mensink, 2003). Myristic acid had also been criticized for elevating cholesterol. However, these negative effects of myristic acid had been described with massive doses, doses which are much higher than usual consumption (Staiger et al., 2006). At usual level, myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDLcholesterol (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Legrand 2008). Moreover, myristic acid at usual level (1.6% total energy intake) is necessary for protein acylation and thus activation (Legrand, 2008). The recommendation should take into account the difference between the SFA. SFA have different physiological functions depending on their chain length, so should not be evaluated as one single group. Line 1868 A recommendation of "as low as possible" would not be achievable in normal life with a normal diet and would result in strict and impossible guidelines to follow. Moreover, this recommendation "as low as possible" is not relevant due to recent scientific results showing the real effect of SFA on health - especially on cardiovascular health (Skeaff and Miller, 2009; He et al., 2007; Mozaffarian, 2005, Hooper et al., 2001 and 2002) (for details see comments lines 1627-1644). A low intake of SFA could lead to an excessive consumption of MUFA and PUFA, which could represent health hazards, especially with regard to intake of n-6 fatty acids (Lecerf, 2009; Ailhaud, 2006).
Association de la transformation laitière française	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Line 1882 An optimal intake with a ratio of n-3/n-6 PUFA should also be fixed by EFSA, like it is the case in all the national and international recommendations. In order to determine this ratio, a conversion factor can be applied to LC PUFAs (LA to ARA, and ALA to EPA and DHA). For adults, this leads to an optimal n-6 PUFA: n-3 PUFA of 5:1. Line 1906 The Panel proposes to set an AI for linoleic acid of 4 E%, with no UL for total or any of the n-6 PUFA. There has been evidence on negative effects on health of excessive intakes of n-6 PUFA and lipid peroxidation (Elmadfa and Kornsteiner, 2009). It could also contribute to excessive adipose tissue development (Ailhaud, 2006; Lecerf, 2009). Therefore, an upper limit should be considered in order to protect consumer health.
Association de la transformation laitière française	6.5. Trans fatty acids (TFA)	Line 1948 According to the recent WHO scientific update on TFA the intake of ruminant TFA is low in most populations. To date there is no conclusive evidence supporting an association with coronary heart diseases risks in the amount of ruminant TFA consumed. In its recent report, AFSSA concluded that TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at very low level (0.5-0.9% of the total energy intake) (AFSSA, 2009a). The EFSA recommendation concerning the dietary reference value for TFAs should therefore deal only with industrially

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		derived TFA. Line 1952 Intake of TFA from industrial origin should be as low as possible. Natural TFA should not be included in this recommendation. Line 1959 This is due to the reduction in industrial TFA.
Association de la transformation laitière française	6.7. Cholesterol	Line 1971 It is important to add that dietary cholesterol has very little influence on plasma cholesterol values which are regulated by numerous genetic and nutritional factors through cholesterol absorption or synthesis. Besides, there is no strong evidence that dietary cholesterol is related to CHD or stroke (Hu andWillett, 2002; He et al., 2003)
Association de la transformation laitière française	Conclusions and recommendations	Line 1978 20 E% does not seem representative of the European fat intake. Indeed according to Annex 1b of this draft opinion means intakes are almost all above 30 E%. The population with very lower intake is obviously a specific population (elderly men in Portugal). This confirms that the 20 E% as the lower bound of the intake range is not adapted for the general population. Lines 1980-1981 Value of 20 E% is not appropriate: it is not representative of the low intake in Europe and according to AFSSA, 2001 below 30 E% the balance of fatty acid intake (especially PUFA) is more difficult to achieve because of the composition of the usual food products. Besides, a growing body of evidence (observational, experimental, clinical trials and meta-analysis) indicates that the traditional diet – CHD paradigm (reduction of total and saturated fats and increase of carbohydrates) is inadequate. First no positive relation in prospective cohorts and randomized trials between total fat reduction and incidence of CHD has been found. Second, reducing total fat leads to increase carbohydrates (Skeaff and Miller, 2009; Mozaffarian 2005; Elmadfa and Kornsteiner, 2009; Hooper et al., 2001 and 2002; Gordon et al., 1981). A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005). Lines 1992-1993 Recommendation of "as low as possible" would not be achievable in normal life with a normal diet and would result in strict and impossible guidelines to follow. Moreover, this recommendation "as low as possible" is not relevant due to recent scientific results showing the real effect of SFA on health - especially on cardiovascular health (Skeaff and Miller, 2009; He et al., 2007; Mozaffarian, 2005, Hooper et al., 2001 and 2002) (for details see comments lines 1627-1644). Lines 2001-2002 An optimal intake with a ratio of n-3/n-6 PUFA should also be fixed by EFSA, like it is the case in all the national and international recommendations. In order to determine this ratio, a conversion factor can be applied to LC PUFAs (LA to ARA, and ALA to EPA and DHA). For adults, this leads to an optimal n-6 PUFA: n-3 PUFA of 5:1. Line 2017 There has been evidence on negative effects on health of excessive intakes of n-6 PUFA and lipid peroxidation (Elmadfa and

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Kornsteiner, 2009). It could also contribute to excessive adipose tissue development (Ailhaud, 2006; Lecerf, 2009). Therefore, an upper limit should be considered to protect consumer health. Lines 2041-2042 Recommendation to reduced TFA intake to «as low as possible» should only concern industrial TFA. This has been recommended in numerous countries in Europe (Nordic Nutrition Recommendations, 2004; AFSSA, 2009b) as well as in the recent WHO scientific update on TFA (Uauy et al., 2009). EFSA recommendation concerning dietary reference value for TFA should therefore deal only with industrially produced TFA. Line 2055 An AI 4% of LA is indeed based on lowest estimated mean intakes in E% (Elmadfa and Kornsteiner, 2009). However, this is not the level at which overt deficiency symptoms occur (this level is at least 2-fold lower): ISSFAL http://www.issfal.org.uk/lipid-matters/issfal-policy-statements/statement-3-pufa-in-adults.html Authors of these adult studies generally concluded that LA intakes of 1.0-2.5 E% would meet requirements but this conclusion was based mostly on minimizing the plasma level of 20:3 w9 (mead acid; a presumed biochemical marker of n-6 PUFA deficiency). Clinical condition of the infants was also considered in one study but otherwise, in these studies, clinical status was not informative. Several authors noted the difficulty in drawing conclusions about LA requirement from measuring plasma fatty acid profiles alone. On the basis of these results, it is concluded that 2E% LA is adequat for healthy adult humans
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BEUC	6.5. Trans fatty acids (TFA)	lines 145-146 and lines 2041-2042 Given the large body of evidence which exists linking the high consumption of tfa to increased risk of CHD, BEUC believes that there is no reason to keep industrially produced trans fats in the food supply when they hold such a potential danger and can be removed. BEUC asks for the EFSA opinion to reflect the recommendations of WHO/FAO and several MS that trans fat intake should not exceed 1% of total calories – a figure which has been achieved in certain populations such as UK (which had set a target of 2%) .

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
CAOBISCO	3. Dietary sources and intake data	CAOBISCO is of the opinion that the conclusions in the summary do not in all cases accurately reflect the content of the report. More precise, the nuance in the report is lacking in the summary. It is not immediately obvious on what basis the conclusions are drawn. Since the summary is generally the part that policy makers will read, it is important that the summary reflects the scientific state of the art, including the recent developments and nuances. Recently, two WHO scientific updates have been published in the European Journal of Clinical Nutrition (vol. 63, supplement 2s, pp S1-S75) and Annals of Nutrition and Metabolism (vol.55, no. 1-3: pp 5-300). It seems logical to take these two updates into account in the document. In conclusion, we would like to point out the following. Consumers do not eat saturated fats or unsaturated fats as such. They eat these nutrients in a matrix (food stuffs), as part of a balanced diet. In practice, the matrix influences the effects of the fatty acids, meaning that negative effects may not occur, or may be less pronounced, due to the presence of other nutrients in the food. on DRV's for saturated fatty acids Saturated fat: Why are all the saturated fats treated as one group in the summary? The unsaturated fats are split up in separate groups, but the saturated fats are treated as one group. Based on their different functions in human physiology and their different effects on cholesterol metabolism wouldn't it be more logical to talk about individual fatty acids instead of treating them as one single group (WHO update 2009: Elmadfa and Kornsteiner (2009) Ann Nutr Metabol 55:56-75 2009. In the EFSA report it is acknowledged that the four main dietary fatty acids have different effects on the lipoprotein profiles on one hand. On the other hand, there is only one DRV for saturated fatty acids defined – and the reason is that there are not enough data for setting individual reference values. Over the past years many papers have been written on the neutral lipoproteinaemic effect of stearic acid and we wonder whether these documents should be made available to EFSA. In the Summary in line 66,67 the following is written: 'The Panel recommends that SFA intake should be as low as possible within the context of a nutritionally adequate diet'. In the discussed scientific research in chapter 5 this recommendation is not supported. Furthermore, according to Table 5 (page 32), most Countries and also the WHO/FAO do set maximum of SFA at 10 E%. In adults, average SFA intakes vary between less than 9 to nearly 17 E% and nearly 30% of the reported average intakes were 15 E% or higher (line 620-629). In addition, in several economically developed countries where the SAFA has fallen close to 10%, the capacity to decrease SFA much further is limited without major changes in dietary patterns, and is only likely to result in modest reductions in TC and LDL-C. We therefore believe it is appropriate to set a goal for SFA at 10 E%. In table 6 (line 2915) the dietary reference value in the Netherlands is mentioned. However, these are the values from 2001, whereas the Dutch Health Council updated its advice in 2006. Therefore we recommend to use the most recent dietary guidelines. For saturated fat we can add that French food safety authority is currently reviewing the recommendations for the different fatty acids (expert Philippe Legrand)
CAOBISCO	6.2. Saturated fatty acids (SAT)	We are of the opinion that the conclusions in the summary do not in all cases accurately reflect the content of the report. More precise, the nuance in the report is lacking in the summary. Therefore, it is not immediately obvious on what basis the conclusions are drawn. Since the summary is generally the part that policy makers will read, it is important that the summary reflects the scientific state of the art, including the recent developments and nuances.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		2. Recently, two WHO scientific updates have been published in the European Journal of Clinical Nutrition (vol. 63, supplement 2s, pp S1-S75) and Annals of Nutrition and Metabolism (vol.55, no. 1-3: pp 5-300). It seems logical to take these two updates into account in the document. 3. In conclusion, we would like to point out the following. Consumers does not eat saturated fats or unsaturated fats as such. They eat these nutrients in a matrix (food stuffs), as part of a balanced diet. In practice, the matrix influences the effects of the fatty acids, meaning that negative effects may not occur, or may be less pronounced, due to the presence of other nutrients in the food. on DRV's for saturated fatty acids Saturated fat: Why are all the saturated fats treated as one group in the summary? The unsaturated fats are split up in separate groups, but the saturated fats are treated as one group. Based on their different functions in human physiology and their different effects on cholesterol metabolism wouldn't it be more logical to talk about individual fatty acids instead of treating them as one single group (WHO update 2009: Elmadfa and Kornsteiner (2009) Ann Nutr Metabol 55:56-75 2009 In the EFSA report it is acknowledged that the four main dietary fatty acids have different effects on the lipoprotein profiles on one hand. On the other hand, there is only one DRV for saturated fatty acids defined – and the reason is that there are not enough data for setting individual reference values. Over the past years many papers have been written on the neutral lipoproteinaemic effect of stearic acid and I wonder whether these documents should be made available to EFSA. As an example Penny Kris-Etherton had written a review for Kraft shared with Caobisco. This could be used, among others. In the Summary in line 66,67 the following is written: 'The Panel recommends that SFA intake should be as low as possible within the context of a nutritionally adequate diet'. In the discussed scientific research in chapter 5 this recommendation is not supported. Furthermore, according to Table 5 (page 32), most Countries and also the WHO/FAO do set maximum of SFA at 10 E%. In adults, average SFA intakes vary between less than 9 to nearly 17 E% and nearly 30% of the reported average intakes were 15 E% or higher (line 620-629). In addition, in several economically developed countries where the SAFA has fallen close to 10%, the capacity to decrease SFA much further is limited without major changes in dietary patterns, and is only likely to result in modest reductions in TC and LDL-C. We therefore believe it is appropriate to set a goal for SFA at 10 E%. In table 6 (line 2915) the dietary reference value in the Netherlands is mentioned. However, these are the values from 2001, whereas the Dutch Health Council updated its advice in 2006. Therefore we recommend to use the most recent dietary guidelines. For saturated fat we can add that French food safety authority is currently reviewing the recommendations for the different fatty acids (expert Philippe Legrand)

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Centre National Interprofessionnel de l''Economie Laitiere	2. Categories, structure and function	Line 394 Protein palmitoylation should be mentioned as well since it is one of the post-translational modifications found on proteins (Bijlmakers and March, 2003). Line 396 The role of the position of fatty acids on the triglyceride backbone should be addressed. Addition of following paragraphs: The first key step governing the bioavailability and metabolic impact of dietary lipids is their digestion. Therefore, fats with the same fatty acid composition might differ in their metabolic impact, due to difference in triglyceride composition. Gastric lipase acts preferentially on fatty acids esterified at the sn-3 position, while pancreatic lipase has a preference for the sn-1 and sn-3 positions. In the chylomicrons, 75% of all fatty acids located at the sn-2 in dietary triacyl-glycerols are maintained at this sn-2 position in the triacyl-glycerols of chylomicrons (Michalski, 2009; Armand, 2007). Especially for babies, C16:0 at the sn-2 position instead of sn-1 or sn-3 position is beneficial. It has been shown in a study with preterm infants (>35 weeks of gestation) that both palmitic acid and calcium absorption are improved and are comparable to infants who were breast-fed when an infant formula was used having 74% of the C16:0 at the sn2 position compared to an infant formula with the same amount of C16:0 but only 28% was positioned at sn2 (Lucas et al., 1997). Furthermore, for formula fed infants it has been shown that palmitic acid at sn-2 (instead of palmitic acid at sn-1 and sn- 3) results in a significant increase in whole body bone mineral content and density, softer stool and less stool soap fatty acids (Kennedy et al., 1999b). Line 414 Saturated fats are essential for cell membranes. In our brain, the two dominant fatty acids are palmitic acid and steraric acid (both around 20-25%) (Carver et al., 2001). Classification of saturated fatty acids (SFA) only from a biochemical point of view is no longer relevant (Lecerf, 2009). SFA must be considered individually according to their chain length because they all have different effects. Short-chain and medium-chain SFA are metabolised differently than long-chain SFA. Metabolism of SFA should be included in this scientific opinion. Lines 423-424 The human body can synthesise substantial amounts of SFA. During a low fat / high carbohydrate diet up to 45% of the VLDL triglycerides can be newly synthesized. The preferentially formed fatty acid by mammalian fatty acid synthase is palmitate (C16:0) (Cooper Hudgins et al., 1996). Recent studies show that a lower fat-diet but rich in carbohydrates stimulated saturated fatty acid synthesis (especially palmitate) at high rates (Wilke et al., 2009).

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Centre National Interprofessionnel de l''Economie Laitiere	2. Categories, structure and function	Line 461 "The conversion of linoleic acid is very limited": what is limited? For children: Olegard and Svennerholm (1971) found no differences in plasma and erythrocyte phoshoglyceride AA of 3-month-old infants who either had been fed breast milk or were bottle fed with a milk formula with only traces of AA. This implies that LA is readily converted to AA in young infants. Line 475 Goyens et al. (2006) does not give conversion rates of 8-12%. It rather states that "After the low-LA diet, the percentage of dietary ALA incorporated into the ALA plasma phospholipid compartment was significantly increased by 4% compared with the control diet (P 0.012). In contrast, consumption of the high-ALA diet significantly decreased the incorporation by 8% and 12% compared with the control diet (P 0.001) and the low-LA diet (P 0.001), respectively." Lines 483-486 This paragraph should be extended and would fit better at line 441. Lines 487-492 Add this paragraph: Vaccenic acid (the predominant TFA from ruminants) is converted into rumenic acid (cis-9, trans-11 CLA). Endogenous synthesis from vaccenic acid (trans-11 18:1; VA), the major biohydrogenation intermediate produced in the rumen, is the predominant source of cis-9, trans-11 CLA in milk fat (Lock et al. 2004). Some animal studies show that vaccenic acid could have a beneficial effect on plasma triglycerides, LDL cholesterol and inflammation (Wang et al.,2008). Line 492 Add to the following sentence "TFA do not serve any vital functions" this: "in the present state of scientific data". If there are scientific publications attesting the absence of vital function of TFA, those references should be specified and added. Lines 494-495 Replace with following sentence: "CLA is a generic term for a group of..." The use of term "natural PUFA" is confusing here as it suggests that CLA is not from natural origin. Cis-9, trans-11 CLA (rumenic acid) is from natural origin as it comes from bioconversion of trans-vaccenic acid through the action of ¿9desaturases (Lock et al. 2004). By contrast, trans-10, cis-12 CLA is mainly produced by industrial processing. Line 497 The different types of cholesterol transporters should be explained within this scientific draft opinion (HDL, VLDL…) Line 502 Cholesterol is not "also" synthesised by the body but "mainly" synthesised by the body. Moreover, this endogenous production is regulated by the dietary intakes in healthy subjects.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Line 503 Cholesterol also plays an important role in “lipid raft” mechanisms for protein sorting at various stages of the secretory and endocytic pathways (van Meer and Sprong, 2004). Cholesterol is involved in the synthesis of vitamin D, in cell membranes construction, and participates to the digestion process with the creation of specific acids (AFSSA, 2001). Line 508 Phytosterols should be covered in this scientific draft opinion as EFSA recently released a scientific opinion on this topic.
Centre National Interprofessionnel de l''Economie Laitiere	2. Categories, structure and function	Lines 414-424 As for PUFA, additional information about structure and functions of SFA should be added. SFA are components of reserve triglycerides, glycerophospholipids and sphingolipids (membrane structure, myeline…). SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions. They have to be classified regarding their chain length: Structure and function of short and medium-chain fatty acids : Short and medium-chain SFA have a specific metabolism. As reported by Bach and Babayan (1982), triglycerides made of C6:0, C8:0, C10:0 and C12:0 (MCTs) have unique physical, chemical, and structural characteristics and their modifications (structured lipids) make special lipids tools for solving certain medical problems. They are indeed hydrolyzed both faster and more completely than long-chain triglycerides (LCTs). The products of this hydrolysis are absorbed as fast as glucose. MCTs are oxidized rapidly in the organism and they have a very low tendency to deposit as body fat. As reported by Sengupta et al. (2006), short-chain butyric acid is likely to have a protective function against colon cancer (inhibition of tumour proliferation, apoptosis induction). Short and medium-chain SFA have a hypocholesterolemic effect at physiological dose. This effect of diets high in C8:0 and C10:0 was shown in humans by Hashim (1960). Mediumchain SFA have also a beneficial role in adiposis. The human study of Tsuji et al. (2001) suggests weight loss with a diet high in medium-chain fatty acids. C6:0, C8:0 and C10:0 have a role in weight reduction, reduced fat deposition, decrease of VLDL production, hypocholesterolemic effect and antiviral role (Rioux et al., 2007; Legrand, 2008; Neyts et al., 2000). Structure and function of long-chain fatty acids Long-chain SFA are converted, in part, by ¿9-desaturation in monounsaturated fatty acids, but with significantly different effectiveness, increasing with the length of the chain. Stearic acid is the best substrate of ¿9-desaturase; and its conversion to oleic acid is important (Legrand, 2002; Legrand, 200;, Kritchevsky, 1988). The long-chain stearic acid has no negative effects on cholesterol level (Yu et al.; 1995) and, as presented by Kelly (2001), it has a beneficial effect on thrombogenic and atherogenic risk factors in males. Myristic acid has a positive action through an increase of HDL-cholesterol when consume at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000). Some SFA regulate specifically the activity of proteins by acylation (myristoylation, palmitoylation). Some studies show that, for example, myristic acid plays a key role through its ability to acylate proteins, a

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		reaction which is called N-terminal myristoylation. Various examples of important cellular regulations where the intervention of myristic acid is proven have been described (Casey, 1995; Rioux, 2002; Peitzsch, 1993; Borgese, 1996). Myristic acid also has a function in the biosynthesis of EPA and DHA (Dabadie et al., 2005; Rioux et al., 2005) and of sphyngolipids (Beauchamp et al., 2007). C20:0, C22:0, C24:0 have a role in nervous structure (myelinisation) (Bourre et al., 1976a and b). Line 430 No information is given to what extent humans can synthesise MUFA. Line 441 The role of n-3/n-6 PUFA ratio should be addressed. Because n-3 and n-6 PUFA are metabolised to LCPUFA by the same enzyme system, excess dietary LA (n-6) may decrease the formation of DHA (LCPUFA n-3) from LNA. In addition, AA (LCPUFA n-6) formation is lower when excess (n-3) LNA is provided (Uauy and Castillo, 2003). Both n-3 and n-6 LCPUFA are needed. However, inWestern diets with ample n-6 PUFA, the balance between tissue n-3 and n-6 LCPUFA might be sub-optimal (Lands, 2008).
Centre National Interprofessionnel de l''Economie Laitiere	3. Dietary sources and intake data	Line 572 The 18:1 TFA profiles of ruminant fat and hydrogenated vegetable oils show considerable overlap for many isomers. However, in contrast to ruminant fat non-palm-based-vegetable cooking oil can contain considerable amounts (0.4-2.7%) of C18:2 trans-cis, cis-trans and trans-trans, and C18:3 trans (up to 2.7%) (Tang, 2002). Partially hydrogenated vegetable oils can contain 1–65% of TFA, of which isomers of elaidic acid (trans-9 and trans-10 18:1) are the two most common isomers. On the other hand, dairy products contain smaller amounts of TFA (1–8% of total fatty acids in milk fat), and the main isomer is vaccenic acid (trans-11 18:1). Humans can utilize vaccenic acid, in the endogenous synthesis of rumenic acid (cis-9, trans-11 18:2), a fatty acid that may not have a negative effect on biomarkers of CVD risk. These two sources of TFA differ in their TFA isomer distribution and contribution to dietary intake, and, as a consequence, they also may have different biological effects (Chardigny et al., 2008) Lines 574 and 579 The actual content of TFA in wt% of total fatty acids in animal fat and industrial fat should be included in the table 4. The concentration of industrial hydrogenated TFA may be as high as 60%, whereas the maximum content of natural TFA in ruminant fat is about 6% (Stender et al., 2008). This information should also be included in the text in connection of the table 4. Line 583 In humans the conversion rate of trans-vaccenic acid to rumenic acid is around 19% (Turpeinen et al., 2002) to 20% (Lock et al., 2005). Line 593

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		In France, more recent data than Volatier (2000) and Deschamp (2005) is available. The INCA 2 study, for example, is more recent and could be used for this paragraph and the annexes (AFSSA, 2009b). Line 605 The presented data are not representative of the whole population but rather for a specific target group of the population (elderly in Portugal for example). Besides, some methods (like FFQ) are not accurate. Line 618 Data for the lowest intake in Portugal are not representative as it concerns the elderly population which is not an average but an extreme level. Besides, data are not very accurate as it is FFQ method. Line 627 In France, according to the INCA 2 study, the SFA intake is more around 15% than 17% (AFSSA, 2009b). Line 669 For those countries where separate intake data for industrial TFA and natural TFA are available, those should be provided (Craig-Schmidt, 2006; Jakobsen, 2007). Lines 676-678 The available data shows that total TFA intake has decreased close to WHO recommendation of 1 E%. This is due to reformulation of food products containing TFA originating from partially hydrogenated vegetable fats and oils. In the same report, WHO also mentions that most TFA are contributed by industrially hardened oils and that to promote cardiovascular health, diets should provide a very low intake of TFA from hydrogenated oils and fats (Uauy et al., 2009). Lines 681-682 Leave out "including … from other sources". Replace by (after line 684): In most European countries with a high TFA intake (>2.5 g/d), the major part of the TFA was from industrial sources (Craig-Schmidt, 2006). Line 690 "In adults, average intakes range from nearly 200 mg/day to 655 mg/day". This is not an average intake (replace "average" by "extreme range"): 655 mg/day concerns only one study for adult men.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Centre National Interprofessionnel de l''Economie Laitiere	3. Dietary sources and intake data	Lines 509-519 Why are a US database used and a European database reference not required? Dietary databases indeed exist in Europe, for example, CIQUAL 2008 in France. European intake data should be given, where possible. No distinction is made between short-chain, medium-chain and long-chain SFA (see our comments to line 530). Lines 513 The purpose of including table 2 is not clear. The selection of fats does not cover the major food groups in the diet. Other animal fats, such as tallow, fish fat and vegetable oils and margarine as well as shortenings for industrial processing should be included in table 2. Isomers of trans 18:1 should also be included in the table. Lines 514 In table 2 the ratio n-6/n-3 PUFA should be added as this is relevant information for the fatty acid balance of fats and oils. Lines 520-529 The Dutch NEVO table for fatty fish provides following data: total fat (g) 23.8, SFA 5.6, MUFA 10.5 PUFA 5.1 (high SFA fish (g total fat/g SFA) = Mackerel (30.7, 7.4); Eel (35, 8.7); Herring (14, 3.3); Salmon (14.2, 3.7)). These numbers differ quite a lot from the fatty fish data given in table 3. The basis for the selection of animal-derived food products is not entirely clear as, for example, eggs are missing. Besides, it is inconsistent to choose on one side only lean meat but on the other side present only standard butter and full fat milk. Semi-skimmed milk should be used instead as it is the most consumed type of milk in Europe. In France, for example, 73% of the milk consumed is semi-skimmed milk (data from CNIEL, Centre National Interprofessionnel de l''Economie Laitière, 2007). Line 523 Several dietary databases exist in Europe, for example, CIQUAL 2008 in France. Why was US data used? Line 530 The main characteristic of milk fat is the variety of fatty acids it contains: more than 400 different fatty acids. Milk fat contains typically around 65-70% SFA and 30-35% unsaturated fatty acids. Amongst saturated fatty acids in milk fat, there are typically around 10-13% short- and medium-chain SFA and typically around 50-55% long-chain SFA, including palmitic (min. 20 – max. 32%), myristic (min. 8 – max. 15%) and stearic acid (min. 6 – max. 13%). Milk fat is also relatively rich in the short-chain SFA C4:0 (butyric acid, min. 7 – max. 14%). Line 532 The lauric acid content in milk fat is more than 10-fold lower than that of coconut oil and palm kernel oil. Therefore, milk fat can - compared to these fats - not be called lauric acid rich (see table 2).

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		Lines 538-539 For example, dairy fat contains a substantial amount of oleic acid (Legrand, 2008). In the French population, dairy products are also the first contributor of MUFA according to the INCA 2 study (AFSSA, 2009b) Line 551 Appreciable amounts of ALA can also be found in animal and dairy fat. In France, for example, dairy products are the first contributor to ALA intake according the SUVIMAX adult consumption survey (SUVIMAX is a French survey done between 1994 and 2002 on 13 000 people) (Astorg et al., 2004) Line 568 There should not be a focus only on C18:1. Ruminant trans fats may contain up to 20% C16:1 (Stender et al., 2008) which shows that profiles of ruminant TFA and industrially produced TFA differ quite substantially (Mendis et al., 2008; Shingfield et al., 2008; IDF Bulletin 377, 2002). Lines 569-570 The TFA content of margarine and fat spreads may vary, depending on the proportion of partially hydrogenated oils used. However, recent analyses have shown that products with high levels of industrially produced TFA are still available on the market (Stender et al., 2008). The range of TFA content in wt% of total fatty acids of those products should be added.

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Centre National Interprofessionnel de l''Economie Laitiere	4. Overview of dietary reference values and recommendations	For the whole part 4 it is not clear on which criteria the chosen dietary guidelines were selected. Line 705 It is important to mention that some national recommendations in Europe such as in France take into account the different effects of TFA according to their sources (natural or industrial) (AFSSA, 2009a). Lines 749-756 The 2009 Joint FAO/WHO Expert Consultation on "Fats and Fatty Acids in Human Nutrition" sets dietary recommendations for total fat at 20-35 E% (acceptable macronutrient distribution range) compared to the population nutrient intake goal of 15-30 E% mentioned in the 2003 WHO report (Elmadfa and Kornsteiner, 2009). For children from 2 to 18 years, the recommendation for the total dietary fat intake is 30-40 E% depending on activity (Uauy and Dangour, 2009). Lines 771-775 Different SFA should be considered independently as there is evidence to indicate that certain SFA might have a beneficial role. Recent data show that the different SFA in milk fat have different effects on health. Several studies show that short-chain and medium-chain SFA do not have a negative impact on the blood lipid profile. They are easily digested and metabolised differently in the body compared to longer chain fatty acids. Certain long-chain SFA such as stearic acid act neutral on the cholesterol level. Myristic acid has various physiological roles in the body such as protein metabolism and the synthesis of n-3 long-chain fatty acids (Lecerf 2009, Legrand 2008, Rioux and Legrand 2007). Lines 776-779 Only the newest guideline available should be used. The Health Council of the Netherlands has published updated dietary reference intakes for fats and fatty acids for the Netherlands in 2006. It is stated there that "The average intake of saturated fatty acids in the diet needs to be cut from 13 to 14 per cent of energy intake to less than 10 per cent." Therefore, the dietary reference value for SFA for adults is < 10 E%. A mentioning of "as low as possible" cannot be found in the summary of the Dutch guidelines. Line 780 The 2009 Joint FAO/WHO Expert Consultation on "Fats and Fatty Acids in Human Nutrition" confirms that the intake of SFA should not exceed a maximum level of 10 E% (Elmadfa and Kornsteiner, 2009). Lines 918-921 Within the Nordic Nutrition Recommendations (2004), a maximum intake of 10 E% of SFA plus TFA is given. It is also mentioned that the intake of TFA from hydrogenated oils should be as "low as possible" (table 1).

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Centre National Interprofessionnel de l''Economie Laitiere	4. Overview of dietary reference values and recommendations	Lines 930-933 In 2005, AFSSA has done a review of studies on the metabolism and toxicity of TFA and their impact on health. They concluded that consumption of total TFA above 2% of total energy intake resulted in a significantly increased risk of CVD. At that time, they did not really distinguish the origin – natural or industrial - of TFA. New data concerning TFA content of food, population intakes as well as new scientific results from epidemiological and clinical studies have conducted AFSSA to reassess its previous conclusions (AFSSA, 2009a). AFSSA considers that: • The estimated average intake of TFA in the French population (around 1%) is lower than the threshold of 2% of the total energy intake. This is true for adults as well as for children independently of age and sex. The intake is lower than in 2005. • It is necessary to pursue the improvement of the food composition tables with regard to TFA. The contribution of different types of food to TFA intake should be considered in more detail, in particular the cheapest priced products, discount products, catering and small-scale ("artisanal") products etc. which are insufficiently known at this moment. • Considering the total TFA intake, the origin of the TFA, natural or industrial, should be taken into account. Concerning TFA of natural origin; consumption levels in the French population (0.5-0.9% of the total energy intake) are lower than levels identified as not posing a risk of CVD (1.5% of the total energy intake); TFA from industrial origin that are present in foods only have a technological function. Thus, AFSSA encourages the efforts to reduce the use of industrial TFA in human food, in order to reduce the risk of exposure. As a conclusion, the recommendation is to decrease TFA intake only concerns industrial TFA. Lines 934-937 Only the newest guideline available should be used. The Health Council of the Netherlands has published updated dietary reference intakes for fats and fatty acids for the Netherlands in 2006. It is stated there that “mono trans fatty acid intake needs to be brought down from 1 to 2 per cent to less than 1 per cent.” Table 6 (line 2915) has to be updated accordingly with the dietary reference value of TFA for adults < 1 E% (instead of “as low as possible”). There only the values for EPA and DHA refer to the 2006 Dutch guidelines. Line 938 The 2009 Joint FAO/WHO Expert Consultation on “Fats and Fatty Acids in Human Nutrition” confirms that the UL for TFA from ruminants and industrially produced sources should be <1% E. This recommendation is done with the focus on industrial trans fat being reduced to 0.5 E%. Ruminant trans fat intake was not recommended to be lowered because the average intake is at approximately 0.5 E% (Elmadfa and Kornsteiner, 2009). Line 939 The Nutritional Recommendations for the French Population (AFSSA, 2001) indicate that the limitation of exogenous cholesterol does not seem to be justified for the general population, as dietary cholesterol has only very limited impact on blood cholesterol. Line 944

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		The Nutritional Recommendations for the French Population (AFSSA, 2001) indicate that for older children and adolescents it does not seem reasonable to recommend fat intake below 30 E%. Line 969 The French recommendations for SFA intake for children are 8 to 12 E% (AFSSA, 2001). Line 1032 The French recommendations for cholesterol intake for children after 3 years of age are 300 mg/day (AFSSA, 2001). Line 1035 The recent AFSSA report should be taken into account for the overview of dietary recommendations in the table (AFSSA, 2009a). Thus, a distinction between natural and industrial TFA should be made. The WHO recommendation also concerns only TFA from industrial origin. This should be specified here (WHO, 2003).
Centre National Interprofessionnel de l''Economie Laitiere	5.1. Dietary requirements	line 1050 In purpose of defining dietary guidelines for nutrients such as fat, a transparent and systematic review of the scientific data has to be performed. In the present scientific overview "5.1 Dietary requirements", the method used for selecting scientific data is not presented. Line 1067 As mentioned in lines 614-616 "In adults average total fat intakes ranged from less than 30 E% to 47 E%. About 43% of the reported average data were between 30 and 35 E%; 13% were 40 E% or higher". This average value (in addition to lower and upper end) is also important as it shows that for adults the fat intake is over 30% in more than 50% of the average data reported. Line 1068-1070 This sentence should also be in the summary. Lines 1072-1073 "Such low fat intakes are highly unlikely in European countries": If very low fat intakes are very unlikely in Europe, the lowest recommended fat intake should not include this kind of low consumption as it is not representative. Under 30 E% of fat consumption, a balanced intake of the different fatty acid is indeed hard to achieve (AFSSA, 2001). Lines 1072-1074 Please provide references for this statement. It seems important to take into account that reducing total fat intake can lead to an increase in carbohydrate intake. A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005) and can lead to a high synthesis of palmitic acid. Recent studies show that a lower fat-diet but rich in carbohydrates stimulated saturated fatty acid synthesis - especially palmitate - at high rates

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		(Wilke et al., 2009). Line 1118 In lines 1109-1112 a clear example is given that diets containing less than 30 E% from fat can have negative effects on weight and vitamin intake. Only in the STRIP Trial evidence is provided that 25-30% has no negative effect on growth and neurological development. Furthermore, none of the studies presented found negative effects of higher fat intake (>35%) compared to lower fat intakes. Why than come to 25% as appropriate (line 1118) and in the table "Summary of DRVs for fats" (line 2055) to an RI of 20-35% for >4 year olds? It appears more prudent to advise a level of 30-40%. Line 1121 Previous studies have suggested that interventions to lower dietary fat content and improved fat quality lead to a compensatory increase in sucrose content. There has been a concern that dietary recommendations aimed at achieving a low saturated fat diet might lead to inappropriately increased sugar intake (Gibney et al., 1995) and some studies suggest that an inverse relationship exists between the intake of fat and simple sugars (Gibson, 1997; Lewis et al., 1992; Hackett, 1993). Other studies show that children with an intake of <30% of energy from fat consumed more carbohydrates (mainly sucrose) than those children whose diets contained >40% of energy from fat (Nicklas et al., 1992; Kennedy et al., 1999a). Moreover, restriction of fat in children is questionable (Olson, 2000). There is no evidence that low-fat diets in childhood will prevent atherosclerosis in adulthood. The claim that low-fat diets are safe in childhood is based on observations over a too short time to establish safety. If growth and development of children are not changed with low-fat diets, the proof of long-term safety is not substantiated. Lines 1139-1142 Editorial comment: "A LA intake of less … the form of LA." is also taken from Hansen et al., 1963. The reference should be cited after that sentence.

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Centre National Interprofessionnel de l''Economie Laitiere	5.10. Cancer	Line 1778 It should be added that it concerns TFA from industrial origin as the author indicate that ”a high serum level of trans monounsaturated fatty acids, presumably reflecting a high intake of industrially processed foods, is probably one factor contributing to increased risk of invasive breast cancer in women.” Line 1780 It is not “associated” as there is “limited evidence” (WCRF/AICR, 2007) Line 1781 There are only “limited-suggestive evidence” and no association (WCRF/AICR, 2007). Line 1785 The WCRF/AICR Expert Report “Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective” (five years of work driven by an independent panel of 21 world renowned scientists) is the most recent and complete synthesis of the available scientific data on this topic. It would be pertinent to refer to this report systematically. For example, WCRF judged that: - There is “limited evidence-no conclusion” to support a link between fats and oils or fatty acids composition and breast cancer risk, whatever the menopausal status. - There is “limited evidence-suggestive” that butter increases lung cancer risk - There is limited-suggestive evidence that foods containing animal fats increases colorectal cancer risk (not any word about olive oil) A new study from China suggests that increasing the intake of n-3 fatty acids, and decreasing intakes of n-6, could reduce the risk of colorectal cancer. The highest dietary ratio of n/3-n-6 was associated with a 95 per cent increase in the risk of women developing colorectal cancer, according to results of a study with 73.242 Chinese women participating in the Shanghai Women"s Health Study (Murff et al., 2009).

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Centre National Interprofessionnel de l''Economie Laitiere	5.2. Serum lipids and lipoproteins	Line 1223 In purpose of defining dietary guidelines for nutrients such as fat, a transparent and systematic review of the scientific data has to be performed. In the present scientific overview "5.2 Serum lipids and lipoproteins" the method used for selecting scientific data is not presented. Lines 1223-1228 The relevance of lipoprotein markers should be mentioned and discussed in relation to their relevance for hard endpoints. A randomized clinical trial (RCT) that shows a statistically significant benefit in disease mortality rather than a benefit for a surrogate endpoint is the pinnacle of evidence–based medicine. However, this is not always feasible. Cholesterol markers have been used as surrogate endpoints to study the effect of dietary fat in RCTs - especially as a marker for CVD risk. For many years, the only biomarkers of CHD risk recognized by health authorities have been total cholesterol and LDL cholesterol. Recently, the Expert Panel of the WHO Scientific Update on trans fatty acids pronounced the ratio of total cholesterol to HDL cholesterol as the "best single lipid predictor of CHD risk" (Uauy et al., 2009). Extensive research has changed the simplistic view of atherosclerosis (the major underlying cause for CHD (Das, 2007)) as a disorder of pathological lipid deposition to a more complex concept of an ongoing inflammatory response (Stoll and Bendszus, 2006). Therefore, effects on inflammatory markers are often included in newer RCTs. Lines 1231-1234 No references are provided for this statement. Lines 1229-1236 The conclusion of 5.2.1 is missing. According to EDA interpretation, these results show that at low intake of SFA (<10 E%) decreasing total fat intakes worsen the lipid profile leading to higher atherosclerosis risk (increases the total/HDL cholesterol ratio and TG, decreases serum concentrations of HDL cholesterol) (See also Mensink et al., 2003). The decrease of fat intake in men to 28% or 24% at stable body weight, leads to a decrease of LDL cholesterol but also to an decrease of HDL cholesterol, an increase of TG and LDL small and dense) (Lefebvre et al., 2005; Wood, 2006; Dreon, 1999).
Centre National Interprofessionnel de l''Economie Laitiere	5.2. Serum lipids and lipoproteins	Line 1237 Not only long-chain, but also medium-chain and short-chain fatty acids should be discussed for disease risk. Short and medium-chain fatty acids are not transported via the chylomicron system, and are not linked to changes is lipoprotein profiles. This is also relevant for paragraphs 5.8 and 6.2. Their effects on CAD and cholesterol have not been a dietary issue (German and Dillard, 2004). There is some evidence that short and medium-chain fatty acids have antiviral and antitumor activity (German and Dillard, 2004). SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions (Parodi, 2009). Short and medium-chain SFA have a hypocholesterolemic effect at physiological dose (this effect of diets high in C8 and C10 was shown in humans by Hashim (1960).

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		In a recent meta-analysis, the effects of the individual SFA on the serum lipoprotein profile have been estimated (Mensik et al., 2003). Iso-energetic replacement of carbohydrates with lauric, myristic and palmitic acids all resulted in increased total, LDL and HDL cholesterol concentrations. But as the cholesterol-raising effects of lauric acid were proportionally higher on HDL than on LDL cholesterol, replacement of carbohydrates by lauric acid resulted in a significantly lower total / HDL cholesterol ratio (The ratio of total to HDL cholesterol is a more powerful predictor of CHD risk than either total or LDL cholesterol levels (Stampfer et al., 1991)), which suggests a decrease in atherosclerotic risk. Stearic acid had the smallest effect on HDL cholesterol but lowered total and LDL cholesterol, and thus also decreased the total / HDL cholesterol ratio. Palmitic acid is the only fatty acids which increased the total / HDL cholesterol ratio (Mensink et al., 2003), fact confirmed in other studies (Salter et al., 1998; Billet MA, 2000). Stearic acid decreases LDL cholesterol, similar effect that oleic acid (Mensink, 2005). No differences between the effects of the different SFA on fasting serum triacylglycerol concentrations were detected (Mensink, 2003) (see especially figure 3 of this study). Myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol when consume at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Dabadie, 2005; Tholstrup et al., 1994 and 2003b). Negative effects of myristic acid that have been described were only the result of massive doses that are well above the usual consumption (Staiger K et al., 2006). Lines 1238-1241 The term “mixture” used here leads to an oversimplification and does not indicate which SFA are concerned. EFSA should indicate what the SFA involved are. Besides, SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions. Doses, population and references should also be indicated to support this statement. Line 1251 The analysis of sub fractions in subjects given low carbohydrate diets with either higher or lower content of SFA shows that the saturated fat intake results in an increase in the larger buoyant LDL rather than the smaller LDL particles. The small, dense LDL particles have been associated with increased risk of CVD, whereas large LDL particles have not (Krauss, 2006). Mozaffarian et al. (2004) also show that in postmenopausal women with relatively low total fat intake, a greater saturated fat intake is associated with less progression of coronary atherosclerosis. The proposed hypothesis is that a decrease in fat intake leads to worsen the lipid profile: decrease of HDL cholesterol, increase of TG and B-phenotype of LDL (small and dense LDL) (Dreon et al., 1998; Dreon et al., 1999; Krauss et al., 2006; Lefebvre et al., 2005).

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Centre National Interprofessionnel de l''Economie Laitiere	5.2. Serum lipids and lipoproteins	Line 1314 However, the intake of ruminant TFA is low in most populations. In the French diet, for example, the natural TFA intake ranges from 0.5-0.9% of the total energy intake (AFSSA, 2009a). This amount is far lower than the 3.7% tested in the Motard-Bélanger study (2008). The French intake values have been established by a consumption survey, INCA2 (2006-2007), on more than 4000 persons (AFSSA, 2009b). Lines 1326-1327 "The intervention studies do not provide evidence that a mixture of CLA isomers, cis-9, trans-11 CLA, or trans-10, cis-12 CLA have an impact on the serum lipoprotein profile." However, as explained in this scientific opinion on line 1319-1321 some studies are showing that cis-9, trans-11 is more favourable as compared with trans-10, cis-12 CLA on lipoprotein profile. The conclusion should be also that more studies are needed on purified CLA isomers. Line 1340 Kratz also conducted a systematic review on animal and human (intervention and observational) studies. Based on the results of these studies, the author found that an increase in dietary cholesterol intake resulted in only a minimal increase in the total/HDL cholesterol ratio, as most subjects can effectively adapt to higher levels of cholesterol intakes (Kratz, 2005). Lines 1342-1344 "Under iso-energetic conditions, the most favourable lipoprotein profile to lower atherosclerotic risk is achieved when a mixture of SFA and TFA is replaced by a mixture of oleic acid, linoleic acid and fish fatty acids. These effects are dosedependent". Those sentences should be removed from the scientific draft opinion: "mixture" does not mean anything and as shown in our previous comments it is not possible to consider SFA as a whole in terms of structure, metabolism and cellular functions. The same remark can be made for TFA: the difference should be made between industrial or natural TFA. The intake of ruminant TFA is indeed low in most populations. In the French diet, for example, the natural TFA intake ranges from 0.5-0.9% of the total energy intake (AFSSA, 2009a). This amount is far lower than the 3.7% tested in the Motard- Bélanger study (2008). The French intake values have been established by a consumption survey, INCA2 (2006-2007), on more than 4000 persons (AFSSA, 2009b). Lines 1341-1346 The effect of stearic acid is neutral (Yu et al., 1995). The effects are also dose dependant. Myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol when consumed at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000). Consumption of naturally occurring TFA at levels found in regular diets does not contribute to elevated risk of cardiovascular disease (see the European Parliament study, 2008).

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Centre National Interprofessionnel de l''Economie Laitiere	5.2. Serum lipids and lipoproteins	Lines 1253-1254 Cis-MUFA had similar effects on serum total cholesterol concentrations as carbohydrates in Hegsted et al. (1965). Thus, many researchers compared the effects on MUFA, in particular oleic acid, and carbohydrates on the distribution of cholesterol over the different lipoproteins (Grundy, 1986; Mensink and Katan, 1987). From these studies it appeared that effects of oleic acid and carbohydrates are indeed similar on total cholesterol concentrations, but that oleic acid increased HDL cholesterol and lowered VLDL cholesterol and triacylglycerol concentrations (Thijssen and Mensink, 2005). Line 1266 Please provide reference for this statement Lines 1281-1282 Remove: “like diets containing mixtures of SFA“. This sentence is not relevant in this part about TFA. Besides, the term “mixture” is not precise and does not mean anything about which fatty acids are concerned. Line 1284 Clarke (2009) is not an intervention study. It is just a simulation. Lines 1294-1296 Please provide reference for this statement. Lines 1297-1298 “In most of the human intervention studies reviewed above, the effects of trans-MUFA from hydrogenated vegetable oils were assessed”. This sentence should be the introduction of the paragraph as there are two parts here, one about industrially produced TFA, the other one about ruminant TFA, starting line 1298. Lines 1298-1299 Extreme high intakes of ruminant TFA (3.7 E% or 5 E%) indeed appear to have adverse effects on blood lipid profiles. However, these high levels of ruminant TFA cannot be reached with a normal diet. The habitual intake of ruminant TFA is far below this amount (Craig-Schmidt, 2006; Willett and Mozaffarian, 2008). On the other hand, ingesting 20-40g (> 5 E%) industrially produced TFA is not at all unrealistic (Stender et al., 2008). Why is this not mentioned? Line 1301 “3.7% of energy from TF” This high percentage does not reflect the usual intake in European countries. In France, TFA intake from natural origin represent only 0.5-0.9% of the total energy intake (AFSSA, 2009a). Line 1307 The European Parliament study on TFA (2008) aimed at providing background information to Members of the European

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		Parliament on TFA. The report highlighted the fact that although there was considerable scientific evidence showing a causative link between intake of industrially produced TFA and cardiovascular disease, scientific studies also revealed that consumption of naturally occurring TFA at levels found in regular diets do not contribute to elevated risk of cardiovascular disease. Therefore the authors mentioned that it is important to make a clear distinction between naturally occurring and industrially produced TFA when developing possible guidelines for action to reduce the intake of TFA. Any legal restrictions should be limited to industrially produced TFA. Line 1309 Remove "like diets containing mixtures of SFA". This sentence is not relevant in this part about TFA. Besides, the term "mixture" is not precise and does not mean anything about which fatty acids are concerned. Line 1311 "Consumption of diets containing trans-MUFA also…" "Also" has to be removed as TFA and some SFA do not have the same effects on HDL cholesterol. Lines 1312-1314 "The available evidence indicates that TFA from ruminant sources have similar adverse effects on blood lipids and lipoproteins to those from industrial sources". This is true only at very high levels of TFA intake, corresponding to diets with 3.7% of energy from TFA - indeed 9 litres of semi-skimmed milk, 4 kg of yoghurt or 800g of camembert cheese – as the average content of TFA in milk fat is 5.39% of total fatty acids (AFSSA, 2005).
Centre National Interprofessionnel de l''Economie Laitiere	5.3. Haemostatic function	Line 1362 If the studies are far from consistent, those sentences should be reformulated. Suggestion: "Although C12:0 to C16:0 SFA have been suspected to increase factor VII levels as compared to stearic acid (C18:0), the studies were far from consistent and no conclusion can be made. Moreover, in one study, post-prandial increases in activity of factor VII were less after consumption of meals rich in SFA, especially stearic acid, than after a consumption of meals enriched with unsaturated fatty acids (Thijssen and Mensink, 2005; Tholstrup et al., 2003a)." Line 1364 Relative to oleic acid, and unlike to n-6 PUFA, either medium-chain SFA or lauric or myristic or palmitic acids did not affect collagen-induced whole blood aggregation. Furthermore, ADP-induced platelet aggregation was not changed by medium-chain saturated fatty acids or myristic acid (Thijssen and Mensink, 2005; Temme et al., 1998). Line 1375 According to the Thijssen and Mensik (2005), thromboxanes (TX) and prostaglandins (PG), two eicosanoids, play an important role in the haemostatic balance. Both types of eicosanoids are synthesised from the C20 fatty acids, arachidonic acid (C20:4n-6) and EPA (C20:5n-3), after release from membrane phospholipids.

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		Eicosanoids of the n-2 series, such as TXA2, are synthesized from the n-6 arachidonic acid in platelets, while prostaglandins I2 (PGI2) is synthesised in the vascular endothelium. TXA2 is a potent vasoconstrictor and a stimulus for platelet aggregation, whereas PGI2 has opposite effects. Eicosanoids of the n-3 series such as TXA3 and PGI3 are principal metabolites of the n-3 fatty acid EPA. TXA3 is less active than TXA2, meaning than the vasoconstrictor effects due to n-6 fatty acids is higher than the ones induced by the n-3 fatty acids. The anti-aggregation effects of PGI3 and PGI2 are however comparable. Furthermore, n-6 PUFA increased urinary 11-dehydro-TXB2 excretion compared with saturated and monounsaturated fatty acids, which seemed to reflect an ADP-induced platelet aggregation (Lahoz et al., 1997; Thijssen and Mensik, 2005). Increased ADP-induced platelet aggregation is associated with increased atherosclerotic risk (Elwood et al., 1991; Thijssen and Mensik, 2005).
Centre National Interprofessionnel de l''Economie Laitiere	5.4. Inflammation and immne function	Line 1422 Additional information: A randomized, controlled, 3-diet, 3-period crossover study was published in 2007 in the American Journal of Clinical Nutrition (Zhao et al., 2007). Hypercholesterolemic subjects (n=23) were assigned to 3 experimental diets: a diet high in ALA (6.5 E%), a diet high in LA (12.6 E%), and an average American diet for 6 weeks. Results showed that increased intakes of dietary ALA elicited anti-inflammatory effects by inhibiting pro-inflammatory cytokine production (IL-6, IL-1ß and TNF-a) in cultured PBMCs (Peripheral Blood Mononuclear Cells). Changes in PBMC ALA and EPA were associated with beneficial changes in TNF-a release. ALA could thus have some effects of reduction in the production of inflammatory cytokines. Line 1426 This line correctly reports that TFA from hydrogenated sources (not ruminant sources) have been linked to adverse effects on inflammatory profile in epidemiological studies. Why is this not mentioned in the overall summary (line 129-146)? Lines 1434-1439 While it is mentioned in the conclusion that no consistent picture has emerged on effects on n-6 PUFA, no references are provided for that in part 5.4.1.
Centre National Interprofessionnel de l''Economie Laitiere	5.7. Body weight control and energy balance	Lines 1583-1593 Profound quantitative and qualitative changes have taken place in the last four decades in the Western industrialised world, particularly the rising intake of n-6 and declining intake of n-3 PUFA. A recent review (Ailhaud et al., 2008) suggests that this imbalance in PUFA intake is an emerging risk factor contributing in addition to long-term net positive energy balance. The authors propose that several aspects of unbalanced PUFA metabolism conspire to stimulate fat cell formation and to increase the prevalence of overweight and obesity such as low n-3 PUFA intake, overestimation of linoleic acid requirement and significant increase in the LA:LNA ratio. Thus, nutritional recommendation should not stress the n-6 PUFA over consumption, and promote instead a good equilibration between n-3 PUFA and n-6 PUFA.

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		Line 1618 It is important to add in the conclusion that based on some recent studies, nutritional recommendation on n-6 PUFA intake should not promote their over consumption but rather a good balance between n-3 PUFA and n-6 PUFA (Ailhaud et al., 2008).
Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Line 1626 General comment on this part about "Cardiovascular disease: the analysis on the effect of lipids on cardiovascular disease is quite poor compared to the analysis made on serum lipids and lipoproteins made in part 5.2. For example there is almost no data on stroke, which is actually a part of cardiovascular diseases and should be considered. Ecological studies suggest that saturated fat (mostly animal fat) is inversely associated with stroke. Some studies suggest that high intake of PUFA could have a negative effect on oxidation process and inflammatory mechanism involved in the stability of the plaque (Thies et al., 2003). Epidemiological studies show that saturated fat is either associated to a significant decreased risk of stroke (Framingham Study – ischemic stroke, Gilman, 1997; Nurses' Health study – hemorrhagic stroke, Iso, 2001; Japanese cohort of 4500 subjects - hemorrhagic stroke, Iso, 2003) or no related to the risk of stroke (Health professional Study, He, 2003) Line 1632 What are the selection criteria for selecting only those four studies? Line 1628 Concerning total fat, a reduction in fat intake is frequently construed as a recommendation in cardiovascular disease prevention. However, the question is now increasingly subject to debate (Mozaffarian et al., 2004). Line 1644 Howard et al. (2006) also shows that no benefit was observed in terms of coronary disease, cardiovascular or cerebrovascular disease with the decrease of fat intake and decrease of SFA to 9.5%. On the contrary, for some women with cardiovascular history, there was an increase of their cardiovascular disease risk linked to a decrease of lipids and SFA intake.
Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Line 1627 to 1644 (continuation of our comments already done on this lines) Elmadfa and Kornsteiner (2009) stated that "The meta-analysis by Skeaff and Miller (2009) demonstrated that the relative risk of CHD death in the highest (14–18 E%) category of SFA consumption was not significantly different from that in the lowest (7–11 E%) category. High compared with low SFA consumption was not significantly related with diverse risk factors of CHD events." Skeaff and Miller (2009) carried out a very recent and exhaustive review of cohort studies and controlled trials of dietary fats and CHD mortality or morbidity (search in the Cochrane Library, Cochrane reviews, article databases, systematic reviews, meta-analysis, etc.). 28 individual cohort studies were selected, in which there were about 6,600 CHD deaths amongst 280,000

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		participants during approximately 3.7 million person-years of follow-up. The authors state on p. 191: "According to the classic 'diet-heart' hypothesis, high intake of SFAs and cholesterol and low intake of PUFAs increase serum cholesterol levels and risk of CHD. However, few within-population studies have been able to demonstrate consistent associations with any specific dietary lipids, with the exception of trans fats and n-3 fatty acids. The available evidence from cohort and randomized controlled trials is unsatisfactory and unreliable to make judgment about and substantiate the effects of dietary fat on risk of CHD." Continuing further it is mentioned that "Furthermore, the evidence from cohort studies of dietary intake of fats and CHD is mostly unreliable (with few exceptions) because most studies have ignored the effects of measurement error and regression dilution bias." According to the results of this study : - Total fat: Intake of total fat was not significantly associated with CHD mortality, with a RR for highest compared with the lowest category of 0.94 (95% CI of 0.74-1.18, p=0.583); Intake of total fat was also unrelated to CHD events (RR 0.93, 95% CI 0.84-1.03, p=0.177); No significant association of total fat intake with CHD mortality (RR 1.06, 95% CI 0.88-1.28, p=0.517) or CHD events (RR 1.02, 95% CI 0.98-1.05, p=0.404) per 5% total energy increment in total fat intake ; Overall, the mean or median total fat intake in all cohort studies varied from 27-47% total energy. - SFA: Intake of SFA was not significantly associated with CHD mortality (RR 1.14, 95% CI 0.82-1.60, p=0.431) for highest compared to lowest category of SFA intake SFA intake was not significantly associated with CHD events (RR 0.93, 95% CI 0.83-1.05, p=0.269 for high vs. low category) No significant association of SFA intake with CHD death (RR 1.11, 95% CI 0.75-1.65, p=0.593) per 5% total energy increment in SFA intake Overall, the mean or median SFA intake in all cohort studies varied from 9-20% total energy. - MUFA: No significant association with CHD mortality / CHD deaths or CHD events - PUFA: Intake of PUFA was strongly significantly associated with CHD mortality with a RR 1.25, 95% CI 1.06-1.47, p=0.009) for highest compared to lowest category High compared with low PUFA intake was not associated with CHD events (RR 0.97, 95% CI 0.74-1.27, p=0.825) for highest compared to lowest category Significant lower risk of CHD events (RR 0.84, 95% CI 0.70-1.00, p=0.049) per 5% total energy increment in PUFA intake, but not with CHD mortality. Moreover, the results of this review showed that the RR of fatal CHD was not reduced by either low-fat diets or diets with a high polyunsaturated to saturated fat ratio (P/S ratio). to continue....

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Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Line 1627 to 1644 (end of our comment already done on those lines) In conclusion, the results of the studies described above tend to show that dietary intervention in healthy people of diets low in total fat or SFA were unsuccessful or provided insufficient evidence in reducing the incidence of cardiovascular disease (for more details, see also Ravnskov, 1998; Ramsden et al., 2009). It also appears that in coronary heart disease, the overconsumption of n-6 PUFA must not be encouraged since it can increase plaque instability (Lecerf, 2009). A recent systematic review of 146 prospective cohort studies and 43 RCTs from Europe, the US and Asia, investigating dietary factors related to CHD carried out by Mente et al. (2009) found insufficient evidence of an association between intake of total fat, SFA, PUFA, milk, meat and eggs and risk of CHD, but found protective associations for intakes of MUFA, fish, n-3 fatty acids, folate, whole grains, vitamins E and C, beta carotene, alcohol, fruit and fibre. A harmful association was found for TFA and foods with a high glycemic index. One of the conclusions stated "it is unlikely that modifying the intake of a few nutrients or foods would substantially influence coronary outcomes." In a review paper from Parodi (2009), 24 reports of 11 cohorts were the only prospective cohort studies found which evaluated the association between SFA and risk of CHD. Among these, 4 studies found a significantly positive association between SFA intake and risk of CHD, 3 found no association and 2 found a negative association. Overall, these results are inconsistent and do not provide convincing evidence of an association between SFA and risk of CHD. The evidence extracted by Gibson et al. (2009) from 12 major prospective cohort studies involving more than 280.000 subjects does not consistently demonstrate a direct relationship between the intake of dairy foods and increased risk of CVD (CHD, IHD or myocardial infarct), even though it is recognized that dairy fat is a contributor of saturated fat intake and excess saturated fat intakes has been associated with a higher incidence of CVD. The authors noted that "the studies available for examining the effect of dairy food consumption on CHD are too varied in design, quality and dietary assessment methodology to evaluate the nature of the relationship." From a meta-analysis of 15 cohort studies carried out by Elwood et al. (2008), the relative risk of stroke or heart disease in subjects with high milk or dairy consumption was 0.84 and 0.79 respectively, relative to the risk in those with low consumption.

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Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Line 1716 The words “of SFA” should be deleted as not all SFA have the same effects. TFA should be replaced by “industrial TFA”. All research (either epidemiological or interventional studies) tends to show that in healthy people diets low in SFA were unsuccessful in reducing the incidence of cardiovascular disease. In this context, the recommendation “as low as possible” has neither scientific value nor scientific justification. Line 1720 The genetic aspect should be included in this scientific draft opinion. There is a wide inter-individual variability in the response to dietary changes since genetic polymorphisms modulate the effects of nutrients. In terms of cardiovascular diseases, polymorphisms at multiple genes have been associated with differential effects in terms of lipid metabolism. Many examples can be given. A habitually low saturated fat diet is associated with a beneficial lipoprotein profile only among homozygotes of the APOC3 promoter 455T-625T polymorphism. (25% of the population) (Brown S et al., 2003). Another example of a well-documented nutrigenetic interaction is that of the apoAI gene which is a major structural and functional component of HDL cholesterol. A significant interaction between this polymorphism and PUFA intake in determining plasma HDL cholesterol concentration has been demonstrated in women in the Framingham Study. In carriers of the A allele, higher PUFA intakes (>8 E%) were shown to be associated with higher HDL cholesterol, whereas in G/G homozygotes, the opposite effect was observed (Lovegrove and Gitau, 2008). The concept of gene-environment interactions modulating common disease risk factors is now well founded and should be taken into consideration for more individually targeted approaches to disease prevention and therapy (Ordovas, 2009).
Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Lines 1627-1644 While CHD and ischemic stroke share some major risk factors, limited epidemiological data on dietary fats and vascular disease risk indicate that ischemic stroke is affected differently (different or opposite effect) by these fatty acids than is CHD. Specifically, the association between saturated fat / animal fat intake and ischemic stroke remains elusive (He et al. 2007). A clear distinction should be made between CVD, CHD and stroke, and the newest literature should be included. Besides, there are no intervention studies that analyse the effect of specific SFA variation: all those studies are based on a variation linked to the total fat intake or other fatty acids intakes (Lecerf, 2009). A growing body of evidence (observational, experimental, and clinical trial) indicates that the traditional diet – CHD paradigm (reduction of total and saturated fats and increase of carbohydrates) is inadequate. Mozaffarian (2005) conducted a systematic MEDLINE search in order to identify observational studies, clinical trials, experimental studies and reviews of dietary fats or carbohydrates and CHR risk in humans from 1966 to June 2005. The author conducted a careful selection based on relevance, strength (designs and methods), precision of effects, endpoints etc. Precedence was given to randomized controlled trials and prospective observational studies. Globally, results showed that there was little evidence that replacement of SFA with carbohydrates (which lowers total fat intake) reduced CHD risk. In details, results showed that: - For total fat: A lower total fat intake also reduce serum HDL cholesterol and increase TG, resulting in little overall net change in CHD risk in

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		men and potentially high risk CHD in women Reducing total fat leads to an increase in carbohydrates. A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain No positive relation in prospective cohorts and randomized trials between total fat reduction and incidence of CHD (ex: Nurses' Health Study) - For saturated fats: In metabolic trials, replacement of SFA with carbohydrates produce little change in the total:HDL ratio and specific SFA have differing effects on lipid physiology (Mensik 2003) The author found in this search: 2 prospective studies observing a positive relation between SFA intake and CHD (the Western Electric Study; the Ireland-Boston Diet-Heart Study) 3 other studies observing a positive relation from some CHD endpoints or in some population but not others (Framingham Study; Lipid Research Clinics, Cohort follow up study in the US) 7 other studies observing no significant association between SFA intake and CHD (including Nurses' Health Study, Puerto Rico Heart Health Program, Zutphen Study, Honolulu Program, the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study and 2 studies from Morris et al. 1977 and Gordon et al., 1981). Results of randomized trials replacing SFA with PUFA have been inconsistent No clinical trials have been specifically designed to evaluate the effect of replacing SFA with carbohydrates on the incidence of CHD. For more details on the effects of SFA on cardiovascular disease, see also Morris et al. (1977) and Gordon et al. (1981). A Cochrane and MEDLINE meta-analysis (Hooper et al., 2001 and 2002) based on 18,196 subjects with 30,901 personyears of observation from 27 randomised intervention trials, and a total of 40 intervention arms lasting at least 6 months found small effects with reduced or modified dietary fat on overall mortality (0.98, 95% CI 0.86-1.12), with a nonsignificant trend towards reduced cardiovascular mortality (0.91, 95% CI 0.77-1.07) or events (0.86; 95% CI 0.72-1.03). Results were different if participants were at high initial cardiovascular risk (0.84; 95% CI: 0.70-0.99), suggesting a protection from fat reduction, or at low cardiovascular risk (0.82; 0.56-1.20), suggesting no effect.

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Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Lines 1645-1694 (end of our comments already done on those lines) Skeaff and Miller (2009) conducted a very recent and exhaustive review of cohort studies and controlled trials of dietary fats and CHD mortality or morbidity (search in the Cochrane Library, Cochrane reviews, article databases, systematic reviews, meta-analysis, etc.). Results found that: - ALA: No association with intake of ALA and CHD death (RR 0.84, 95% CI 0.53-1.31, p=0.439) or CHD events (RR 1.05, 95% CI 0.78-1.42, p=0.730) for highest compared to lowest category of intake - LC PUFA: For cohort studies on n-3 LC PUFA, there were about 5,361 deaths amongst 256,000 participants during 4 million person-years of follow-up. Intake of n-3 LC PUFA or fish consumption were strongly associated with CHD mortality (RR 0.82, 95% Cl 0.71-0.94, p=0.006) for the highest compared with lowest category. Intake of n-3 LC PUFA was not associated with decreased risk of CHD events, non fatal CHD, total myocardial infarction, sudden cardiac death. For meta-analysis of randomized controlled trials of n-3 LC PUFA or fish and CHD, there were about 1,300 CHD deaths amongst 37,000 participants during 140,000 person-years of follow-up. Depending on the inclusion or exclusion of DART 2 study, risk ratios of the different parameters were totally changed (either a reduction or a non significance), limiting the interpretation.
Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Lines 1645-1694 (first part of our comments on those lines) Two other clinical trials of dietary supplementation with n-3 fatty acids exist: the DART and Lyon Heart studies, which are both secondary prevention trials. The DART study (Burr et al., 1989; Burr et al., 2007) was conducted in 2003 men after myocardial infarction, with 3 treatment arms: reduction of SFA intake to 30% energy with a P/S ration of 1:0, an increase of fatty fish (200-400 g/week), or an increase in cereal fibres to 18g/d. Advice to modify fat intake did not confer any obvious benefit, perhaps partly because it entailed greater changes in dietary habits and was therefore inadequately followed. Indeed, the advice about dietary fat did not achieve the expected differences in intakes, partly because of incomplete compliance with the advice and partly because of spontaneous changes in the control group. After 2 years, total fat accounted for 31.4% and 35.2% in the fat-advice and the non-fat advice groups respectively, and the corresponding mean P/S ratio were 0.8 and 0.4, although patients had regularly nutritional recommendations and advice given by a professionals of dietetics. However, the fish advice was associated with a 29% reduction in overall mortality, and this result was unaffected by adjusting variables at baseline. The Lyon Heart study (de Lorgeril et al., 1994; Renaud et al., 1994; de Lorgeril et al., 1999) was a randomized secondary prevention trial aimed at testing whether a Mediterranean type diet may reduce the rate of recurrence after a first myocardial infarction. The intervention diet was rich in a-linolenic acid (0.8% versus 0.3% in the control group) and provided around 30 E% from fat, 8 E% from SFA (12% in the control group), 13 E% from MUFA (10% in the control group)

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		and <4 E% from linoleic acid (n-6 LA) (>5% in the control group). The study lasted over a 5-year period and was conducted on 302 patients, compared to 303 control patients. There was also an additional follow-up after the 5 initial years for 46 months. The recurrent myocardial infarction, all cardiovascular events, and cardiac and total death were significantly decreased by > 70% in the group consuming the Mediterranean diet. These protective effects were not related to serum concentrations of total, LDL or HDL cholesterol. With regard to any association between the plasma concentration of major fatty acids and recurrence, only 18:3 n-3 and 22:6 n-3 tended to be inversely associated with recurrence of outcomes (p=0,11 and p=0,16 respectively) for myocardial infarction and cardiovascular deaths (no significance for other outcomes as heart failure, stroke, pulmonary or peripheral embolism, angina, thrombophlebitis). to continue...
Centre National Interprofessionnel de l''Economie Laitiere	5.8. Cardiovascular disease	Lines 1695-1700 Non-conjugated polyunsaturated TFA should be addressed in relation to disease risk. There is evidence that polyunsaturated TFA (trans 18:2) could pose a higher risk for ischemic heart disease and sudden cardiac death and CHD than monounsaturated TFA (trans 18:1) (Lemaitre et al., 2006; Baylin et al., 2003) These polyunsaturated TFA are from industrial sources, and can only be found in trace levels in ruminant fats. The WHO experts come to a different conclusion. They do make a difference between ruminant and industrially produced TFA: "The current growing body of evidence from controlled trials and observational studies indicates that TFA consumption from partially hydrogenated oils adversely affects multiple cardiovascular risk factors and contributes significantly to increased risk of CHD events. Although ruminant TFAs cannot be removed entirely from the diet, their intake is low in most populations and to date there is no conclusive evidence supporting an association with CHD risks in the amounts usually consumed. In contrast, TFA produced by partial hydrogenation of fats and oils should be considered industrial food additives having no demonstrable health benefits and clear risks to human health. The WHO Scientific Update on TFA concludes that restaurants and food manufacturers should avoid using industrially derived TFA in food products and that governments should take steps to support alternative fats or oils for TFA replacement. The evidence on the effects of TFA and disease outcomes strongly supports the need to remove PHVO from the human food supply." (Uauy et al., 2009). The limited data suggest that the experimental effects of ruminant and industrial TFA are similar when consumed in similar quantities, but very few persons consume such high levels of ruminant TFA, and observational studies do not support adverse CHD effects of ruminant TFA in amounts actually consumed (Mozaffarian et al., 2009). AFSSA concluded it its recent report that TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at very low level (0.5-0.9% of the total energy intake) (AFSSA, 2009a). Lines 1701-1712 Incidence of nonfatal and fatal CHD and stroke corresponding to the daily egg consumption was determined in 37,851 men and 80,082 women in 2 large prospective cohort studies (the Health Professionals Study and the Nurses Health study). Results showed no evidence for an overall significant association between egg consumption and risk of CHD and stroke, after adjustments for age, smoking and other potential CHD risk factors. The authors found a significant association between egg

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		consumption and CHD and stroke in only a subgroup of diabetic patients (thus with abnormalities in lipid metabolism). Kratz also conducted a systematic review on animal and human (intervention and observational) studies. A large number of observational studies (Honolulu Heart Study, the Puerto-Rico Heart Health Program, the Lipid Research Clinics Prevalence Follow-up Study, the Nurses Health Study, the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study and the Hawaii Cardiovascular Study) did not find any relationship between the intake of dietary cholesterol and the risk of CHD. Moreover, some other studies which primarily found a potential positive link between cholesterol intakes and CHD noted that the results were no longer significant after adjustments for consumption of vegetable, proteins and fibres, since they usually go hand in hand in individual diets (Kratz, 2005).
Centre National Interprofessionnel de l''Economie Laitiere	6.1. Total fat	Line 1831 As mentioned in this scientific draft opinion (lines 1068-1070), "Very low fat diets tend to increase the risk of an insufficient intake of PUFA, can impair the absorption of fat-soluble vitamins and be associated with insufficiency of other essential nutrients like zinc and B vitamins". Line 1840 The 20 E% does not seem representative of the European fat intake. Indeed according to Annex 1b of this draft opinion means intakes are almost all above 30 E%. The population with very lower intake is obviously a specific population (elderly men in Portugal). This confirms that the 20 E% as the lower bound of the intake range is not appropriate for the general population. Line 1843 The value of 20 E% is not appropriate: it is not representative of the low intake in Europe and according to AFSSA (2001) below 30 E% the balance of fatty acid intake (especially PUFA) is more difficult to achieve because of the composition of the usual food products. Besides, a growing body of evidence (observational, experimental, clinical trials and meta-analysis) indicates that the traditional diet – CHD paradigm (reduction of total and saturated fats and increase of carbohydrates) is inadequate. Firstly, no positive relation in prospective cohorts and randomized trials between total fat reduction and incidence of CHD has been found. Secondly, reducing total fat leads to increase carbohydrates (Skeaff and Miller, 2009; Mozaffarian 2005; Elmadfa and Kornsteiner, 2009; Hooper et al., 2001 and 2002; Gordon et al., 1981). A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005). Line 1847 The recommendation for total fat intake between 3 years and adult is missing.

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Centre National Interprofessionnel de l''Economie Laitiere	6.2. Saturated fatty acids (SAT)	Line 1851 It should be clear what is meant with expressions like “a mixture of SFA” and also if this mixture is nutritionally relevant. In order to determine dietary reference values for nutrients, it is important to be aware of that no biochemical measurement in the human body can represent the effect of various nutrients. It is thus of greatest importance to examine the direct relationship between consumption of the food item/nutrient and the risk of disease. In the second paragraph of 6.2, the main discussion is made on SFA and LDL cholesterol and not cardiovascular disease. According toWHO, the ratio of total and HDL cholesterol is a more reliable biomarker. Lines 1851-1852 This sentence does not represent the conclusion of the scientific opinion on line 1238-1240 where it is stated that “There s a positive, dose-dependent relationship between the intake of a mixture of SFA and serum LDL and HDL cholesterol cncentrations, when compared to carbohydrates. As a consequence, the total to HDL cholesterol ratio does not change”. Line 1855 However, Mozaffarian (2004) shows that in some case a greater saturated fat intake is associated with less progression of coronary atherosclerosis, whereas carbohydrate intake is associated with a greater progression. Besides, the Women Health Initiative (WHI) study indicates that no benefit was observed in terms of coronary disease, cardiovascular or cerebro-vascular disease with the decrease of fat intake and 9.5% SFA (Howard, 2006).
Centre National Interprofessionnel de l''Economie Laitiere	6.2. Saturated fatty acids (SAT)	Line 1858 The only link between SFA and health concerns total blood cholesterol (LDL and HDL). However, and contrary to carbohydrates which only increase the LDL cholesterol, SFA increase both HDL and LDL. Moreover, not all SFA but only a few have impacts on cholesterol so on this matter SFA cannot be considered as a whole. Only lauric, myristic and palmitic acids are known to increase total cholesterol, while short and medium-chain fatty acids are neutral (Mensink 2005 and 2003; Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Dabadie, 2005; Tholstrup et al., 1994 and 2003b; Hashim, 1960; Parodi, 2009). In a recent meta-analysis, the effects of individual SFA on the serum lipoprotein profile have been estimated (Mensik et al., 2003). Iso-energetic replacement of carbohydrates with lauric, myristic and palmitic acids all resulted in increased total, LDL and HDL cholesterol concentrations. But as the cholesterol-raising effects of lauric acid were proportionally higher on HDL than on LDL cholesterol, replacement of carbohydrates by lauric acid resulted in a significantly lower total / HDL cholesterol ratio, which suggests a decrease in atherosclerotic risk. Stearic acid had the smallest effect on HDL cholesterol but lowered total and LDL cholesterol, and thus also decreased the total / HDL cholesterol ratio. Palmitic acid is the only fatty acid which increased the total / HDL cholesterol ratio (Mensink, 2003), a fact confirmed in other studies (Salter et al., 1998; Billet MA, 2000). No differences between the effects of the different SFA on fasting serum triacylglycerol concentrations were detected (Mensink, 2003). Myristic acid had also been criticized for elevating cholesterol. However, these negative effects of myristic acid had been described with massive doses, doses which are much higher than usual consumption (Staiger et al., 2006). At usual level, myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol (Temme

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		et al., 1997; Salter et al., 1998; Billet MA, 2000; Legrand 2008). Moreover, myristic acid at usual level (1.6% total energy intake) is necessary for protein acylation and thus activation (Legrand, 2008).The recommendation should take into account the difference between the SFA. SFA have different physiological functions depending on their chain length, so should not be evaluated as one single group. Line 1868 A recommendation of "as low as possible" would not be achievable in normal life with a normal diet and would result in strict and impossible guidelines to follow. Moreover, this recommendation "as low as possible" is not relevant due to recent scientific results showing the real effect of SFA on health - especially on cardiovascular health (Skeaff and Miller, 2009; He et al., 2007; Mozaffarian, 2005, Hooper et al., 2001 and 2002) (for details see comments lines 1627-1644). A low intake of SFA could lead to an excessive consumption of MUFA and PUFA, which could represent health hazards, especially with regard to intake of n-6 fatty acids (Lecerf, 2009; Ailhaud, 2006).
Centre National Interprofessionnel de l''Economie Laitiere	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Line 1882 An optimal intake with a ratio of n-3/n-6 PUFA should also be fixed by EFSA, like it is the case in all the national and international recommendations. In order to determine this ratio, a conversion factor can be applied to LC PUFAs (LA to ARA, and ALA to EPA and DHA). For adults, this leads to an optimal n-6 PUFA: n-3 PUFA of 5:1. Line 1906 The Panel proposes to set an AI for linoleic acid of 4 E%, with no UL for total or any of the n-6 PUFA. There has been evidence on negative effects on health of excessive intakes of n-6 PUFA and lipid peroxidation (Elmadfa and Kornsteiner, 2009). It could also contribute to excessive adipose tissue development (Ailhaud, 2006; Lecerf, 2009). Therefore, an upper limit should be considered in order to protect consumer health.
Centre National Interprofessionnel de l''Economie Laitiere	6.5. Trans fatty acids (TFA)	Line 1948 According to the recent WHO scientific update on TFA the intake of ruminant TFA is low in most populations. To date there is no conclusive evidence supporting an association with coronary heart diseases risks in the amount of ruminant TFA consumed. In its recent report, AFSSA concluded that TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at very low level (0.5-0.9% of the total energy intake) (AFSSA, 2009a). The EFSA recommendation concerning the dietary reference value for TFAs should therefore deal only with industrially derived TFA. Line 1952 Intake of TFA from industrial origin should be as low as possible. Natural TFA should not be included in this recommendation. Line 1959 This is due to the reduction in industrial TFA.

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Centre National Interprofessionnel de l''Economie Laitiere	6.7. Cholesterol	Line 1971 It is important to add that dietary cholesterol has very little influence on plasma cholesterol values which are regulated by numerous genetic and nutritional factors through cholesterol absorption or synthesis. Besides, there is no strong evidence that dietary cholesterol is related to CHD or stroke (Hu andWillett, 2002; He et al., 2003)
Centre National Interprofessionnel de l''Economie Laitiere	References	Additional references (part 3) Gordon T, Kagan A, Garcia-Palmieri M, Kannel WB, Zukel WJ, Tillotson J, Sorlie P, Hjortland M (1981) Diet and itsrelation to coronary heart disease and death in three populations. Circulation Mar;63(3):500-15. Goyens PL, Spilker ME, Zock PL, Katan MB, Mensink RP (2005) Compartmental modeling to quantify a-linolenic acid conversion after longer term intake of multiple tracer boluses. J Lipid Res 46:1474-1483 Goyens PL, Spilker ME, Zock PL, Katan MB, Mensink RP (2006) Conversion of alpha-linolenic acid in humans is influenced by the absolute amounts of alpha-linolenic acid and linoleic acid in the diet and not by their ratio. Am J Clin Nutr 84(1):44-53. Griel AE, Kris-Etherton PM (2006) Beyond saturated fat: the importance of the dietary fatty acid profile on cardiovascular disease. Nutr Rev May;64(5 Pt 1):257-62. Grundy SM (1986) Comparison of monounsaturated fatty acids and carbohydrates for lowering plasma cholesterol. N Engl J Med Mar 20;314(12):745-8. Hackett A (1993) National and community food policies for dental health in the UK. In: Rugg-Gunn AJ, ed. Nutrition and Dental Health. Oxford, United Kingdom: Oxford University Press; 1993:410–451 Hashim SA, Arteaga A, Van Itallie TB (1960) Effect of a saturated medium-chain triglyceride on serum-lipids in man. Lancet May 21;1(7134):1105-8. Harvey-Berino J (1999) Calorie restriction is more effective for obesity treatment than dietary fat restriction. Ann Behav Med Spring;21(1):35-9 He K, Merchant A, Rimm EB, Rosner BA, Stampfer MJ, Willett WC (2003) Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study BMJ 327(7418): 777-82. He K, Xu Y, Van Horn L (2007) The puzzle of dietary fat intake and risk of ischemic stroke: a brief review of epidemiologic data. J Am Diet Assoc 107:287-295 Hegsted DM, McGandy RB, Myers ML, Stare FJ (1965) Quantitative effects of dietary fat on serum cholesterol in man, AJCN 17:281-295 Hooper L, Summerbell CD, Higgins JP, Thompson RL, Clements G, Capps N, Davey S, Riemersma RA, Ebrahim S (2002) In: The Cochrane Library, JohnWiley & Sons, Ltd, Chichester, UK. Hooper L, Summerbell CD, Higgins JP, Thompson RL, Clements G, Capps N, Davey S, Riemersma RA, Ebrahim (2001) Dietary fat intake and prevention of cardiovascular disease: systematic review, British Medical Journal, 322: 757-763 Howard BV, Van Horn L, Hsia J, Manson JE, Stefanick ML (2006) Low-fat dietary pattern and risk of cardiovascular disease: theWomen"s Health Initiative Randomized Controlled Dietary Modification Trial. JAMA Feb 8;295(6):655-66. Hu FB, Stampfer MJ, Rimm EB, Manson JE, Ascherio A, Colditz GA, Rosner BA, Spiegelman D, Speizer FE, Sacks FM, Hennekens CH, Willett WC (1999) A prospective study of egg consumption and risk of cardiovascular disease in men and women. JAMA Apr 21;281(15):1387-94.

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CF&R	6.1. Total fat	line 50 : Who in Europe is eating with only 20% of total fat in the food intake ? What amount of food intake would need someone eating a ration with only 20 % of the energy coming from fat ? How could we achieve it with the current food supply ? the recommandations from the different european institutes are between 30 an 35% for normal weight population. It should not been lowered to 20 to 35 % just like this.
CF&R	6.2. Saturated fatty acids (SAT)	line 67 : - "as low as possible" for SFA is an impossible guideline to use for labelling. When you want to express the proportion of the recommanded daily amount of SFA brought by a portion of any food, you cannot devide by zero or "as low as possible" example : 30 g of cheese brings 4 g of SFA - The actual GDA is 20 g for SFA. So 30 g of cheese brings 25% of the GDA. Quid with "as low as possible" ? I do not know how to calculate 4/"as low as possible" - there are SFA in animal products. The guideline "as low as possible" means "animal product as low as possible" Is it really what we want ? The european nutritionnal way is composed with animal products for centuries : has it fail for such a long time ? Where will we get calcium, iron, some vitamins from ?
Chambre Syndicale de la Margarine (French Margarine Association)	Conclusions and recommendations	For LA and ALA DRVs, EFSA recommends a level based on the lowest estimated mean intakes of the various populations groupe in Europe where deficiencies symptoms are not present. i.e. 4 E% for LA and 0.5 E% for ALA. However: - ALA/LA deficiency is virtually non-existent in Western societies - FAO/WHO recommands higher intakes of ALA/LA, because it has shown to reduce the risk of CV disease (LA 5-8 E% and ALA 1-2 E% for the total population) and not only to prevent ALA/LA deficiency. => higher intake would help th e population to reach dietary intakes recommanded to prevent the major chronic diseases, which are the real public health issue EFSA set DRV for LA to 4 E% and for 0,5 E%, wich leads to a ratio w6/w3 of 8. However recommandation asks for a higher ratio (5 for adults according to AFSSA, French agency for food safety).

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		For SAFA and TFA ,no accurate limit of intake have been set. Indeed EFSA recommans both to be as low as possible. But deleterious health effects of SAFA in cardiovascular disease have been shown, and we regret no upper limit have been set. EFSA states (ligne 60/63) that "There is also evidence from dietary intervention studies that decreasing the intakes of products rich in SAFA by replacement with products rich in n-6 PUFA [...]decreased the number of cardiovascular events." It should be highlighted than replacement by n-3 PUFA decreased the number of CV events too. In view of the importance of dietary cholesterol in the blood cholestreol concentration, we regrets however that EFSA does not propose a recommendation on cholesterol intake. The Panel also proposes to set the total fat recommanded intake between 20 E% and 35 E%, wich is not in line with the french recommandation of AFSSA.
EDA	2. Categories, structure and function	¿ Line 394 Protein myristoylation is only one way to regulate enzyme activity. Protein palmitoylation should be mentioned as well since it is one of the most frequent post-translational modifications found on proteins (Bijlmakers and March, 2003). ¿ Line 396 The role of the position of fatty acids on the triglyceride backbone should be addressed. Addition of following paragraphs: The first key step governing the bioavailability and metabolic impact of dietary lipids is their digestion. Therefore, fats with the same fatty acid composition might differ in their metabolic impact, due to difference in triglyceride composition. Gastric lipase acts preferentially on fatty acids esterified at the sn-3 position, while pancreatic lipase has a preference for the sn-1 and sn-3 positions. In the chylomicrons, 75% of all fatty acids located at the sn-2 in dietary triacyl-glycerols are maintained at this sn-2 position in the triacyl-glycerols of chylomicrons (Michalski, 2009; Armand, 2007). Especially for babies, C16:0 at the sn-2 position instead of sn-1 or sn-3 position is beneficial. It has been shown in a study with preterm infants (>35 weeks of gestation) that both palmitic acid and calcium absorption are improved and are comparable to infants who were breast-fed when an infant formula was used having 74% of the C16:0 at the sn2 position compared to an infant formula with the same amount of C16:0 but only 28% was positioned at sn2 (Lucas et al., 1997). Furthermore, for formula fed infants it has been shown that palmitic acid at sn-2 (instead of palmitic acid at sn-1 and sn-3) results in a significant increase in whole body bone mineral content and density, softer stool and less stool soap fatty acids (Kennedy et al., 1999b). ¿ Line 414 Saturated fats are essential for cell membranes. In our brain, the two dominant fatty acids are palmitic acid and steraric acid (both around 20-25%) (Carver et al., 2001). Classification of saturated fatty acids (SFA) only from a biochemical point of view is no longer relevant (Lecerf, 2009). SFA must be considered individually according to their chain length because they all have different effects. Short-chain and medium-chain SFA are metabolised differently than long-chain SFA. Metabolism of SFA should be included in this scientific opinion.

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		¿ Lines 423-424 The human body can synthesise substantial amounts of SFA. During a low fat / high carbohydrate diet up to 45% of the VLDL triglycerides can be newly synthesized. The preferentially formed fatty acid by mammalian fatty acid synthase is palmitate (C16:0) (Cooper Hudgins et al., 1996). Recent studies show that a lower fat-diet but rich in carbohydrates stimulated saturated fatty acid synthesis (especially palmitate) at high rates (Wilke et al., 2009).
EDA	2. Categories, structure and function	¿ Line 461 "The conversion of linoleic acid is very limited": what is limited? For children: Olegard and Svennerholm (1971) found no differences in plasma and erythrocyte phoshoglyceride AA of 3-month-old infants who either had been fed breast milk or were bottle fed with a milk formula with only traces of AA. This implies that LA is readily converted to AA in young infants. ¿ Line 475 Goyens et al. (2006) does not give conversion rates of 8-12%. It rather states that "After the low-LA diet, the percentage of dietary ALA incorporated into the ALA plasma phospholipid compartment was significantly increased by 4% compared with the control diet (P 0.012). In contrast, consumption of the high-ALA diet significantly decreased the incorporation by 8% and 12% compared with the control diet (P 0.001) and the low-LA diet (P 0.001), respectively." ¿ Lines 483-486 This paragraph should be extended and would fit better at line 441. ¿ Lines 487-492 Add this paragraph: Vaccenic acid (the predominant TFA from ruminants) is converted into rumenic acid (cis-9, trans-11 CLA). Endogenous synthesis from vaccenic acid (trans-11 18:1; VA), the major biohydrogenation intermediate produced in the rumen, is the predominant source of cis-9, trans-11 CLA in milk fat (Lock et al. 2004). Some animal studies show that vaccenic acid could have a beneficial effect on plasma triglycerides, LDL cholesterol and inflammation (Wang et al., 2008). ¿ Line 492 Add to the following sentence "TFA do not serve any vital functions" this: "in the present state of scientific data". If there are scientific publications attesting the absence of vital function of TFA, those references should be specified and added. ¿ Lines 494-495 Replace with following sentence: "CLA is a generic term for a group of..." The use of term "natural PUFA" is confusing here as it suggests that CLA is not from natural origin. Cis-9, trans-11 CLA (rumenic acid) is from natural origin as it comes from bioconversion of trans-vaccenic acid through the action of ¿9 desaturases

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		(Lock et al. 2004). By contrast, trans-10, cis-12 CLA is mainly produced by industrial processing. ¿ Line 497 The different types of cholesterol transporters should be explained within this scientific draft opinion (HDL, VLDL…) ¿ Line 502 Cholesterol is not "also" synthesised by the body but "mainly" synthesised by the body. Moreover, this endogenous production is regulated by the dietary intakes in healthy subjects. ¿ Line 503 Cholesterol also plays an important role in "lipid raft" mechanisms for protein sorting at various stages of the secretory and endocytic pathways (van Meer and Sprong, 2004). Cholesterol is involved in the synthesis of vitamin D, in cell membranes construction, and participates to the digestion process with the creation of specific acids (AFSSA, 2001). ¿ Line 508 Phytosterols should be covered in this scientific draft opinion as EFSA recently released a scientific opinion on this topic.
EDA	2. Categories, structure and function	¿ Lines 414-424 As for PUFA, additional information about structure and functions of SFA should be added. SFA are components of reserve triglycerides, glycerophospholipids and sphingolipids (membrane structure, myeline…). SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions. They have to be classified regarding their chain length: Structure and function of short and medium-chain fatty acids Short and medium-chain SFA have a specific metabolism. As reported by Bach and Babayan (1982), triglycerides made of C6:0, C8:0, C10:0 and C12:0 (MCTs) have unique physical, chemical, and structural characteristics and their modifications (structured lipids) make special lipids tools for solving certain medical problems. They are indeed hydrolyzed both faster and more completely than long-chain triglycerides (LCTs). The products of this hydrolysis are absorbed as fast as glucose. MCTs are oxidized rapidly in the organism and they have a very low tendency to deposit as body fat. As reported by Sengupta et al. (2006), short-chain butyric acid is likely to have a protective function against colon cancer (inhibition of tumour proliferation, apoptosis induction). Short and medium-chain SFA have a hypocholesterolemic effect at physiological dose. This effect of diets high in C8:0 and C10:0 was shown in humans by Hashim (1960). Medium-chain SFA have also a beneficial role in adiposis. The human study of Tsuji et al. (2001) suggests weight loss with a diet high in medium-chain fatty acids. C6:0, C8:0 and C10:0 have a role in weight reduction, reduced fat deposition, decrease of VLDL production, hypocholesterolemic effect and antiviral role (Rioux et al., 2007; Legrand, 2008; Neyts et al., 2000). Structure and function of long-chain fatty acids Long-chain SFA are converted, in part, by ¿9-desaturation in monounsaturated fatty acids, but with significantly different effectiveness, increasing with the length of the chain. Stearic acid is the best substrate of ¿9-desaturase; and its conversion to

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		oleic acid is important (Legrand, 2002; Legrand, 200;, Kritchevsky, 1988). The long-chain stearic acid has no negative effects on cholesterol level (Yu et al.; 1995) and, as presented by Kelly (2001), it has a beneficial effect on thrombogenic and atherogenic risk factors in males. Myristic acid has a positive action through an increase of HDL-cholesterol when consume at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000). Some SFA regulate specifically the activity of proteins by acylation (myristoylation, palmitoylation). Some studies show that, for example, myristic acid plays a key role through its ability to acylate proteins, a reaction which is called N-terminal myristoylation. Various examples of important cellular regulations where the intervention of myristic acid is proven have been described (Casey, 1995; Rioux, 2002; Peitzsch, 1993; Borgese, 1996). Myristic acid also has a function in the biosynthesis of EPA and DHA (Dabadie et al., 2005; Rioux et al., 2005) and of sphyngolipids (Beauchamp et al., 2007). C20:0, C22:0, C24:0 have a role in nervous structure (myelinisation) (Bourre et al., 1976a and b). ¿ Line 430 No information is given to what extent humans can synthesise MUFA. ¿ Line 441 The role of n-3/n-6 PUFA ratio should be addressed. Because n-3 and n-6 PUFA are metabolised to LCPUFA by the same enzyme system, excess dietary LA (n-6) may decrease the formation of DHA (LCPUFA n-3) from LNA. In addition, AA (LCPUFA n-6) formation is lower when excess (n-3) LNA is provided (Uauy and Castillo, 2003). Both n-3 and n-6 LCPUFA are needed. However, in Western diets with ample n-6 PUFA, the balance between tissue n-3 and n-6 LCPUFA might be sub-optimal (Lands, 2008).
EDA	3. Dietary sources and intake data	¿ Line 530 The main characteristic of milk fat is the variety of fatty acids it contains: more than 400 different fatty acids. Milk fat contains typically around 65-70% SFA and 30-35% unsaturated fatty acids. Amongst saturated fatty acids in milk fat, there are typically around 10-13% short- and medium-chain SFA and typically around 50-55% long-chain SFA, including palmitic (min. 20 – max. 32%), myristic (min. 8 – max. 15%) and stearic acid (min. 6 – max. 13%). Milk fat is also relatively rich in the short-chain SFA C4:0 (butyric acid, min. 7 – max. 14%). Degree of unsaturation Common name Structure Average (%) Min (%) Max (%) Saturated 69 57 80 Short and medium-chain Butyric acid C4:0 8.5 7 14 Caproic Acid C6:0 4 2 7 Caprylic Acid C8:0 1.8 1 3.5 Capric Acid C10:0 3 1.5 5 Long-chain Lauric Acid C12:0 3.6 2.5 7 Myristic Acid C14:0 10.5 8 15 Palmitic Acid C16:0 23.5 20 32

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		Stearic Acid C18:0 10 6 13 Odd-numbered 2.5 1.5 3.5 Branched 1.1 0.7 1.8 Other 0.7 0.3 2 Monounsaturated 27 18 36 Palmitoleic Acid C16:1 1.4 Oleic Acid C18:1 21 13 28 Other 5.5 Diunsaturated 2.5 1 4.3 Linoleic Acid (LA) C18:2 1.8 Other 0.7 Polyunsaturated 0.8 0.4 2 Linolenic Acid (ALA) C18:3 0.4 Other 0.4 Fatty acid derivatives 0.6 Keto 0.3 Hydroxy 0.3 Fatty alcohol 0 Fatty aldehyde 0 TOTAL 99.9 Table: Fatty acids in milk fat, Walstra P., Woulters J.T., Geurts T.J., 2006, Dairy Science and Technology, 2nd edition
EDA	3. Dietary sources and intake data	¿ Line 532 The lauric acid content in milk fat is more than 10-fold lower than that of coconut oil and palm kernel oil. Therefore, milk fat can - compared to these fats - not be called lauric acid rich (see table 2). ¿ Lines 538-539 For example, dairy fat contains a substantial amount of oleic acid (Legrand, 2008). In the French population, dairy products are also the first contributor of MUFA according to the INCA 2 study (AFSSA, 2009b) ¿ Line 545 Safflower oil should be included as an example since it is higher in linoleic acid (72%) than the product examples given. ¿ Line 551 Appreciable amounts of ALA can also be found in animal and dairy fat. In France, for example, dairy products are the first

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		contributor to ALA intake according the SUVIMAX adult consumption survey (SUVIMAX is a French survey done between 1994 and 2002 on 13 000 people) (Astorg et al., 2004) ¿ Line 568 There should not be a focus only on C18:1. Ruminant trans fats may contain up to 20% C16:1 (Stender et al., 2008) which shows that profiles of ruminant TFA and industrially produced TFA differ quite substantially (Mendis et al., 2008; Shingfield et al., 2008; IDF Bulletin 377, 2002). ¿ Lines 569-570 The TFA content of margarine and fat spreads may vary, depending on the proportion of partially hydrogenated oils used. However, recent analyses have shown that products with high levels of industrially produced TFA are still available on the market (Stender et al., 2008). The range of TFA content in wt% of total fatty acids of those products should be added. ¿ Line 572 The 18:1 TFA profiles of ruminant fat and hydrogenated vegetable oils show considerable overlap for many isomers. However, in contrast to ruminant fat non-palm-based-vegetable cooking oil can contain considerable amounts (0.4-2.7%) of C18:2 trans-cis, cis-trans and trans-trans, and C18:3 trans (up to 2.7%) (Tang, 2002). Partially hydrogenated vegetable oils can contain 1–65% of TFA, of which isomers of elaidic acid (trans-9 and trans-10 18:1) are the two most common isomers. On the other hand, dairy products contain smaller amounts of TFA (1–8% of total fatty acids in milk fat), and the main isomer is vaccenic acid (trans-11 18:1). Humans can utilize vaccenic acid, in the endogenous synthesis of rumenic acid (cis-9, trans-11 18:2), a fatty acid that may not have a negative effect on biomarkers of CVD risk. These two sources of TFA differ in their TFA isomer distribution and contribution to dietary intake, and, as a consequence, they also may have different biological effects (Chardigny et al., 2008) ¿ Lines 574 and 579 The actual content of TFA in wt% of total fatty acids in animal fat and industrial fat should be included in the table 4. The concentration of industrial hydrogenated TFA may be as high as 60%, whereas the maximum content of natural TFA in ruminant fat is about 6% (Stender et al., 2008). This information should also be included in the text in connection of the table 4. ¿ Line 583 In humans the conversion rate of trans-vaccenic acid to rumenic acid is around 19% (Turpeinen et al., 2002) to 20% (Lock et al., 2005).

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EDA	3. Dietary sources and intake data	¿ Line 593 In France, more recent data than Volatier (2000) and Deschamp (2005) is available. The INCA 2 study, for example, is more recent and could be used for this paragraph and the annexes (AFSSA, 2009b). ¿ Line 605 The presented data are not representative of the whole population but rather for a specific target group of the population (elderly in Portugal for example). Besides, some methods (like FFQ) are not accurate. ¿ Line 618 Data for the lowest intake in Portugal are not representative as it concerns the elderly population which is not an average but an extreme level. Besides, data are not very accurate as it is FFQ method. ¿ Line 627 In France, according to the INCA 2 study, the SFA intake is more around 15% than 17% (AFSSA, 2009b). ¿ Line 669 For those countries where separate intake data for industrial TFA and natural TFA are available, those should be provided (Craig-Schmidt, 2006; Jakobsen, 2007). ¿ Lines 676-678 The available data shows that total TFA intake has decreased close to WHO recommendation of 1 E%. This is due to reformulation of food products containing TFA originating from partially hydrogenated vegetable fats and oils. In the same report, WHO also mentions that most TFA are contributed by industrially hardened oils and that to promote cardiovascular health, diets should provide a very low intake of TFA from hydrogenated oils and fats (Uauy et al., 2009). ¿ Lines 681-682 Leave out “including … from other sources”. Replace by (after line 684): In most European countries with a high TFA intake (>2.5 g/d), the major part of the TFA was from industrial sources (Craig-Schmidt, 2006). ¿ Line 690 “In adults, average intakes range from nearly 200 mg/day to 655 mg/day”. This is not an average intake (replace “average” by “extreme range”): 655 mg/day concerns only one study for adult men.

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EDA	3. Dietary sources and intake data	¿ Lines 509-519 Why are a US database used and a European database reference not required? Dietary databases indeed exist in Europe, for example, CIQUAL 2008 in France. European intake data should be given, where possible. No distinction is made between short-chain, medium-chain and long-chain SFA (see table in comments to line 530). ¿ Lines 513 The purpose of including table 2 is not clear. The selection of fats does not cover the major food groups in the diet. Other animal fats, such as tallow, fish fat and vegetable oils and margarine as well as shortenings for industrial processing should be included in table 2. Isomers of trans 18:1 should also be included in the table. ¿ Lines 514 In table 2 the ratio n-6/n-3 PUFA should be added as this is relevant information for the fatty acid balance of fats and oils. ¿ Lines 520-529 The Dutch NEVO table for fatty fish provides following data: total fat (g) 23.8, SFA 5.6, MUFA 10.5 PUFA 5.1 (high SFA fish (g total fat/g SFA) = Mackerel (30.7, 7.4); Eel (35, 8.7); Herring (14, 3.3); Salmon (14.2, 3.7)). These numbers differ quite a lot from the fatty fish data given in table 3. The basis for the selection of animal-derived food products is not entirely clear as, for example, eggs are missing. Besides, it is inconsistent to choose on one side only lean meat but on the other side present only standard butter and full fat milk. Semi-skimmed milk should be used instead as it is the most consumed type of milk in Europe. In France, for example, 73% of the milk consumed is semi-skimmed milk (data from CNIEL, Centre National Interprofessionnel de l"Economie Laitière, 2007). ¿ Line 523 Several dietary databases exist in Europe, for example, CIQUAL 2008 in France. Why was US data used?

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EDA	4. Overview of dietary reference values and recommendations	¿ Lines 930-933 In 2005, AFSSA has done a review of studies on the metabolism and toxicity of TFA and their impact on health. They concluded that consumption of total TFA above 2% of total energy intake resulted in a significantly increased risk of CVD. At that time, they did not really distinguish the origin – natural or industrial - of TFA. New data concerning TFA content of food, population intakes as well as new scientific results from epidemiological and clinical studies have conducted AFSSA to reassess its previous conclusions (AFSSA, 2009a). AFSSA considers that: •The estimated average intake of TFA in the French population (around 1%) is lower than the threshold of 2% of the total energy intake. This is true for adults as well as for children independently of age and sex. The intake is lower than in 2005. •It is necessary to pursue the improvement of the food composition tables with regard to TFA. The contribution of different types of food to TFA intake should be considered in more detail, in particular the cheapest priced products, discount products, catering and small-scale ("artisanal") products etc. which are insufficiently known at this moment. •Considering the total TFA intake, the origin of the TFA, natural or industrial, should be taken into account. Concerning TFA of natural origin; consumption levels in the French population (0.5-0.9% of the total energy intake) are lower than levels identified as not posing a risk of CVD (1.5% of the total energy intake); TFA from industrial origin that are present in foods only have a technological function. Thus, AFSSA encourages the efforts to reduce the use of industrial TFA in human food, in order to reduce the risk of exposure. As a conclusion, the recommendation is to decrease TFA intake only concerns industrial TFA. ¿ Lines 934-937 Only the newest guideline available should be used. The Health Council of the Netherlands has published updated dietary reference intakes for fats and fatty acids for the Netherlands in 2006. It is stated there that “mono trans fatty acid intake needs to be brought down from 1 to 2 per cent to less than 1 per cent.” Table 6 (line 2915) has to be updated accordingly with the dietary reference value of TFA for adults < 1 E% (instead of “as low as possible”). There only the values for EPA and DHA refer to the 2006 Dutch guidelines. ¿ Line 938 The 2009 Joint FAO/WHO Expert Consultation on “Fats and Fatty Acids in Human Nutrition” confirms that the UL for TFA from ruminants and industrially produced sources should be <1% E. This recommendation is done with the focus on industrial trans fat being reduced to 0.5 E%. Ruminant trans fat intake was not recommended to be lowered because the average intake is at approximately 0.5 E% (Elmadfa and Kornsteiner, 2009). ¿ Line 939 The Nutritional Recommendations for the French Population (AFSSA, 2001) indicate that the limitation of exogenous cholesterol does not seem to be justified for the general population, as dietary cholesterol has only very limited impact on blood cholesterol. ¿ Line 944

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		The Nutritional Recommendations for the French Population (AFSSA, 2001) indicate that for older children and adolescents it does not seem reasonable to recommend fat intake below 30 E%. ¿ Line 969 The French recommendations for SFA intake for children are 8 to 12 E% (AFSSA, 2001). ¿ Line 1032 The French recommendations for cholesterol intake for children after 3 years of age are 300 mg/day (AFSSA, 2001). ¿ Line 1035 The recent AFSSA report should be taken into account for the overview of dietary recommendations in the table (AFSSA, 2009a). Thus, a distinction between natural and industrial TFA should be made. The WHO recommendation also concerns only TFA from industrial origin. This should be specified here (WHO, 2003).

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EDA	4. Overview of dietary reference values and recommendations	It is not clear on which criteria the chosen dietary guidelines were selected. ¿ Line 705 It is important to mention that some national recommendations in Europe such as in France take into account the different effects of TFA according to their sources (natural or industrial) (AFSSA, 2009a). ¿ Lines 749-756 The 2009 Joint FAO/WHO Expert Consultation on "Fats and Fatty Acids in Human Nutrition" sets dietary recommendations for total fat at 20-35 E% (acceptable macronutrient distribution range) compared to the population nutrient intake goal of 15-30 E% mentioned in the 2003 WHO report (Elmadfa and Kornsteiner, 2009). For children from 2 to 18 years, the recommendation for the total dietary fat intake is 30-40 E% depending on activity (Uauy and Dangour, 2009). ¿ Lines 771-775 Different SFA should be considered independently as there is evidence to indicate that certain SFA might have a beneficial role. Recent data show that the different SFA in milk fat have different effects on health. Several studies show that short-chain and medium-chain SFA do not have a negative impact on the blood lipid profile. They are easily digested and metabolised differently in the body compared to longer chain fatty acids. Certain long-chain SFA such as stearic acid act neutral on the cholesterol level. Myristic acid has various physiological roles in the body such as protein metabolism and the synthesis of n-3 long-chain fatty acids (Lecerf 2009, Legrand 2008, Rioux and Legrand 2007). ¿ Lines 776-779 Only the newest guideline available should be used. The Health Council of the Netherlands has published updated dietary reference intakes for fats and fatty acids for the Netherlands in 2006. It is stated there that "The average intake of saturated fatty acids in the diet needs to be cut from 13 to 14 per cent of energy intake to less than 10 per cent." Therefore, the dietary reference value for SFA for adults is < 10 E%. A mentioning of "as low as possible" cannot be found in the summary of the Dutch guidelines. ¿ Line 780 The 2009 Joint FAO/WHO Expert Consultation on "Fats and Fatty Acids in Human Nutrition" confirms that the intake of SFA should not exceed a maximum level of 10 E% (Elmadfa and Kornsteiner, 2009). ¿ Lines 918-921 Within the Nordic Nutrition Recommendations (2004), a maximum intake of 10 E% of SFA plus TFA is given. It is also mentioned that the intake of TFA from hydrogenated oils should be as "low as possible" (table 1).

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EDA	5.1. Dietary requirements	In purpose of defining dietary guidelines for nutrients such as fat, a transparent and systematic review of the scientific data has to be performed. In the present scientific overview "5.1 Dietary requirements", the method used for selecting scientific data is not presented. ¿ Line 1067 As mentioned in lines 614-616 "In adults average total fat intakes ranged from less than 30 E% to 47 E%. About 43% of the reported average data were between 30 and 35 E%; 13% were 40 E% or higher". This average value (in addition to lower and upper end) is also important as it shows that for adults the fat intake is over 30% in more than 50% of the average data reported. ¿ Line 1068-1070 This sentence should also be in the summary. ¿ Lines 1072-1073 "Such low fat intakes are highly unlikely in European countries": If very low fat intakes are very unlikely in Europe, the lowest recommended fat intake should not include this kind of low consumption as it is not representative. Under 30 E% of fat consumption, a balanced intake of the different fatty acid is indeed hard to achieve (AFSSA, 2001). ¿ Lines 1072-1074 Please provide references for this statement. It seems important to take into account that reducing total fat intake can lead to an increase in carbohydrate intake. A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005) and can lead to a high synthesis of palmitic acid. Recent studies show that a lower fat-diet but rich in carbohydrates stimulated saturated fatty acid synthesis - especially palmitate - at high rates (Wilke et al., 2009). ¿ Line 1118 In lines 1109-1112 a clear example is given that diets containing less than 30 E% from fat can have negative effects on weight and vitamin intake. Only in the STRIP Trial evidence is provided that 25-30% has no negative effect on growth and neurological development. Furthermore, none of the studies presented found negative effects of higher fat intake (>35%) compared to lower fat intakes. Why than come to 25% as appropriate (line 1118) and in the table "Summary of DRVs for fats" (line 2055) to an RI of 20-35% for >4 year olds? It appears more prudent to advise a level of 30-40%. ¿ Line 1121 Previous studies have suggested that interventions to lower dietary fat content and improved fat quality lead to a compensatory increase in sucrose content. There has been a concern that dietary recommendations aimed at achieving a low saturated fat diet might lead to inappropriately increased sugar intake (Gibney et al., 1995) and some studies suggest that an inverse relationship exists between the intake of fat and simple sugars (Gibson, 1997; Lewis et al., 1992; Hackett, 1993). Other studies show that children with an intake of <30% of energy from fat consumed more carbohydrates (mainly sucrose) than those children whose

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		diets contained >40% of energy from fat (Nicklas et al., 1992; Kennedy et al., 1999a). Moreover, restriction of fat in children is questionable (Olson, 2000). There is no evidence that low-fat diets in childhood will prevent atherosclerosis in adulthood. The claim that low-fat diets are safe in childhood is based on observations over a too short time to establish safety. If growth and development of children are not changed with low-fat diets, the proof of long-term safety is not substantiated. ¿ Lines 1139-1142 Editorial comment: "A LA intake of less … the form of LA." is also taken from Hansen et al., 1963. The reference should be cited after that sentence.
EDA	5.10. Cancer	¿ Line 1778 It should be added that it concerns TFA from industrial origin as the author indicate that "a high serum level of trans monounsaturated fatty acids, presumably reflecting a high intake of industrially processed foods, is probably one factor contributing to increased risk of invasive breast cancer in women." ¿ Line 1780 It is not "associated" as there is "limited evidence" (WCRF/AICR, 2007) ¿ Line 1781 There are only "limited-suggestive evidence" and no association (WCRF/AICR, 2007). ¿ Line 1785 The WCRF/AICR Expert Report "Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective" (five years of work driven by an independent panel of 21 world renowned scientists) is the most recent and complete synthesis of the available scientific data on this topic. It would be pertinent to refer to this report systematically. For example, WCRF judged that: There is "limited evidence-no conclusion" to support a link between fats and oils or fatty acids composition and breast cancer risk, whatever the menopausal status. There is "limited evidence-suggestive" that butter increases lung cancer risk. There is limited-suggestive evidence that foods containing animal fats increases colorectal cancer risk (not any word about olive oil). A new study from China suggests that increasing the intake of n-3 fatty acids, and decreasing intakes of n-6, could reduce the risk of colorectal cancer. The highest dietary ratio of n/3-n-6 was associated with a 95 per cent increase in the risk of women developing colorectal cancer, according to results of a study with 73.242 Chinese women participating in the Shanghai Women"s Health Study (Murff et al., 2009).

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EDA	5.2. Serum lipids and lipoproteins	¿ Line 1237 Not only long-chain, but also medium-chain and short-chain fatty acids should be discussed for disease risk. Short and medium-chain fatty acids are not transported via the chylomicron system, and are not linked to changes is lipoprotein profiles. This is also relevant for paragraphs 5.8 and 6.2. Their effects on CAD and cholesterol have not been a dietary issue (German and Dillard, 2004). There is some evidence that short and medium-chain fatty acids have antiviral and antitumor activity (German and Dillard, 2004). SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions (Parodi, 2009). Short and medium-chain SFA have a hypocholesterolemic effect at physiological dose (this effect of diets high in C8 and C10 was shown in humans by Hashim (1960). In a recent meta-analysis, the effects of the individual SFA on the serum lipoprotein profile have been estimated (Mensik et al., 2003). Iso-energetic replacement of carbohydrates with lauric, myristic and palmitic acids all resulted in increased total, LDL and HDL cholesterol concentrations. But as the cholesterol-raising effects of lauric acid were proportionally higher on HDL than on LDL cholesterol, replacement of carbohydrates by lauric acid resulted in a significantly lower total / HDL cholesterol ratio (The ratio of total to HDL cholesterol is a more powerful predictor of CHD risk than either total or LDL cholesterol levels (Stampfer et al., 1991)), which suggests a decrease in atherosclerotic risk. Stearic acid had the smallest effect on HDL cholesterol but lowered total and LDL cholesterol, and thus also decreased the total / HDL cholesterol ratio. Palmitic acid is the only fatty acids which increased the total / HDL cholesterol ratio (Mensink et al., 2003), fact confirmed in other studies (Salter et al., 1998; Billet MA, 2000). Stearic acid decreases LDL cholesterol, similar effect that oleic acid (Mensink, 2005). No differences between the effects of the different SFA on fasting serum triacylglycerol concentrations were detected (Mensink, 2003) (see especially figure 3 of this study). Myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol when consume at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Dabadie, 2005; Tholstrup et al., 1994 and 2003b). Negative effects of myristic acid that have been described were only the result of massive doses that are well above the usual consumption (Staiger K et al., 2006). ¿ Lines 1238-1241 The term “mixture” used here leads to an oversimplification and does not indicate which SFA are concerned. EFSA should indicate what the SFA involved are. Besides, SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions. Doses, population and references should also be indicated to support this statement. ¿ Line 1251 The analysis of sub fractions in subjects given low carbohydrate diets with either higher or lower content of SFA shows that the saturated fat intake results in an increase in the larger buoyant LDL rather than the smaller LDL particles. The small, dense LDL particles have been associated with increased risk of CVD, whereas large LDL particles have not (Krauss, 2006). Mozaffarian et al. (2004) also show that in postmenopausal women with relatively low total fat intake, a greater saturated fat intake is associated with less progression of coronary atherosclerosis. The proposed hypothesis is that a decrease in fat intake

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		leads to worsen the lipid profile: decrease of HDL cholesterol, increase of TG and B-phenotype of LDL (small and dense LDL) (Dreon et al., 1998; Dreon et al., 1999; Krauss et al., 2006; Lefebvre et al., 2005).
EDA	5.2. Serum lipids and lipoproteins	¿ Lines 1253-1254 Cis-MUFA had similar effects on serum total cholesterol concentrations as carbohydrates in Hegsted et al. (1965). Thus, many researchers compared the effects on MUFA, in particular oleic acid, and carbohydrates on the distribution of cholesterol over the different lipoproteins (Grundy, 1986; Mensink and Katan, 1987). From these studies it appeared that effects of oleic acid and carbohydrates are indeed similar on total cholesterol concentrations, but that oleic acid increased HDL cholesterol and lowered VLDL cholesterol and triacylglycerol concentrations (Thijssen and Mensink, 2005). ¿ Line 1266 Please provide reference for this statement ¿ Lines 1281-1282 Remove: "like diets containing mixtures of SFA". This sentence is not relevant in this part about TFA. Besides, the term "mixture" is not precise and does not mean anything about which fatty acids are concerned. ¿ Line 1284 Clarke (2009) is not an intervention study. It is just a simulation. ¿ Lines 1294-1296 Please provide reference for this statement. ¿ Lines 1297-1298 "In most of the human intervention studies reviewed above, the effects of trans-MUFA from hydrogenated vegetable oils were assessed". This sentence should be the introduction of the paragraph as there are two parts here, one about industrially produced TFA, the other one about ruminant TFA, starting line 1298. ¿ Lines 1298-1299 Extreme high intakes of ruminant TFA (3.7 E% or 5 E%) indeed appear to have adverse effects on blood lipid profiles. However, these high levels of ruminant TFA cannot be reached with a normal diet. The habitual intake of ruminant TFA is far below this amount (Craig-Schmidt, 2006; Willett and Mozaffarian, 2008). On the other hand, ingesting 20-40g (> 5 E%) industrially produced TFA is not at all unrealistic (Stender et al., 2008). Why is this not mentioned? ¿ Line 1301 "3.7% of energy from TF" This high percentage does not reflect the usual intake in European countries. In France, TFA intake from natural origin represent only 0.5-0.9% of the total energy intake (AFSSA, 2009a).

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		¿ Line 1307 The European Parliament study on TFA (2008) aimed at providing background information to Members of the European Parliament on TFA. The report highlighted the fact that although there was considerable scientific evidence showing a causative link between intake of industrially produced TFA and cardiovascular disease, scientific studies also revealed that consumption of naturally occurring TFA at levels found in regular diets do not contribute to elevated risk of cardiovascular disease. Therefore the authors mentioned that it is important to make a clear distinction between naturally occurring and industrially produced TFA when developing possible guidelines for action to reduce the intake of TFA. Any legal restrictions should be limited to industrially produced TFA. ¿ Line 1309 Remove "like diets containing mixtures of SFA". This sentence is not relevant in this part about TFA. Besides, the term "mixture" is not precise and does not mean anything about which fatty acids are concerned. ¿ Line 1311 "Consumption of diets containing trans-MUFA also…" "Also" has to be removed as TFA and some SFA do not have the same effects on HDL cholesterol.
EDA	5.2. Serum lipids and lipoproteins	¿ Lines 1312-1314 "The available evidence indicates that TFA from ruminant sources have similar adverse effects on blood lipids and lipoproteins to those from industrial sources". This is true only at very high levels of TFA intake, corresponding to diets with 3.7% of energy from TFA - indeed 9 litres of semi-skimmed milk, 4 kg of yoghurt or 800g of camembert cheese – as the average content of TFA in milk fat is 5.39% of total fatty acids (AFSSA, 2005). ¿ Line 1314 However, the intake of ruminant TFA is low in most populations. In the French diet, for example, the natural TFA intake ranges from 0.5-0.9% of the total energy intake (AFSSA, 2009a). This amount is far lower than the 3.7% tested in the Motard-Bélanger study (2008). The French intake values have been established by a consumption survey, INCA2 (2006-2007), on more than 4000 persons (AFSSA, 2009b). ¿ Lines 1326-1327 "The intervention studies do not provide evidence that a mixture of CLA isomers, cis-9, trans-11 CLA, or trans-10, cis-12 CLA have an impact on the serum lipoprotein profile." However, as explained in this scientific opinion on line 1319-1321 some studies are showing that cis-9, trans-11 is more favourable as compared with trans-10, cis-12 CLA on lipoprotein profile. The conclusion should be also that more studies are needed on purified CLA isomers.

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		¿ Line 1340 Kratz also conducted a systematic review on animal and human (intervention and observational) studies. Based on the results of these studies, the author found that an increase in dietary cholesterol intake resulted in only a minimal increase in the total/HDL cholesterol ratio, as most subjects can effectively adapt to higher levels of cholesterol intakes (Kratz, 2005). ¿ Lines 1342-1344 "Under iso-energetic conditions, the most favourable lipoprotein profile to lower atherosclerotic risk is achieved when a mixture of SFA and TFA is replaced by a mixture of oleic acid, linoleic acid and fish fatty acids. These effects are dose-dependent". Those sentences should be removed from the scientific draft opinion: "mixture" does not mean anything and as shown in our previous comments it is not possible to consider SFA as a whole in terms of structure, metabolism and cellular functions. The same remark can be made for TFA: the difference should be made between industrial or natural TFA. The intake of ruminant TFA is indeed low in most populations. In the French diet, for example, the natural TFA intake ranges from 0.5-0.9% of the total energy intake (AFSSA, 2009a). This amount is far lower than the 3.7% tested in the Motard-Bélanger study (2008). The French intake values have been established by a consumption survey, INCA2 (2006-2007), on more than 4000 persons (AFSSA, 2009b). ¿ Lines 1341-1346 The effect of stearic acid is neutral (Yu et al., 1995). The effects are also dose dependant. Myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol when consumed at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000). Consumption of naturally occurring TFA at levels found in regular diets does not contribute to elevated risk of cardiovascular disease (see the European Parliament study, 2008).

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EDA	5.2. Serum lipids and lipoproteins	In purpose of defining dietary guidelines for nutrients such as fat, a transparent and systematic review of the scientific data has to be performed. In the present scientific overview "5.2 Serum lipids and lipoproteins" the method used for selecting scientific data is not presented. ¿ Lines 1223-1228 The relevance of lipoprotein markers should be mentioned and discussed in relation to their relevance for hard endpoints. A randomized clinical trial (RCT) that shows a statistically significant benefit in disease mortality rather than a benefit for a surrogate endpoint is the pinnacle of evidence–based medicine. However, this is not always feasible. Cholesterol markers have been used as surrogate endpoints to study the effect of dietary fat in RCTs - especially as a marker for CVD risk. For many years, the only biomarkers of CHD risk recognized by health authorities have been total cholesterol and LDL cholesterol. Recently, the Expert Panel of the WHO Scientific Update on trans fatty acids pronounced the ratio of total cholesterol to HDL cholesterol as the "best single lipid predictor of CHD risk" (Uauy et al., 2009). Extensive research has changed the simplistic view of atherosclerosis (the major underlying cause for CHD (Das, 2007)) as a disorder of pathological lipid deposition to a more complex concept of an ongoing inflammatory response (Stoll and Bendszus, 2006). Therefore, effects on inflammatory markers are often included in newer RCTs. ¿ Lines 1231-1234 No references are provided for this statement. ¿ Lines 1229-1236 The conclusion of 5.2.1 is missing. According to EDA interpretation, these results show that at low intake of SFA (<10 E%) decreasing total fat intakes worsen the lipid profile leading to higher atherosclerosis risk (increases the total/HDL cholesterol ratio and TG, decreases serum concentrations of HDL cholesterol) (See also Mensink et al., 2003). The decrease of fat intake in men to 28% or 24% at stable body weight, leads to a decrease of LDL cholesterol but also to an decrease of HDL cholesterol, an increase of TG and LDL small and dense) (Lefebvre et al., 2005; Wood, 2006; Dreon, 1999).

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EDA	5.3. Haemostatic function	¿ Line 1362 If the studies are far from consistent, those sentences should be reformulated. Suggestion: "Although C12:0 to C16:0 SFA have been suspected to increase factor VII levels as compared to stearic acid (C18:0), the studies were far from consistent and no conclusion can be made. Moreover, in one study, post-prandial increases in activity of factor VII were less after consumption of meals rich in SFA, especially stearic acid, than after a consumption of meals enriched with unsaturated fatty acids (Thijssen and Mensink, 2005; Tholstrup et al., 2003a)." ¿ Line 1364 Relative to oleic acid, and unlike to n-6 PUFA, either medium-chain SFA or lauric or myristic or palmitic acids did not affect collagen-induced whole blood aggregation. Furthermore, ADP-induced platelet aggregation was not changed by medium-chain saturated fatty acids or myristic acid (Thijssen and Mensink, 2005; Temme et al., 1998). ¿ Line 1375 According to the Thijssen and Mensik (2005), thromboxanes (TX) and prostaglandins (PG), two eicosanoids, play an important role in the haemostatic balance. Both types of eicosanoids are synthesised from the C20 fatty acids, arachidonic acid (C20:4n-6) and EPA (C20:5n-3), after release from membrane phospholipids. Eicosanoids of the n-2 series, such as TXA2, are synthesized from the n-6 arachidonic acid in platelets, while prostaglandins I2 (PGI2) is synthesised in the vascular endothelium. TXA2 is a potent vasoconstrictor and a stimulus for platelet aggregation, whereas PGI2 has opposite effects. Eicosanoids of the n-3 series such as TXA3 and PGI3 are principal metabolites of the n-3 fatty acid EPA. TXA3 is less active than TXA2, meaning than the vasoconstrictor effects due to n-6 fatty acids is higher than the ones induced by the n-3 fatty acids. The anti-aggregation effects of PGI3 and PGI2 are however comparable. Furthermore, n-6 PUFA increased urinary 11-dehydro-TXB2 excretion compared with saturated and monounsaturated fatty acids, which seemed to reflect an ADP-induced platelet aggregation (Lahoz et al., 1997; Thijssen and Mensik, 2005). Increased ADP-induced platelet aggregation is associated with increased atherosclerotic risk (Elwood et al., 1991; Thijssen and Mensik, 2005).

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EDA	5.4. Inflammation and immne function	¿ Line 1422 Additional information: A randomized, controlled, 3-diet, 3-period crossover study was published in 2007 in the American Journal of Clinical Nutrition (Zhao et al., 2007). Hypercholesterolemic subjects (n=23) were assigned to 3 experimental diets: a diet high in ALA (6.5 E%), a diet high in LA (12.6 E%), and an average American diet for 6 weeks. Results showed that increased intakes of dietary ALA elicited anti-inflammatory effects by inhibiting pro-inflammatory cytokine production (IL-6, IL-1ß and TNF-a) in cultured PBMCs (Peripheral Blood Mononuclear Cells). Changes in PBMC ALA and EPA were associated with beneficial changes in TNF-a release. ALA could thus have some effects of reduction in the production of inflammatory cytokines. ¿ Line 1426 This line correctly reports that TFA from hydrogenated sources (not ruminant sources) have been linked to adverse effects on inflammatory profile in epidemiological studies. Why is this not mentioned in the overall summary (line 129-146)? ¿ Lines 1434-1439 While it is mentioned in the conclusion that no consistent picture has emerged on effects on n-6 PUFA, no references are provided for that in part 5.4.1.
EDA	5.7. Body weight control and energy balance	¿ Lines 1583-1593 Profound quantitative and qualitative changes have taken place in the last four decades in the Western industrialised world, particularly the rising intake of n-6 and declining intake of n-3 PUFA. A recent review (Ailhaud et al., 2008) suggests that this imbalance in PUFA intake is an emerging risk factor contributing in addition to long-term net positive energy balance. The authors propose that several aspects of unbalanced PUFA metabolism conspire to stimulate fat cell formation and to increase the prevalence of overweight and obesity such as low n-3 PUFA intake, overestimation of linoleic acid requirement and significant increase in the LA:LNA ratio. Thus, nutritional recommendation should not stress the n-6 PUFA over consumption, and promote instead a good equilibration between n-3 PUFA and n-6 PUFA. ¿ Line 1618 It is important to add in the conclusion that based on some recent studies, nutritional recommendation on n-6 PUFA intake should not promote their over consumption but rather a good balance between n-3 PUFA and n-6 PUFA (Ailhaud et al., 2008).

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EDA	5.8. Cardiovascular disease	¿ Line 1626 General comment on this part about "Cardiovascular disease: the analysis on the effect of lipids on cardiovascular disease is quite poor compared to the analysis made on serum lipids and lipoproteins made in part 5.2. For example there is almost no data on stroke, which is actually a part of cardiovascular diseases and should be considered. Ecological studies suggest that saturated fat (mostly animal fat) is inversely associated with stroke. Some studies suggest that high intake of PUFA could have a negative effect on oxidation process and inflammatory mechanism involved in the stability of the plaque (Thies et al., 2003). Epidemiological studies show that saturated fat is either associated to a significant decreased risk of stroke (Framingham Study – ischemic stroke, Gilman, 1997; Nurses' Health study – hemorrhagic stroke, Iso, 2001; Japanese cohort of 4500 subjects - hemorrhagic stroke, Iso, 2003) or no related to the risk of stroke (Health professional Study, He, 2003) ¿ Line 1632 What are the selection criteria for selecting only those four studies? ¿ Line 1628 Concerning total fat, a reduction in fat intake is frequently construed as a recommendation in cardiovascular disease prevention. However, the question is now increasingly subject to debate (Mozaffarian et al., 2004). ¿ Line 1644 Howard et al. (2006) also shows that no benefit was observed in terms of coronary disease, cardiovascular or cerebro-vascular disease with the decrease of fat intake and decrease of SFA to 9.5%. On the contrary, for some women with cardiovascular history, there was an increase of their cardiovascular disease risk linked to a decrease of lipids and SFA intake.
EDA	5.8. Cardiovascular disease	¿ Lines 1627-1644 A Cochrane and MEDLINE meta-analysis (Hooper et al., 2001 and 2002) based on 18,196 subjects with 30,901 person-years of observation from 27 randomised intervention trials, and a total of 40 intervention arms lasting at least 6 months found small effects with reduced or modified dietary fat on overall mortality (0.98, 95% CI 0.86-1.12), with a non-significant trend towards reduced cardiovascular mortality (0.91, 95% CI 0.77-1.07) or events (0.86; 95% CI 0.72-1.03). Results were different if participants were at high initial cardiovascular risk (0.84; 95% CI: 0.70-0.99), suggesting a protection from fat reduction, or at low cardiovascular risk (0.82; 0.56-1.20), suggesting no effect. Elmadfa and Kornsteiner (2009) stated that "The meta-analysis by Skeaff and Miller (2009) demonstrated that the relative risk of CHD death in the highest (14–18 E%) category of SFA consumption was not significantly different from that in the lowest (7–11 E%) category. High compared with low SFA consumption was not significantly related with diverse risk factors of CHD events." Skeaff and Miller (2009) carried out a very recent and exhaustive review of cohort studies and controlled trials of dietary fats and CHD mortality or morbidity (search in the Cochrane Library, Cochrane reviews, article databases, systematic reviews,

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		meta-analysis, etc.). 28 individual cohort studies were selected, in which there were about 6,600 CHD deaths amongst 280,000 participants during approximately 3.7 million person-years of follow-up. The authors state on p. 191: "According to the classic 'diet-heart' hypothesis, high intake of SFAs and cholesterol and low intake of PUFAs increase serum cholesterol levels and risk of CHD. However, few within-population studies have been able to demonstrate consistent associations with any specific dietary lipids, with the exception of trans fats and n-3 fatty acids. The available evidence from cohort and randomized controlled trials is unsatisfactory and unreliable to make judgment about and substantiate the effects of dietary fat on risk of CHD." Continuing further it is mentioned that "Furthermore, the evidence from cohort studies of dietary intake of fats and CHD is mostly unreliable (with few exceptions) because most studies have ignored the effects of measurement error and regression dilution bias." According to the results of this study Total fat: ¿Intake of total fat was not significantly associated with CHD mortality, with a RR for highest compared with the lowest category of 0.94 (95% CI of 0.74-1.18, p=0.583); ¿Intake of total fat was also unrelated to CHD events (RR 0.93, 95% CI 0.84-1.03, p=0.177); ¿No significant association of total fat intake with CHD mortality (RR 1.06, 95% CI 0.88-1.28, p=0.517) or CHD events (RR 1.02, 95% CI 0.98-1.05, p=0.404) per 5% total energy increment in total fat intake ; ¿Overall, the mean or median total fat intake in all cohort studies varied from 27-47% total energy. SFA: ¿Intake of SFA was not significantly associated with CHD mortality (RR 1.14, 95% CI 0.82-1.60, p=0.431) for highest compared to lowest category of SFA intake ¿SFA intake was not significantly associated with CHD events (RR 0.93, 95% CI 0.83-1.05, p=0.269 for high vs. low category) ¿No significant association of SFA intake with CHD death (RR 1.11, 95% CI 0.75-1.65, p=0.593) per 5% total energy increment in SFA intake ¿Overall, the mean or median SFA intake in all cohort studies varied from 9-20% total energy.
EDA	5.8. Cardiovascular disease	¿ Lines 1627-1644 continued: MUFA: ¿No significant association with CHD mortality / CHD deaths or CHD events PUFA: ¿Intake of PUFA was strongly significantly associated with CHD mortality with a RR 1.25, 95% CI 1.06-1.47, p=0.009) for highest compared to lowest category ¿High compared with low PUFA intake was not associated with CHD events (RR 0.97, 95% CI 0.74-1.27, p=0.825) for highest compared to lowest category

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		¿Significant lower risk of CHD events (RR 0.84, 95% CI 0.70-1.00, p=0.049) per 5% total energy increment in PUFA intake, but not with CHD mortality. Moreover, the results of this review showed that the RR of fatal CHD was not reduced by either low-fat diets or diets with a high polyunsaturated to saturated fat ratio (P/S ratio). In conclusion, the results of the studies described above tend to show that dietary intervention in healthy people of diets low in total fat or SFA were unsuccessful or provided insufficient evidence in reducing the incidence of cardiovascular disease (for more details, see also Ravnskov, 1998; Ramsden et al., 2009). It also appears that in coronary heart disease, the overconsumption of n-6 PUFA must not be encouraged since it can increase plaque instability (Lecerf, 2009). A recent systematic review of 146 prospective cohort studies and 43 RCTs from Europe, the US and Asia, investigating dietary factors related to CHD carried out by Mente et al. (2009) found insufficient evidence of an association between intake of total fat, SFA, PUFA, milk, meat and eggs and risk of CHD, but found protective associations for intakes of MUFA, fish, n-3 fatty acids, folate, whole grains, vitamins E and C, beta carotene, alcohol, fruit and fibre. A harmful association was found for TFA and foods with a high glycemic index. One of the conclusions stated "it is unlikely that modifying the intake of a few nutrients or foods would substantially influence coronary outcomes." In a review paper from Parodi (2009), 24 reports of 11 cohorts were the only prospective cohort studies found which evaluated the association between SFA and risk of CHD. Among these, 4 studies found a significantly positive association between SFA intake and risk of CHD, 3 found no association and 2 found a negative association. Overall, these results are inconsistent and do not provide convincing evidence of an association between SFA and risk of CHD. The evidence extracted by Gibson et al. (2009) from 12 major prospective cohort studies involving more than 280.000 subjects does not consistently demonstrate a direct relationship between the intake of dairy foods and increased risk of CVD (CHD, IHD or myocardial infarct), even though it is recognized that dairy fat is a contributor of saturated fat intake and excess saturated fat intakes has been associated with a higher incidence of CVD. The authors noted that "the studies available for examining the effect of dairy food consumption on CHD are too varied in design, quality and dietary assessment methodology to evaluate the nature of the relationship." From a meta-analysis of 15 cohort studies carried out by Elwood et al. (2008), the relative risk of stroke or heart disease in subjects with high milk or dairy consumption was 0.84 and 0.79 respectively, relative to the risk in those with low consumption.
EDA	5.8. Cardiovascular disease	¿ Lines 1627-1644 While CHD and ischemic stroke share some major risk factors, limited epidemiological data on dietary fats and vascular disease risk indicate that ischemic stroke is affected differently (different or opposite effect) by these fatty acids than is CHD. Specifically, the association between saturated fat / animal fat intake and ischemic stroke remains elusive (He et al. 2007). A clear distinction should be made between CVD, CHD and stroke, and the newest literature should be included. Besides, there are no intervention studies that analyse the effect of specific SFA variation: all those studies are based on a variation linked to the total fat intake or other fatty acids intakes (Lecerf, 2009). A growing body of evidence (observational, experimental, and clinical trial) indicates that the traditional diet – CHD paradigm (reduction of total and saturated fats and increase of carbohydrates) is inadequate.

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		Mozaffarian (2005) conducted a systematic MEDLINE search in order to identify observational studies, clinical trials, experimental studies and reviews of dietary fats or carbohydrates and CHR risk in humans from 1966 to June 2005. The author conducted a careful selection based on relevance, strength (designs and methods), precision of effects, endpoints etc. Precedence was given to randomized controlled trials and prospective observational studies. Globally, results showed that there was little evidence that replacement of SFA with carbohydrates (which lowers total fat intake) reduced CHD risk. In details, results showed that: For total fat: A lower total fat intake also reduce serum HDL cholesterol and increase TG, resulting in little overall net change in CHD risk in men and potentially high risk CHD in women Reducing total fat leads to an increase in carbohydrates. A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain No positive relation in prospective cohorts and randomized trials between total fat reduction and incidence of CHD (ex: Nurses' Health Study) For saturated fats: In metabolic trials, replacement of SFA with carbohydrates produce little change in the total:HDL ratio and specific SFA have differing effects on lipid physiology (Mensik 2003) The author found in this search: 2 prospective studies observing a positive relation between SFA intake and CHD (the Western Electric Study; the Ireland-Boston Diet-Heart Study) 3 other studies observing a positive relation from some CHD endpoints or in some population but not others (Framingham Study; Lipid Research Clinics, Cohort follow up study in the US) 7 other studies observing no significant association between SFA intake and CHD (including Nurses' Health Study, Puerto Rico Heart Health Program, Zutphen Study, Honolulu Program, the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study and 2 studies from Morris et al. 1977 and Gordon et al., 1981). Results of randomized trials replacing SFA with PUFA have been inconsistent No clinical trials have been specifically designed to evaluate the effect of replacing SFA with carbohydrates on the incidence of CHD. For more details on the effects of SFA on cardiovascular disease, see also Morris et al. (1977) and Gordon et al. (1981).

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EDA	5.8. Cardiovascular disease	¿ Lines 1645-1694 continued: Skeaff and Miller (2009) conducted a very recent and exhaustive review of cohort studies and controlled trials of dietary fats and CHD mortality or morbidity (search in the Cochrane Library, Cochrane reviews, article databases, systematic reviews, meta-analysis, etc.). Results found that: ALA: No association with intake of ALA and CHD death (RR 0.84, 95% CI 0.53-1.31, p=0.439) or CHD events (RR 1.05, 95% CI 0.78-1.42, p=0.730) for highest compared to lowest category of intake LC PUFA: For cohort studies on n-3 LC PUFA, there were about 5,361 deaths amongst 256,000 participants during 4 million person-years of follow-up. Intake of n-3 LC PUFA or fish consumption were strongly associated with CHD mortality (RR 0.82, 95% Cl 0.71-0.94, p=0.006) for the highest compared with lowest category. Intake of n-3 LC PUFA was not associated with decreased risk of CHD events, non fatal CHD, total myocardial infarction, sudden cardiac death. For meta-analysis of randomized controlled trials of n-3 LC PUFA or fish and CHD, there were about 1,300 CHD deaths amongst 37,000 participants during 140,000 person-years of follow-up. Depending on the inclusion or exclusion of DART 2 study, risk ratios of the different parameters were totally changed (either a reduction or a non significance), limiting the interpretation. ¿ Lines 1695-1700 Non-conjugated polyunsaturated TFA should be addressed in relation to disease risk. There is evidence that polyunsaturated TFA (trans 18:2) could pose a higher risk for ischemic heart disease and sudden cardiac death and CHD than monounsaturated TFA (trans 18:1) (Lemaitre et al., 2006; Baylin et al., 2003) These polyunsaturated TFA are from industrial sources, and can only be found in trace levels in ruminant fats. The WHO experts come to a different conclusion. They do make a difference between ruminant and industrially produced TFA: “The current growing body of evidence from controlled trials and observational studies indicates that TFA consumption from partially hydrogenated oils adversely affects multiple cardiovascular risk factors and contributes significantly to increased risk of CHD events. Although ruminant TFAs cannot be removed entirely from the diet, their intake is low in most populations and to date there is no conclusive evidence supporting an association with CHD risks in the amounts usually consumed. In contrast, TFA produced by partial hydrogenation of fats and oils should be considered industrial food additives having no demonstrable health benefits and clear risks to human health. The WHO Scientific Update on TFA concludes that restaurants and food manufacturers should avoid using industrially derived TFA in food products and that governments should take steps to support

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		alternative fats or oils for TFA replacement. The evidence on the effects of TFA and disease outcomes strongly supports the need to remove PHVO from the human food supply." (Uauy et al., 2009). The limited data suggest that the experimental effects of ruminant and industrial TFA are similar when consumed in similar quantities, but very few persons consume such high levels of ruminant TFA, and observational studies do not support adverse CHD effects of ruminant TFA in amounts actually consumed (Mozaffarian et al., 2009). AFSSA concluded it its recent report that TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at very low level (0.5-0.9% of the total energy intake) (AFSSA, 2009a).
EDA	5.8. Cardiovascular disease	¿ Lines 1645-1694 Two other clinical trials of dietary supplementation with n-3 fatty acids exist: the DART and Lyon Heart studies, which are both secondary prevention trials. The DART study (Burr et al., 1989; Burr et al., 2007) was conducted in 2003 men after myocardial infarction, with 3 treatment arms: reduction of SFA intake to 30% energy with a P/S ration of 1:0, an increase of fatty fish (200-400 g/week), or an increase in cereal fibres to 18g/d. Advice to modify fat intake did not confer any obvious benefit, perhaps partly because it entailed greater changes in dietary habits and was therefore inadequately followed. Indeed, the advice about dietary fat did not achieve the expected differences in intakes, partly because of incomplete compliance with the advice and partly because of spontaneous changes in the control group. After 2 years, total fat accounted for 31.4% and 35.2% in the fat-advice and the non-fat advice groups respectively, and the corresponding mean P/S ratio were 0.8 and 0.4, although patients had regularly nutritional recommendations and advice given by a professionals of dietetics. However, the fish advice was associated with a 29% reduction in overall mortality, and this result was unaffected by adjusting variables at baseline. The Lyon Heart study (de Lorgeril et al., 1994; Renaud et al., 1994; de Lorgeril et al., 1999) was a randomized secondary prevention trial aimed at testing whether a Mediterranean type diet may reduce the rate of recurrence after a first myocardial infarction. The intervention diet was rich in a-linolenic acid (0.8% versus 0.3% in the control group) and provided around 30 E% from fat, 8 E% from SFA (12% in the control group), 13 E% from MUFA (10% in the control group) and <4 E% from linoleic acid (n-6 LA) (>5% in the control group). The study lasted over a 5-year period and was conducted on 302 patients, compared to 303 control patients. There was also an additional follow-up after the 5 initial years for 46 months. The recurrent myocardial infarction, all cardiovascular events, and cardiac and total death were significantly decreased by > 70% in the group consuming the Mediterranean diet. These protective effects were not related to serum concentrations of total, LDL or HDL cholesterol. With regard to any association between the plasma concentration of major fatty acids and recurrence, only 18:3 n-3 and 22:6 n-3 tended to be inversely associated with recurrence of outcomes (p=0,11 and p=0,16 respectively) for myocardial infarction and cardiovascular deaths (no significance for other outcomes as heart failure, stroke, pulmonary or peripheral embolism, angina, thrombophlebitis).

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
EDA	5.8. Cardiovascular disease	¿ Lines 1701-1712 Incidence of nonfatal and fatal CHD and stroke corresponding to the daily egg consumption was determined in 37,851 men and 80,082 women in 2 large prospective cohort studies (the Health Professionals Study and the Nurses Health study). Results showed no evidence for an overall significant association between egg consumption and risk of CHD and stroke, after adjustments for age, smoking and other potential CHD risk factors. The authors found a significant association between egg consumption and CHD and stroke in only a subgroup of diabetic patients (thus with abnormalities in lipid metabolism). Kratz also conducted a systematic review on animal and human (intervention and observational) studies. A large number of observational studies (Honolulu Heart Study, the Puerto-Rico Heart Health Program, the Lipid Research Clinics Prevalence Follow-up Study, the Nurses Health Study, the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study and the Hawaii Cardiovascular Study) did not find any relationship between the intake of dietary cholesterol and the risk of CHD. Moreover, some other studies which primarily found a potential positive link between cholesterol intakes and CHD noted that the results were no longer significant after adjustments for consumption of vegetable, proteins and fibres, since they usually go hand in hand in individual diets (Kratz, 2005). ¿ Line 1716 The words “of SFA” should be deleted as not all SFA have the same effects. TFA should be replaced by “industrial TFA”. All research (either epidemiological or interventional studies) tends to show that in healthy people diets low in SFA were unsuccessful in reducing the incidence of cardiovascular disease. In this context, the recommendation “as low as possible” has neither scientific value nor scientific justification. ¿ Line 1720 The genetic aspect should be included in this scientific draft opinion. There is a wide inter-individual variability in the response to dietary changes since genetic polymorphisms modulate the effects of nutrients. In terms of cardiovascular diseases, polymorphisms at multiple genes have been associated with differential effects in terms of lipid metabolism. Many examples can be given. A habitually low saturated fat diet is associated with a beneficial lipoprotein profile only among homozygotes of the APOC3 promoter 455T-625T polymorphism. (25% of the population) (Brown S et al., 2003). Another example of a well-documented nutrigenetic interaction is that of the apoAI gene which is a major structural and functional component of HDL cholesterol. A significant interaction between this polymorphism and PUFA intake in determining plasma HDL cholesterol concentration has been demonstrated in women in the Framingham Study. In carriers of the A allele, higher PUFA intakes (>8 E%) were shown to be associated with higher HDL cholesterol, whereas in G/G homozygotes, the opposite effect was observed (Lovegrove and Gitau, 2008). The concept of gene-environment interactions modulating common disease risk factors is now well founded and should be taken into consideration for more individually targeted approaches to disease prevention and therapy (Ordovas, 2009).

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
EDA	6.1. Total fat	¿ Line 1831 As mentioned in this scientific draft opinion (lines 1068-1070), "Very low fat diets tend to increase the risk of an insufficient intake of PUFA, can impair the absorption of fat-soluble vitamins and be associated with insufficiency of other essential nutrients like zinc and B vitamins". ¿ Line 1840 The 20 E% does not seem representative of the European fat intake. Indeed according to Annex 1b of this draft opinion means intakes are almost all above 30 E%. The population with very lower intake is obviously a specific population (elderly men in Portugal). This confirms that the 20 E% as the lower bound of the intake range is not appropriate for the general population. ¿ Line 1843 The value of 20 E% is not appropriate: it is not representative of the low intake in Europe and according to AFSSA (2001) below 30 E% the balance of fatty acid intake (especially PUFA) is more difficult to achieve because of the composition of the usual food products. Besides, a growing body of evidence (observational, experimental, clinical trials and meta-analysis) indicates that the traditional diet – CHD paradigm (reduction of total and saturated fats and increase of carbohydrates) is inadequate. Firstly, no positive relation in prospective cohorts and randomized trials between total fat reduction and incidence of CHD has been found. Secondly, reducing total fat leads to increase carbohydrates (Skeaff and Miller, 2009; Mozaffarian 2005; Elmadfa and Kornsteiner, 2009; Hooper et al., 2001 and 2002; Gordon et al., 1981). A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005). ¿ Line 1847 The recommendation for total fat intake between 3 years and adult is missing.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
EDA	6.2. Saturated fatty acids (SAT)	¿ Line 1851 It should be clear what is meant with expressions like "a mixture of SFA" and also if this mixture is nutritionally relevant. In order to determine dietary reference values for nutrients, it is important to be aware of that no biochemical measurement in the human body can represent the effect of various nutrients. It is thus of greatest importance to examine the direct relationship between consumption of the food item/nutrient and the risk of disease. In the second paragraph of 6.2, the main discussion is made on SFA and LDL cholesterol and not cardiovascular disease. According to WHO, the ratio of total and HDL cholesterol is a more reliable biomarker. ¿ Lines 1851-1852 This sentence does not represent the conclusion of the scientific opinion on line 1238-1240 where it is stated that "There is a positive, dose-dependent relationship between the intake of a mixture of SFA and serum LDL and HDL cholesterol concentrations, when compared to carbohydrates. As a consequence, the total to HDL cholesterol ratio does not change". ¿ Line 1855 However, Mozaffarian (2004) shows that in some case a greater saturated fat intake is associated with less progression of coronary atherosclerosis, whereas carbohydrate intake is associated with a greater progression. Besides, the Women Health Initiative (WHI) study indicates that no benefit was observed in terms of coronary disease, cardiovascular or cerebro-vascular disease with the decrease of fat intake and 9.5% SFA (Howard, 2006).
EDA	6.2. Saturated fatty acids (SAT)	¿ Line 1858 The only link between SFA and health concerns total blood cholesterol (LDL and HDL). However, and contrary to carbohydrates which only increase the LDL cholesterol, SFA increase both HDL and LDL. Moreover, not all SFA but only a few have impacts on cholesterol so on this matter SFA cannot be considered as a whole. Only lauric, myristic and palmitic acids are known to increase total cholesterol, while short and medium-chain fatty acids are neutral (Mensink 2005 and 2003; Temme et al., 1997; Salter et al., 1998; Billet MA, 2000; Dabadie, 2005; Tholstrup et al., 1994 and 2003b; Hashim, 1960; Parodi, 2009). In a recent meta-analysis, the effects of individual SFA on the serum lipoprotein profile have been estimated (Mensik et al., 2003). Iso-energetic replacement of carbohydrates with lauric, myristic and palmitic acids all resulted in increased total, LDL and HDL cholesterol concentrations. But as the cholesterol-raising effects of lauric acid were proportionally higher on HDL than on LDL cholesterol, replacement of carbohydrates by lauric acid resulted in a significantly lower total / HDL cholesterol ratio, which suggests a decrease in atherosclerotic risk. Stearic acid had the smallest effect on HDL cholesterol but lowered total and LDL cholesterol, and thus also decreased the total / HDL cholesterol ratio. Palmitic acid is the only fatty acid which increased the total / HDL cholesterol ratio (Mensink, 2003), a fact confirmed in other studies (Salter et al., 1998; Billet MA, 2000). No differences between the effects of the different SFA on fasting serum triacylglycerol concentrations were detected (Mensink, 2003). Myristic acid had also been criticized for elevating cholesterol. However, these negative effects of myristic acid had been described with massive doses, doses which are much higher than usual consumption (Staiger et al., 2006). At usual level, myristic acid has no hypercholesterolemic effect but has rather positive action through an increase of HDL-cholesterol (Temme

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		et al., 1997; Salter et al., 1998; Billet MA, 2000; Legrand 2008). Moreover, myristic acid at usual level (1.6% total energy intake) is necessary for protein acylation and thus activation (Legrand, 2008). The recommendation should take into account the difference between the SFA. SFA have different physiological functions depending on their chain length, so should not be evaluated as one single group. ¿ Line 1868 A recommendation of "as low as possible" would not be achievable in normal life with a normal diet and would result in strict and impossible guidelines to follow. Moreover, this recommendation "as low as possible" is not relevant due to recent scientific results showing the real effect of SFA on health - especially on cardiovascular health (Skeaff and Miller, 2009; He et al., 2007; Mozaffarian, 2005, Hooper et al., 2001 and 2002) (for details see comments lines 1627-1644). A low intake of SFA could lead to an excessive consumption of MUFA and PUFA, which could represent health hazards, especially with regard to intake of n-6 fatty acids (Lecerf, 2009; Ailhaud, 2006).
EDA	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	¿ Line 1882 An optimal intake with a ratio of n-3/n-6 PUFA should also be fixed by EFSA, like it is the case in all the national and international recommendations. In order to determine this ratio, a conversion factor can be applied to LC PUFAs (LA to ARA, and ALA to EPA and DHA). For adults, this leads to an optimal n-6 PUFA: n-3 PUFA of 5:1. ¿ Line 1906 The Panel proposes to set an AI for linoleic acid of 4 E%, with no UL for total or any of the n-6 PUFA. There has been evidence on negative effects on health of excessive intakes of n-6 PUFA and lipid peroxidation (Elmadfa and Kornsteiner, 2009). It could also contribute to excessive adipose tissue development (Ailhaud, 2006; Lecerf, 2009). Therefore, an upper limit should be considered in order to protect consumer health.
EDA	6.5. Trans fatty acids (TFA)	¿ Line 1948 According to the recent WHO scientific update on TFA the intake of ruminant TFA is low in most populations. To date there is no conclusive evidence supporting an association with coronary heart diseases risks in the amount of ruminant TFA consumed. In its recent report, AFSSA concluded that TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at very low level (0.5-0.9% of the total energy intake) (AFSSA, 2009a). The EFSA recommendation concerning the dietary reference value for TFAs should therefore deal only with industrially derived TFA. ¿ Line 1952 Intake of TFA from industrial origin should be as low as possible. Natural TFA should not be included in this recommendation. ¿ Line 1959 This is due to the reduction in industrial TFA.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
EDA	6.7. Cholesterol	¿ Line 1971 It is important to add that dietary cholesterol has very little influence on plasma cholesterol values which are regulated by numerous genetic and nutritional factors through cholesterol absorption or synthesis. Besides, there is no strong evidence that dietary cholesterol is related to CHD or stroke (Hu and Willett, 2002; He et al., 2003).
EDA	Conclusions and recommendations	¿ Line 1978 The 20 E% does not seem representative of the European fat intake. Indeed according to Annex 1b of this draft opinion means intakes are almost all above 30 E%. The population with very lower intake is obviously a specific population (elderly men in Portugal). This confirms that the 20 E% as the lower bound of the intake range is not adapted for the general population. ¿ Lines 1980-1981 The value of 20 E% is not appropriate: it is not representative of the low intake in Europe and according to AFSSA, 2001 below 30 E% the balance of fatty acid intake (especially PUFA) is more difficult to achieve because of the composition of the usual food products. Besides, a growing body of evidence (observational, experimental, clinical trials and meta-analysis) indicates that the traditional diet – CHD paradigm (reduction of total and saturated fats and increase of carbohydrates) is inadequate. First no positive relation in prospective cohorts and randomized trials between total fat reduction and incidence of CHD has been found. Second, reducing total fat leads to increase carbohydrates (Skeaff and Miller, 2009; Mozaffarian 2005; Elmadfa and Kornsteiner, 2009; Hooper et al., 2001 and 2002; Gordon et al., 1981). A high intake of carbohydrates (refined, high glycemic index) may adversely affect insulin homeostasis, satiety and weight gain (Mozaffarian, 2005). ¿ Lines 1985 The recommendation for total fat intake between 3 years and adult is missing. ¿ Lines 1992-1993 A recommendation of “as low as possible” would not be achievable in normal life with a normal diet and would result in strict and impossible guidelines to follow. Moreover, this recommendation “as low as possible” is not relevant due to recent scientific results showing the real effect of SFA on health - especially on cardiovascular health (Skeaff and Miller, 2009; He et al., 2007; Mozaffarian, 2005, Hooper et al., 2001 and 2002) (for details see comments lines 1627-1644). ¿ Lines 2001-2002 An optimal intake with a ratio of n-3/n-6 PUFA should also be fixed by EFSA, like it is the case in all the national and international recommendations. In order to determine this ratio, a conversion factor can be applied to LC PUFAs (LA to ARA, and ALA to EPA and DHA). For adults, this leads to an optimal n-6 PUFA: n-3 PUFA of 5:1.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
EDA	Conclusions and recommendations	¿ Line 2017 There has been evidence on negative effects on health of excessive intakes of n-6 PUFA and lipid peroxidation (Elmadfa and Kornsteiner, 2009). It could also contribute to excessive adipose tissue development (Ailhaud, 2006; Lecerf, 2009). Therefore, an upper limit should be considered in order to protect consumer health. ¿ Lines 2041-2042 The recommendation to reduced TFA intake to «as low as possible» should only concern industrial TFA. This has been recommended in numerous countries in Europe (Nordic Nutrition Recommendations, 2004; AFSSA, 2009b) as well as in the recent WHO scientific update on TFA (Uauy et al., 2009). The EFSA recommendation concerning the dietary reference value for TFA should therefore deal only with industrially produced TFA. ¿ Line 2055 An AI 4% of LA is indeed based on lowest estimated mean intakes in E% (Elmadfa and Kornsteiner, 2009). However, this is not the level at which overt deficiency symptoms occur (this level is at least 2-fold lower): ISSFAL http://www.issfal.org.uk/lipid-matters/issfal-policy-statements/statement-3-pufa-in-adults.html The authors of these adult studies generally concluded that LA intakes of 1.0-2.5 E% would meet requirements but this conclusion was based mostly on minimizing the plasma level of 20:3 w9 (mead acid; a presumed biochemical marker of n-6 PUFA deficiency). The clinical condition of the infants was also considered in one study but otherwise, in these studies, clinical status was not informative. Several authors specifically noted the difficulty in drawing conclusions about LA requirement from measuring plasma fatty acid profiles alone. On the basis of these results, it is concluded that 2 E% LA is adequate for healthy adult humans.
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ORGANISATION	CHAPTER TEXT	COMMENT TEXT
EFPRA	6.1. Total fat	Dear Madam, dear Sir, EFPRA, the European Animal Fat Processors and Renderers Association, has read with much interest EFSA's statement on dietary reference values for fat. First of all, we want to underline the point that EFPRA fully supports CLITRAVI's comments sent to EFSA on 15 October 2009. In addition to these comments, EFPRA want to highlight three further points: - On lines 66-67: Recent literature studies (available at the EFPRA secretariat) that also take the TFA content into account show very little or no effect from SFA on CHD. The problem of earlier studies on SFA is that often the "hidden" TFA content was not taken into account and/or the focus was limited to LDL effects. When TFA is not taken into account SFA will be assigned all the negative effect of TFA. Regarding cholesterol level the total HDL:ratio is the most important factor to predict effects on CHD and not only the LDL effects. Just taking HDL into account, SFA would be the healthiest fat. However the ratio predict that SF has no effect on risk of CHD. This is supported by the nurses health study 2005 (Harvard school of public health). SFA does not increase risk of heart disease of women and have little effect in men. - On lines 56-69: There is growing evidence that the CHD paradigm (or American paradox) is inadequate. In practice total fat was replaced by carbohydrates and not by PUFA. EFPRA is of the firm view that a reduction of SF (as low as possible) almost certainly will lead to an increase of intake of carbohydrates. A higher intake of carbohydrates does not improve the total HDL:ratio (Jacobsen et all 2009) and this could cause an even higher risk of CHD. - On lines 56-69: The body needs SFAs because they are necessary for building cell membranes, nervous structures, and phospholipids. As such SF intake at appropriate levels is essential for the body and human health. We trust that EFSA will give EFPRA's position its due consideration. Yours sincerely, Steve Woodgate and Johan van der Veen Technical Director and Scientific Expert EFPRA

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
ENSA	3. Dietary sources and intake data	Lines 685-692: These figures clearly show that European adults tend to have a too high intake of dietary cholesterol compared to recommendations to limit the intake of dietary cholesterol below 300mg/d (cf. lines 939 to 942). As the Panel concluded that there is a positive relationship between the intake of dietary cholesterol with serum LDL concentrations, the fact that the average intake of dietary cholesterol is too high in European countries reinforces the need for clear and understandable information about dietary cholesterol. DRV for dietary cholesterol would enable people to control their dietary cholesterol intake and therefore maintain a healthy cholesterol blood level.
ENSA	4. Overview of dietary reference values and recommendations	Lines 939-942: There are additional sources which recommend to limit the intake of dietary cholesterol below 300mg/d. ENSA calls on the EFSA to also make reference to the following ones: ¿European guidelines on cardiovascular disease prevention in clinical practice – Third Joint Task force of European and other Societies on Cardiovascular disease prevention in clinical practice, European Heart Journal 2003; 24,1601-1610 ¿ Belgian Superior Health Council (SHC) – Food recommendations for Belgium Revision November 2006 HGR 7145-2 ¿AHA Scientific statement – Diet and lifestyle recommendations revision 2006 –A scientific statement from the American Heart Association Nutrition Committee Circulation 2006; 114:82-96
ENSA	6. Data on which to base dietary reference values	Lines 1964 to 1972: ENSA believes that a DRV should be set also for dietary cholesterol. This is justified from a public health perspective given the fact that the negative effects of too high intakes of dietary cholesterol on health have clearly been demonstrated (cf. lines 1328 to 1340; 1701 to 1712; 1745 to 1751). In addition, ENSA sees an urgent need for a DRV to be set for dietary cholesterol in light of the Panel's conclusion that current average intake levels of dietary cholesterol among European adults are often well above the generally accepted and recommended intake limits (cf. lines 685 to 692 and lines 939 to 942). Furthermore, information on dietary cholesterol is a highly relevant marker for consumers to identify foods which are also high in saturated fats. From a consumer point of view, dietary cholesterol is far more easy to understand than the difference between healthy (unsaturated) and less healthy (saturated) fatty acids . Information on dietary cholesterol would enable consumers to make easier, quicker, and more informed food choices which fit in a healthy lifestyle. As a result, ENSA believes that the Panel should set a DRV for dietary cholesterol, which should be in line with the DRV for saturated fats – i.e. as low as possible, or at least in line with the generally accepted and recommended intake limits – i.e. max 300mg/day for adults.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
ENSA	Conclusions and recommendations	Lines 2047 to 2054: ENSA believes that a DRV should be set also for dietary cholesterol. This is justified from a public health perspective given the fact that the negative effects of too high intakes of dietary cholesterol on health have clearly been demonstrated (cf. lines 1328 to 1340; 1701 to 1712; 1745 to 1751). In addition, ENSA sees an urgent need for a DRV to be set for dietary cholesterol in light of the Panel's conclusion that current average intake levels of dietary cholesterol among European adults are often well above the generally accepted and recommended intake limits (cf. lines 685 to 692 and lines 939 to 942). Furthermore, information on dietary cholesterol is a highly relevant marker for consumers to identify foods which are also high in saturated fats. From a consumer point of view, dietary cholesterol is far more easy to understand than the difference between healthy (unsaturated) and less healthy (saturated) fatty acids. Information on dietary cholesterol would enable consumers to make easier, quicker, and more informed food choices which fit in a healthy lifestyle. As a result, ENSA believes that the Panel should set a DRV for dietary cholesterol, which should be in line with the DRV for saturated fats – i.e. as low as possible, or at least in line with the generally accepted and recommended intake limits – i.e. max 300mg/day for adults.
Food Standards Agency	1. Introduction	Introduction In EFSA opinions it is not always clear how evidence has been identified for inclusion. EFSA should consider including a section detailing the methodology used to review the scientific evidence which would provide a more transparent approach and more comprehensive review of the literature. This should include how they selected the studies to include and how study quality was assessed.
Food Standards Agency	3. Dietary sources and intake data	Section 3.2 Intake data This section refers to annex 2b, which details dietary intakes of ALA, EPA and DHA in different EU countries. The data presented is from a limited number of countries (Austria, France, Germany, NL and Sweden). With regards to EPA/DHA intakes we are not surprised that intakes are low in these countries. EFSA should seek out data from Mediterranean countries to improve the comparison. Data from the UK National Diet and Nutrition Survey (NDNS) is missing. Details can be found at http://www.food.gov.uk/science/dietarysurveys/ndnsdocuments/ The NDNS programme aims to provide comprehensive, cross-sectional information on the dietary habits and nutritional status of the population of Great Britain. The results of the surveys within the programme are used to develop nutrition policy at a national and local level and to contribute to the evidence base for Government advice on healthy eating. The UK would be happy to supply this information on request.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Food Standards Agency	4. Overview of dietary reference values and recommendations	Section 4.1.4.2 (p28) We note that several member states including the UK, the Netherlands and France have recommendations for EPA/DHA that are higher than the EFSA proposed DRV. The Netherlands (Health Council) recommend 450mg EPA and DHA, AFSSA (France) value of 500mg/day based on usual consumption. The UK recommendation is based on the Scientific Advisory Committee on Nutrition (SACN) recommendation of 450mg/day. SACN based on the balance of the scientific evidence from RCTS and observational studies and on two portions of fish, one oily (one portion is 2.8g DHA/EPA/week) and one white (one portion average 0.4g/DHA/EPA week). This is a weekly total of 3.2g/week which equates to 450mg/day. EFSA should revisit their opinion on the DRV for EPA/DHA with a view to increasing it to 450mg/day (also see comment on section 5.8.1.1)
Food Standards Agency	5.2. Serum lipids and lipoproteins	Section 5.2.2 serum lipids We note that several meta analyses are mentioned in the introduction to this section (5.2) but more details are required. In addition evidence from good quality prospective studies should be included. A list of references is included at the end of this section. For example in the review by Mensink et al (2003) the combined results of 60 randomised controlled dietary trials of the effects of dietary fatty acids and carbohydrates on the ratio of blood total to high density lipoprotein (HDL) cholesterol found that this ratio decreased when saturated fatty acids were replaced by cis-unsaturated fatty acids. Prospective cohort studies from various countries that followed people for a number of years demonstrate a strong positive association between blood cholesterol levels and the incidence of heart disease; those study populations with higher mean cholesterol levels experience higher heart disease mortality (Martin et al., 1986; Goldbourt et al., 1985; Reed et al., 1986; Rose & Shipley, 1986; Pocock et al., 1989). The randomised controlled trial remains the best study design for demonstrating cause effect relationships. Randomised controlled trials support the positive association between blood cholesterol levels and risk of developing heart disease. A review of 28 randomised controlled trials (Law et al., 1994) showed that most of the benefit in reduction of risk is achieved after two years, and the full benefit after five years. Some of the best evidence for the beneficial effects of lowering LDL-cholesterol levels on the risk of developing heart disease comes from randomised controlled trials of a family of LDL-cholesterol lowering drugs called statins. The combined results of 14 randomised controlled trials of statins with a total of 90,056 participants found that a reduction in LDL-cholesterol of 1 mmol/L sustained over a period of 5 years produces a reduction in major vascular events of 23% (Cholesterol Treatment Trialists' Collaborators, 2005). While the effect of reducing dietary intakes of saturated fat on LDL-cholesterol levels is much smaller than the effect of statin

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		treatment, a benefit remains for reducing population intakes of saturated fat and we believe that EFSA should be able to set an upper level based on the scientific evidence available. References Cholesterol Treatment Trialists' Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins. Lancet 2005;366:1267-78. Goldbourt V, Holtzman E, Neufeld HN. Total and high density lipoprotein cholesterol in the serum and risk of mortality: evidence of a threshold effect. BMJ 1985;290:1239-43. Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? BMJ 1994;308:367-72. Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. Am J Clin Nutr 2003;77(5):1146-1155. Martin MJ, Hulley SB, Browner WS, Kuller LH, Wentworth D. Serum cholesterol, blood pressure, and mortality: implications from a cohort of 361,662 men. Lancet 1986;2:933-6. Reed D, Yano K, Kagan A. Lipids and lipoproteins as predictors of coronary heart disease, stroke and cancer in the Honolulu Heart Program. Am J Med. 1986;80(5):871-8. Rose G and Shipley M. Plasma cholesterol concentration and death from coronary heart disease: 10-year results of the Whitehall study. BMJ 1986;293:306-7. Pocock SJ, Shaper AG, Phillips AN. Concentrations of high density lipoprotein cholesterol, triglycerides, and total cholesterol in ischaemic heart disease. BMJ 1989;298:998-1002.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Food Standards Agency	5.8. Cardiovascular disease	First comment for this section (5.8): Section 5.8.1 CVD and saturated fat The evidence reviewed for beneficial effects of reducing saturated fat intake on risk of developing CVD in this section is incomplete, a list of suggested references is provided at the end of this response. Most noticeably the meta analysis by Truswell (1994) is missing. In this meta-analysis of 17 dietary trials (of which 16 were randomised) with a total of 92,623 participants (Truswell, 1994) found that a 10% fall in blood total cholesterol levels, achieved by dietary means, was associated with a 6% reduction in total mortality and a 13% reduction in coronary events. When the five trials with the largest reductions in total blood cholesterol levels (13%) were analysed separately then there was an 11% reduction in total mortality and a 30% reduction in coronary events. The Nurses' Health Study, a large prospective cohort study conducted in the USA, provides one of the best opportunities to examine the relationship between intake of saturated fat and the risk of developing heart disease. When 80,082 women were followed for 14 years, 939 new cases of coronary heart disease (CHD) were diagnosed (Hu et al., 1997). It was found that an increased intake of saturated or trans fat was associated with an increased risk of CHD while an increased intake of monounsaturated or polyunsaturated fat was associated with decreased risk of CHD. It was estimated that replacement of 5% energy from saturated fat with energy from unsaturated fat reduced CHD risk by 42%. When the 78,778 women remaining after 20 years were studied, 1,766 new cases of CHD were diagnosed (Oh et al., 2005). However, in this analysis the association between saturated fat and CHD risk was no longer significant, suggesting a weaker association between intake of saturated fat and risk of CHD than previously reported from epidemiological studies. The associations between trans fat and polyunsaturated fat and CHD risk persisted. Other prospective cohort studies on the relationship between intakes of saturated fat and the risk of developing heart disease have been carried out and these have been reviewed (Hu et al, 2001; Hu & Willett, 2002). However, only two individual cohort studies, the Honolulu Heart Program (McGee et al., 1984) and the Ireland-Boston Diet-Heart Study (Kushi et al., 1985), have demonstrated a significant positive association between intake of saturated fat and risk of developing heart disease. Overall, the totality of the evidence suggests that reducing dietary saturated fat intake reduces the risk of developing heart disease. Refs Truswell AS. Review of dietary intervention studies: effect on coronary events and on total mortality. Aust NZ J Med 1994;24:98-106. Hu FB, Stampfer MJ, Manson J et al. Dietary fat intake and the risk of coronary heart disease in women. N Engl J Med 1997;337:1491-9.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Hu FB, Manson JE, Willett WC. Types of dietary fat and risk of coronary heart disease: a critical review. JACN 2001;20(1):5-19. Hu FB and Willett WC. Optimal diets for prevention of coronary heart disease. JAMA 2002;288(20):2569-78. Kushi LH, Lew RA, Stare FJ, Ellison CR, el Lozy M, Bourke G, Daly L, Graham I, Hickey N, Mulcahy R, et al. Diet and 20-year mortality from coronary heart disease. The Ireland-Boston Diet-Heart Study. N Engl J Med. 1985;312(13):811-8. McGee DL, Reed DM, Yano K, Kagan A, Tillotson J. Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Am J Epid. 1984;119(5):667-76. Oh K, Hu FB, Manson JE, Stampfer MJ, Willett WC. Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the Nurses' Health Study. Am J Epid. 2005;161:672-679. (please also see second comment for this section on 5.8.1.1)

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Food Standards Agency	5.8. Cardiovascular disease	Second comment on this section Section 5.8.1.1 The EFSA opinion appears to be based on a recent meta analysis by Mozaffarian and Rimm 2006. We believe this meta analysis to be flawed. This meta-analysis does not include details on study quality and includes the DART 2 study (Burr et al 2003) which SACN excluded from their report on " Advice on fish consumption: benefits and risk" due to methodological flaws including compliance only being assessed in a subset of subjects and interruption in the trial due to funding problems. The Cochrane systematic review (Hooper et al 2004) is missing from the paper. Reference Hooper et al (2004) Omega 3 fatty acids for prevention and treatment of cardiovascular disease. Hooper L et al. Cochrane Database Syst Rev. (2004) The peer reviewed literature reflects three different approaches to reviewing the literature for n3 fatty acids and CVD. (1) The review by Mozaffarian and Rimm 2006 combines data 15 prospective cohort studies and five RCTS (including DART 2) of fish or fish oil. (2) The review by Hooper et al focuses on 12 RCTs including DART 2. It is important to note that removal of the methodologically flawed DART 2 study (Burr et al 2003) changes the conclusion of the Hooper review from no effect to a clear benefit. (3) The review by SACN bases its advice on both 23 observational studies and three (of four available) RCTs as they excluded data from DART 2 (Burr et al 2003) due to methodological flaws including compliance only being assessed in a subset of subjects and interruption in the trial due to funding problems. Data from observational studies suggest that there is a plateau effect in high risk population around 0.9g/day. In reaching its conclusions the SACN also looked at data from fatty acid analysis from blood and blood compartments, which suggests a positive effect with no plateau effect. SACNs approach is consistent with other advisory committees. The FDA has recently produced a summary on published research on the beneficial effects of fish consumption, which EFSA may find helpful in informing their review. This can be found at http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2009-N-0018-Rpt%202%20pg1-100.pdf We believe that EFSA should base their DRV on evidence from both cohort studies and good quality RCTs.
Food Standards Agency	6.4. Cis-polyunsaturated fatty acids (Cis-	Section 6.4 n6:n3 ratio N6/n3 ratio, the Agency agrees with EFSAs decision not to set a ratio for n3:n6. In 2006 the Agency convened a research

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
	PUFA)	workshop of international scientific experts which discussed research on the n3:n6 ratio and made the following recommendations including: (1)Based upon theoretical and scientific ground (reviewed at the workshop) use of the n6:n3 ratio to estimate CVD risk should be abandoned (2)Further research on dietary fatty acids would benefit from focusing on the effects of absolute amounts of individual n6 and VLC n3 fatty acids on cardiovascular risk factors and other physiological outcomes related to risk of chronic disease. The workshop report Stanley JC et al (2007) British Journal of Nutrition 98: 1305-1310 is available on the FSA website (http://www.food.gov.uk/science/research/researchinfo/nutritionresearch/dietandcardiovasc/reports/ FSA note that at the national experts meeting one member state disagreed with EFSAs view on the n6:n3 ratio and that EFSA agreed to revisit the evidence for this section. The UK expects that the above workshop report (and studies reported in it) will help strengthen EFSAs view that a specific value should not be set for n6:n3 ratio. 6.4.2 n3 PUFA FSA is concerned regarding the EFSA DRV for EPA/DHA of 250mg/day. We would like to see levels closer to 450mg/day which better reflects the evidence, rather than the EFSA proposed value of 250mg/day. The EFSA 250mg/day level is out of line with several national recommendations including the Netherlands, France and UK. The UK recommendation is based on the Scientific Advisory Committee on Nutrition (SACN) recommendation of 450mg/day. SACN based on the balance of the scientific evidence from RCTS and observational studies and on two portions of fish, one oily (one portion is 2.8g DHA/EPA/week) and one white (one portion average 0.4g/DHA/EPA week). This is a weekly total of 3.2g/week which equates to 450mg/day. (see comment under section 5.8.1.1, regarding meta analysis use for EFSAs recommendation) We appreciate that EFSA's role is risk assessment but they should still be able to make a recommendation to the risk managers at the Commission to guide the policymakers who are not scientific experts in this area and so rely on EFSA to provide technical/ scientific advice. Setting 250 mg for EPA/DHA will mean that 'source of claims' will be allowed on foods such as white fish that contain very little EPA/DHA and will be of little practical benefit to consumers because it will not help the consumer to distinguish between levels of EPA/DHA in oily and white fish.
Food Standards Agency	Conclusions and recommendations	Please see these comments on n-3 fattyacids, total fat and saturated fat and the additional comments on MUFA and trans fat in an additional comment box Conclusions and recommendations:

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		n3 PUFA We are pleased to see that EFSA have decided to set a separate DRV for ALA and EPA/DHA . We agree that the conversion rate of ALA to DHA/EPA in the body is extremely low and so ALA cannot be assumed to have the same effects as EPA/DHA. FSA is concerned regarding the EFSA DRV for EPA/DHA of 250mg/day. We would like to see levels closer to 450mg/day rather than the EFSA proposed value of 250mg/day. (see comment under 5.8.1.1 and 6.4.2 for full details). Total fat FSA agree with the suggested DRV of 20-35% energy but it is not clear how this figure is derived given that EFSA do not propose a DRV for MUFA, saturated fats or trans fats. Saturated fat FSA are concerned that EFSA did not set an upper level for saturated fat but just states "as low as possible". How can this be translated into meaningful dietary guideline in relation to total fat? It should be possible to recommend a guidance level (if it is not possible to set a UL) for saturated fat as this is such an important public health issue. Several national members have set levels for example the UK Committee on Medical Aspects of Food Policy (COMA), DH 1994) advised that people should consume on average no more than 11% of food energy as saturated fat. See comments on section 5.8.1 and section 5.2.2 for comments on saturated fat, cholesterol and CVD and lists of references for consideration by EFSA.
Gentofte University Hospital	4. Overview of dietary reference values and recommendations	We are surprised to find that you in chapter 4, Overview of dietary reference values and recommendations do not include legislation (line 199). In subsection 4.1.5, Trans fatty acids (lines 912 to 938), is only mentioned the Nordic recommendation NNR, 2004, and not the Danish legislation concerning trans fatty acids. Even before the publication of the Nordic Nutrition Recommendation, the Danish Government introduced a legislation requiring that no more than 2 % of the fat in foods was industrially produced trans fat. On March 22, 2007, the European Commission dropped its infringement proceedings against Denmark over the trans fat limit because of increased scientific evidence on the dangers of trans fats. This legislation overrules the Nordic Nutrition recommendation in Denmark and should in our opinion be mentioned. Likewise the legislation in Switzerland and in the US remains unmentioned in the report. A reference to the report from The Danish Nutrition Council "The influence of trans fatty acids on health" is missing in the references. http://www.meraadet.dk/gfx/uploads/rapporter_pdf/Trans%20fatty%20acids_4.th%20ed._UK_www.pdf

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
German Federation for Food Law and Food Science, Godesberger Allee 142-148, 53175 Bonn	1. Introduction	Lines: 70-71 93-94 149-150 1877-1878 1902-1903 1962-1963 1996-1997 2014 2045-2046 Concerning the above mentioned lines we would like to comment as follows: In the Draft Scientific Opinion "Dietary reference values for fat" the following statements are given: "The panel proposes not to set any DRV" [...] for cis-MUFA, n-6-PUFA and CLA. We suggest to express this statement more open, e.g. "According to the current scientific evidence it is actually not possible to set any DRV."

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
German Federation for Food Law and Food Science, Godesberger Allee 142-148, 53175 Bonn	6.3. Cis-monounsaturated fatty acids (Cis-MUFA)	Lines: 70-71 93-94 149-150 1877-1878 1902-1903 1962-1963 1996-1997 2014 2045-2046 Concerning the above mentioned lines we would like to comment as follows: In the Draft Scientific Opinion "Dietary reference values for fat" the following statements are given: "The panel proposes not to set any DRV" [...] for cis-MUFA, n-6-PUFA and CLA. We suggest to express this statement more open, e.g. "According to the current scientific evidence it is actually not possible to set any DRV."

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
German Federation for Food Law and Food Science, Godesberger Allee 142-148, 53175 Bonn	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Lines: 70-71 93-94 149-150 1877-1878 1902-1903 1962-1963 1996-1997 2014 2045-2046 Concerning the above mentioned lines we would like to comment as follows: In the Draft Scientific Opinion "Dietary reference values for fat" the following statements are given: "The panel proposes not to set any DRV" [...] for cis-MUFA, n-6-PUFA and CLA. We suggest to express this statement more open, e.g. "According to the current scientific evidence it is actually not possible to set any DRV."

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
German Federation for Food Law and Food Science, Godesberger Allee 142-148, 53175 Bonn	6.6. Conjugated linoleic acid (CLA)	Lines: 70-71 93-94 149-150 1877-1878 1902-1903 1962-1963 1996-1997 2014 2045-2046 Concerning the above mentioned lines we would like to comment as follows: In the Draft Scientific Opinion "Dietary reference values for fat" the following statements are given: "The panel proposes not to set any DRV" [...] for cis-MUFA, n-6-PUFA and CLA. We suggest to express this statement more open, e.g. "According to the current scientific evidence it is actually not possible to set any DRV."

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
German Federation for Food Law and Food Science, Godesberger Allee 142-148, 53175 Bonn	Conclusions and recommendations	Lines: 70-71 93-94 149-150 1877-1878 1902-1903 1962-1963 1996-1997 2014 2045-2046 Concerning the above mentioned lines we would like to comment as follows: In the Draft Scientific Opinion "Dietary reference values for fat" the following statements are given: "The panel proposes not to set any DRV" [...] for cis-MUFA, n-6-PUFA and CLA. We suggest to express this statement more open, e.g. "According to the current scientific evidence it is actually not possible to set any DRV."
German Nutrition Society (DGE)	2. Categories, structure and function	Line 474: The conversion factors mentioned here are “8 – 12 %” but in line 1177 “5 + 0.5 %”. What is correct ??
German Nutrition Society (DGE)	4. Overview of dietary reference values and recommendations	Line 786: Here is a wrong citation of the DACH Reference Values. Line 836: “A ratio of…..between 3 and 9 : 1” would be the correct wording. Line 874: “recommendation”, this is an ”estimated value” ! Line 940: The Eurodiet also recommended a maximum intake of 300 mg cholesterol [Kafatos AG, Codrington CA (eds): EURODiet. Public Health Nutrition 4 (2001) p 290]

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
German Nutrition Society (DGE)	5. Criteria (endpoints) on which to base the dietary reference values	Line 1070: Here the risk of increasing triglycerides and decreasing HDL-cholesterol is missing. Line 1177: See also line 47: The conversion factors mentioned here are "8 – 12 %" but in line 1177 "5 + 0.5 %". What is correct ?? Line 1202: See line 126: "To this intake should be added 100-200 mg of preformed DHA" The correct recommendation is: "Pregnant and lactating women should aim to achieve an average dietary intake of at least 200 mg DHA/d" [Koletzko et al. Br J Nutr 98 (2007) 873 – 877], but not in addition! Line 1235: See line 48: "total fat 20 E% …neither adverse effects on serum lipids". Low fat diets with <25 E% fat will induce hypertriglyceridemia and decrease HDL-cholesterol [Knopp et al. JAMA 278 (1997) 1509 -1515 and DRI, page 780], especially in obese people which reach in most European countries more than 50 % of the population. In contrast vegetarians reach seldom more than 1 %. The lowest intake level should be changed to 25 E%.
German Nutrition Society (DGE)	6.1. Total fat	Line 1837: A dose-response relationship is documented by Yu Poth et al. [Yu Poth et al. Am J Clin Nutr 69 (1999) 632–646] and is cited in the Guideline "Fat" of the German Nutrition Society (DGE 2006: http://www.dge.de/leitlinie). Line 1841: See line 48 "total fat 20 E% …neither adverse effects on serum lipids". Low fat diets with <25 E% fat will induce hypertriglyceridemia and decrease HDL-cholesterol [Knopp et al. JAMA 278 (1997) 1509 -1515 and DRI, page 780], especially in obese people which reach in most European countries more than 50 % of the population. In contrast vegetarians reach seldom more than 1 %. The lowest intake level should be changed to 25 E%.
German Nutrition Society (DGE)	6.2. Saturated fatty acids (SAT)	Line 1867: "SFA intake should be as low as possible within the context of a nutritionally adequate diet". This recommendation is too weak. SFA <10 E% is recommended by several authorities around the world (section 4.1.2.) and practically achievable (line 1872) and effective (DGE 2006: http://www.dge.de/leitlinie). To specify no guiding value because the average intake of SFA in adults in many EU Member States exceeds 10 E% might not be an argument against this figure, since there is no evidence that the consumption of more then 10 E% as SFA does not increase the risk for CHD… Line 1868: See line 145: "Nutritionally adequate diet": Where is the definition or the description of this phrase?

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
German Nutrition Society (DGE)	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Line 1882: The ratio n-3 / n-6 is very important for the conversion of ALA to EPA and DHA (Goyens et al. 2006). Of course the ratio per se does not have an importance independent of absolute levels of intake, but with the levels recommended (sections 6.4.1. and 6.4.2.) it should be pointed out, that it is more necessary to enhance ALA (consumption) than to decrease LA (and in this connection the ratio would be changed) to increase the synthesis of EPA and DHA [Goyens PLL et al. Am J Clin Nutr 84 (2006) 44-53]. This is not addressed in the present text! We have to keep in mind that sea fish resources are limited and many people don`t like fish. Line 1905: The discussion concerning safety aspects is too limited and should go deeper [Eritsland J. Am J Clin Nutr 71 (2000) 197S – 201S]. The importance of Vitamin E as an antioxidant is not addressed.
German Nutrition Society (DGE)	6.5. Trans fatty acids (TFA)	Line 1937: See line 130: "TFA are not synthesized by the human body". That is not correct, since during the catabolism of PUFA within the cells there are catabolites with trans-configuration. Therefore this sentence should be deleted. Line 1954: An intake of TFA <1% is practically achievable and very well based. There is convincing evidence (DGE 2006: http://www.dge.de/leitlinie) for this recommendation and a convincing support by a recent WHO Scientific Update [Uauy R et al. Eur J Clin Nutr 63 (2009) S68–S75]. It is a pity that the European Food Safety Agency will not banish the TFA of industrial origin!
German Nutrition Society (DGE)	6.7. Cholesterol	Line 1971: See line 157: There are foods with high cholesterol content but less SFA, i.e. eggs, liver, hide, oysters or mussels. These cholesterol carriers will not be covered by this formulation. Therefore 300 mg cholesterol remains a necessary and suitable guiding value (DGE 2006: http://www.dge.de/leitlinie). Compare also lines 1704 to 1709
German Nutrition Society (DGE)	References	It is a pity that the "Evidence based guideline: Fat consumption and certain nutrition-related diseases" of the German Nutrition Society was not noticed preparing this Draft Scientific Opinion. The DGE-Guideline documents the relationship between the consumption of fat (and fatty acids) and the risk of certain nutrition-related diseases, based on a systematic analysis and assessment of the existing literature: http://www.dge.de/leitlinie http://www.dge.de/pdf/ws/ll-fett/11-Summary-DGE-guideline-fat-11-2006.pdf http://www.dge.de/pdf/ws/ll-fett/12-Implementation-of-the-Guideline-DGE-guideline-fat-11-2006.pdf
Global Oranization for EPA and DHA Omega-3s	2. Categories, structure and function	Section 2.1.3.2 L471-L477 – This section identifies the limited ability of alpha-linolenic acid (ALA) to serve as a source of DHA. A recent ISSFAL position paper by Brenna and co-workers confirms that conversion of ALA to DHA is less than 1% in adults, this reference may be a useful addition to the Opinion (Brenna JT, Salem N, et al. Prostaglandins Leukot Essent Fatty Acids 80:85-

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		91, 2009. See Summary Statement #2). Unfortunately, the limited conversion of ALA to DHA is not sufficiently identified throughout the current draft opinion. Specifically, the Summary (L107) recognizes that the body converts ALA to DHA and EPA but fails to quantify the limited extent of conversion. In addition, throughout the entire Opinion, there is an absence of any mention of stearidonic acid (SDA), an intermediate omega-3 fatty acid in the conversion of ALA to EPA. We respectfully suggest that language from L474 be added to the opinion Summary, specifically, "The human body can synthesize EPA and/or DHA from precursor fatty acids including alpha-linolenic acid and stearidonic acid; however, the conversion of these fatty acids into DHA may be even less than 1%" at line 107. L480 – The Committee notes that "the developing brain accumulates large amounts of DHA both pre- and postnatally (until two years of age)…". We respectfully disagree, however, with the limitation of DHA accumulation only "until two years of age". Classic research by Martinez indicates that DHA accumulation by the brain postnatally "is still very significant until at least 2 years of age" [emphasis added], specifically, Martinez provides data for children up to 2.7 years (J Pediatr 120:S129-39, 1992 Pg. S132 Fig. 3A). More recent data from Carver and coworkers (Carver JD, et al. Brain Research Bulletin 56:79-85, 2001. Pg. 82 Fig. 1; Pg. 84 Table 2) indicates that levels of DHA in the cerebral cortex increases steadily up to the age of 18 years. Finally, it is well known that the brain growth spurt begins during the third trimester and continues throughout the first 3-4 years of life (Dobbing J and Sands J. Archives of Disease in Childhood, 48:757-767, 1973. Pg. 765), this important developmental period is recognized as a period of critical brain growth and neuronal development. Collectively, these data support recognition of an expanded range of DHA accumulation by the postnatal brain in the current Opinion or elimination of the "until two years of age" language without an effort to specify further.
Global Oranization for EPA and DHA Omega-3s	4. Overview of dietary reference values and recommendations	Section 4.1.4.2 L866-L867 – notes the U.S. IOM recommendation for DHA and EPA contribution toward reversing an n-3 fatty acid deficiency but fails to recognize the level of contribution specified by the IOM. i.e. up to 10%. We respectfully request the following revised language be considered for L866-867, "Small amounts of EPA and DHA (up to 10%) can contribute towards reversing an n-3 fatty acid deficiency and can therefore contribute towards the AI for alpha-linolenic acid." L1012-L1014 – We respectfully request the following revised language be considered for 1012-1014, "Small amounts of EPA and DHA (up to 10%) can contribute towards reversing an n-3 fatty acid deficiency and can therefore contribute towards the AI for alpha-linolenic acid."
Global Oranization for EPA and DHA Omega-3s	4. Overview of dietary reference values and recommendations	Section 4.1.4.2 L866-L867 – notes the U.S. IOM recommendation for DHA and EPA contribution toward reversing an n-3 fatty acid deficiency but fails to recognize the level of contribution specified by the IOM. i.e. up to 10%. We respectfully request the following revised language be considered for L866-867, "Small amounts of EPA and DHA (up to 10%) can contribute towards reversing an n-3 fatty acid deficiency and can therefore contribute towards the AI for alpha-linolenic acid." L1012-L1014 – We respectfully request the following revised language be considered for 1012-1014, "Small amounts of EPA and DHA (up to 10%) can contribute towards reversing an n-3 fatty acid deficiency and can therefore contribute towards the AI for alpha-linolenic acid."

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Global Oranization for EPA and DHA Omega-3s	5.1. Dietary requirements	Section 5.1.2.2 L1176-L1180 – This section identifies the limited ability of alpha-linolenic acid (ALA) to serve as a source of DHA. A recent ISSFAL position paper by Brenna and co-workers confirms that conversion of ALA to DHA is less than 1% in adults, this reference may be a useful addition to the Opinion (Brenna JT, Salem N, et al. Prostaglandins Leukot Essent Fatty Acids 80:85-91, 2009. See Summary Statement #2). L1199-L1207 – This section provides sound rationale for a DHA requirement during pregnancy and nursing. However, recent expert group recommendations and guidelines are not mentioned. Specifically, the Consensus recommendations on behalf of the European Commission research projects Perinatal Lipid Metabolism (PeriLip) and Early Nutrition Programming (EARNEST) should be recognized. In addition, the benefits to maternal and infant health noted by the PeriLip/EARNEST document should also be recognized, specifically, slightly longer pregnancy duration, reduced risk of preterm birth, and somewhat higher birth weight (Koletzko B, Cetin I, et al. Br J Nutr 98:873-877, 2007; Conclusions and Recommendations #2,6). L1220 – We respectfully request that "such small amounts of" be removed from this sentence. Given the very limited intake and availability of DHA, particularly from 6-24 months of age, classification of 100 mg as a small amount could be misleading as it suggests a goal readily accomplished as part of the normal diet. In fact, the most common source of DHA other than infant formula is fatty fish. Fish and seafood, however, are typically restricted by parents to at least 3 years of age due to allergy related concerns (ESPGHAN Committee on Nutrition, J Pedi Gastro Nutr 46:99-110, 2008. Pg. 104-105).
Global Oranization for EPA and DHA Omega-3s	5.11. Nervous system function	Section 5.11 L1817 – This sentence appears to contradict recommendations made by the Committee in the Conclusions of the current opinion. This sentence notes that optimal amounts of LC-PUFAs cannot be specified for infants in the second six months of life, however, the Conclusions (L2029-2030) indicate a proposed "… AI of 100 mg DHA for older infants (> 7 months of age) and young children below the age of 24 months". We respectfully request that section 5.11 reflect the Panel's conclusion regarding an optimal level of DHA during the second six months of life.
Global Oranization for EPA and DHA Omega-3s	5.2. Serum lipids and lipoproteins	Section 5.2.4.2 L1274-1279 – This section recognizes the role of EPA and/or DHA in triglyceride reduction but does not recognize the independent role of DHA in this regard. A recent analysis of 16 studies of algal DHA supplementation (0.7-6.0 g/d) reports that "clinical trials with algal-DHA as a TG oil have demonstrated a marked reduction in serum TG levels (up to 26%) in normal individuals and in those with HTG or combined hyperlipidemia." (Ryan AS, et al. Am J Therapeutics 16:183-92. Table 2). We respectfully request that the independent role of DHA for TG reduction be recognized in this section. Additionally, recognition of the independent role of DHA for elevation of HDL is also requested (Ryan AS, et al. Am J Therapeutics 16:183-92, 2009 Table 3). L1279 – We respectfully request that the terminology "fish oil fatty acids" be replaced with EPA and/or DHA as it is more appropriate to recognize the beneficial nutrients as opposed to any one dietary source. These nutrients are not limited to fish oil but currently available from fish, marine microalgae and numerous fortified and enriched foods and beverages.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Global Oranization for EPA and DHA Omega-3s	5.3. Haemostatic function	Section 5.3.4.2 L1377-L1384 – These lines recognize the role of EPA and DHA in hemostasis. It is important to note that changes in bleeding times resulting from decreased platelet aggregation as noted in L1380-L1382 are within a clinically normal range and considered a benefit as opposed to a safety issue in the general population (Lavie CJ, et al. J Am Coll Cardiol 54:585-594, 2009). Section 5.3.7 L1399-L1400 – We respectfully request the following revised language be considered, "An exception may be the n-3 LCPUFA, which may decrease platelet aggregation in particular at intakes above 1 g but without clinically adverse changes in bleeding in the general healthy population."
Global Oranization for EPA and DHA Omega-3s	5.4. Inflammation and immne function	Section 5.4.4 L1437 – We respectfully request that "fish oil" be removed as it could be misleading to suggest that only fish oil can provide beneficial n-3 LCPUFA. These nutrients are not limited to fish oil but currently available from fish, marine microalgae and numerous fortified and enriched foods and beverages.
Global Oranization for EPA and DHA Omega-3s	5.5. Blood pressure	Section 5.5.4.2 L1464-L1473 - We respectfully request that the terminology "fish oil" be replaced with EPA and/or DHA since these nutrients are available from multiple sources in addition to fish oil such as DHA from marine microalgae. It seems more appropriate to recognize a particular intake level of the beneficial nutrients as opposed to any one dietary source. Studies of blood pressure in response to algal-DHA supplementation are available and suggest at least equal reductions compared to EPA and DHA from fish oil (Ryan AS, et al. Am J Therapeutics 16:183-92. Table 3). Section 5.5.7 L1486 – We respectively request "fish oil" be removed and n-3 LCPUFA rather than n-3 PUFA be used in this sentence. Authors provide data only for n-3 LCPUFA and blood pressure reduction therefore n-3 LCPUFA is a more appropriate term than n-3 PUFA which would typically include ALA. In addition, it could be misleading to suggest that only fish oil can provide beneficial n-3 LCPUFA. These nutrients are not limited to fish oil but currently available from fish, marine microalgae and numerous fortified and enriched foods and beverages.
Global Oranization for EPA and DHA Omega-3s	5.8. Cardiovascular disease	Section 5.8.4 L1716 - We respectfully request that the term "fish oil" be replaced with EPA and DHA since these nutrients are available from multiple sources in addition to fish oil, such as marine microalgae, and it seems more appropriate to recognize a particular intake level of the beneficial nutrients as opposed to any one dietary source. Modifying the language in this section would also be consistent with that used in EFSA's scientific opinion regarding labelling reference intake values for n-3 and cardiovascular disease prevention (The EFSA Journal, 1176:1-11, 2009) and with L1919-1924 of the current opinion.

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Global Oranization for EPA and DHA Omega-3s	5.8. Cardiovascular disease	We applaud the Panel's proposal to establish a DRV of 250 mg/day for EPA + DHA. While significant benefits can be demonstrated with a dose of 250 mg/day, we believe that optimal benefits for the general population can be achieved with a higher dose. Thus said, 250 mg/day should be considered a minimal, rather than an optimal, intake. We encourage the Panel to reevaluate its current proposal and establish the DRV based on the optimal level. While the Panel proposed 250 mg/day, it recognized that cardiovascular benefits were demonstrated within the range of 250-500 mg/day. See L1920-L1923-"With respect to cardiovascular diseases, prospective epidemiological and dietary intervention studies indicate that oily fish consumption or n-3 LCPUFA dietary supplements (equivalent to a range of 250-500 mg of EPA + DHA/day) decrease the risk of mortality from CHD and sudden cardiac death." Furthermore, the Panel calls 250 mg/day a 'sufficient' not 'optimal' dose for primary prevention in healthy adults. See L1923-L1924-"An intake of 250 mg/day of EPA + DHA appears to be sufficient for primary prevention in healthy subjects." Caution should be exercised in establishing an intake of the n-3 LCPUFAs of 250 mg/day as optimal. Instead, the consumption of 250 mg/day of the n-3 LCPUFAs should be considered a minimum recommended intake. The publications considered in the Opinion include meta-analyses that combine estimates of low intake from background dietary consumption and higher intakes from supplements. It is clear that there is a positive correlation between realized benefits and intake with increasing doses towards 250 mg/day; however, due to the uncertainties inherent in the analysis, the benefit above this level is not as clear, and it can only be concluded that maximum efficacy lies above 250 mg/day, but closer to 500 mg/day as discussed above. Although the population will realize significant benefits by establishing a DRV of 250 mg/day, it is also likely that many in the population will not realize the maximum benefits.
Global Oranization for EPA and DHA Omega-3s	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Section 6.4.2 L1915 - This sentence recognizes the ability of the body to synthesize DHA and EPA from a-linolenic acid but does not identify the limited extent of this conversion. A recent ISSFAL position paper by Brenna and co-workers (Brenna JT, Salem N, et al. Prostaglandins Leukot Essent Fatty Acids 80:85-91, 2009. See Summary Statement #2) confirms that conversion of ALA to DHA is less than 1% in adults. Unfortunately, the limited conversion of ALA to DHA is not sufficiently identified throughout the current draft opinion. In addition, throughout the entire Opinion, there is an absence of any mention of stearidonic acid (SDA), an intermediate omega-3 fatty acid in the conversion of ALA to EPA. We respectfully suggest that language from L474 be added to this sentence, specifically, "The human body can synthesize EPA and/or DHA from precursor fatty acids including alpha-linolenic acid and stearidonic acid; however, the conversion of these fatty acids into DHA may be even less than 1%" at line 107.
Global Oranization for EPA and DHA Omega-3s	Conclusions and recommendations	Conclusions and Recommendations L2024 - This sentence recognizes the ability of the body to synthesize DHA and EPA from a-linolenic acid but does not identify the limited extent of this conversion. A recent ISSFAL position paper by Brenna and co-workers (Brenna JT, Salem N, et al. Prostaglandins Leukot Essent Fatty Acids 80:85-91, 2009. See Summary Statement #2) confirms that conversion of ALA to DHA is less than 1% in adults. We respectfully suggest that language from L474 be added to this sentence, specifically, "The human body can synthesize EPA and/or DHA from alpha-linolenic acid and stearidonic acid; however, the conversion of ALA

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		into DHA may be even less than 1%". L2029-L2030 – Conclusions regarding a DHA AI for children > 7 months until the age of 24 months are not reflected in the opinion Summary. We respectfully request that the conclusions from L2020-L2030 be added to the Summary.
Global Oranization for EPA and DHA Omega-3s	References	The following references correspond to those cited in the comments associated with Chapter/Section: 5.8 Cardiovascular Disease (1) Mozaffarian D, Rimm EB (2006). Fish intake, contaminants, and human health: evaluating the risks and the benefits. JAMA 29(15):1885-1899. (2) Kromhout D, Bosschieter EB, de Lezenne Coulander C (1985). The inverse relation between fish consumption and 20-year mortality from coronary heart disease. N Engl J Med 312:1205-1209. (3) Kromhout D, Feskens EJ, Bowles CH (1995). The protective effect of a small amount of fish on coronary heart disease mortality in an elderly population. Int J Epidemiol 24:340-345. (4) Fraser GE, Sabate J, Beeson WL, Strahan TM (1997). A possible protective effect of nut consumption on risk of coronary heart disease: the Adventist Health Study. Arch Intern Med 152:1416-1424. (5) Daviglus ML, Stamler J, Orencia AJ, Dyer AR, Liu K, Greenland P, Walsh MK, Morris D, Shekelle RB (1997). Fish Consumption and the 30-year risk of fatal myocardial infarction. N Engl J Med 336:1046-1053. (6) Nakamura Y, Ueshima H, Okamura T, Kadowaki T, Hayakawa T, Kita Y, Tamaki S, Okayama A, NIPPON DATA80 Research Group (2005). Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80 , 1980-99. Am J Med 118:239-245. (7) Osler M, Andreasen AH, Hoidrup S (2003). No inverse association between fish consumption and risk of death from all-causes, and incidence of coronary heart disease in middle-aged, Danish adults. J Clin Epidemiol 56:274-279. (8) Harris WS, Kris-Etherton PM, Harris KA (2008). Intakes of long-chain omega-3 fatty acid associated with reduced risk for death from coronary heart disease in healthy adults. Curr Atheroscler Rep 10(6):503-509. (9) Dolecek TA, Grandits G (1991). Dietary polyunsaturated fatty acids and mortality in the multiple risk factor intervention trial (MRFIT). World Rev Nutr Diet 66:205-216.

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		(10) Yuan JM, Ross RK, Gao YT, Yu MC (2001). Fish and shellfish consumption in relation to death from myocardial infarction among men in Shanghai, China. Am J Epidemiol 154(9):809-816. (11) Mozaffarian D, Lemaitre RN, Kuller LH, Burke GL, Tracy RP, Siscovick DS (2003). Cardiac benefits of fish consumption may depend on the type of fish meal consumed: The Cardiovascular Health Study. Circulation 107(10):1372-1377. (12) He K, Song Y, Daviglus ML, Liu K, Van Horn L, Dyer AR, Greenland P (2004). Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. Circulation 109(22):2705-2711. (13) Whelton SP, He J, Whelton PK, Muntner P (2004). Meta-analysis of observational studies on fish intake and coronary heart disease. Am J Cardiol 93(9):1119-1123. (14) König A, Bouzan C, Cohen JT, Connor WE, Kris-Etherton PM, Gray GM et al. (2005). A quantitative analysis of fish consumption and coronary heart disease mortality. Am J Prev Med 29(4):335-346. (15) Iso H, Kobayashi M, Ishihara J, Sasaki S, Okada K, Kita Y, Kokubo Y, Tsugane S, JPHC Study Group (2006). Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I. Circulation 113(2):195-202.
Heart of Mersey	1. Introduction	Lines 293 – 314: Heart of Mersey acknowledges there are difficulties in establishing DRV's when considering their potential use and possible misinterpretation e.g. whether they are to be used for developing population goals in relation to appropriate dietary composition, food labelling purposes, to interpret dietary information for individuals or sub groups within the population. For example the previous RDA's developed in the UK in 1979 (were established as average amounts of a nutrient which should be provided per head in a group of people if the needs of practically all members of the group are to be met) had many disadvantages in that they were used inappropriately, had a limited degree of accuracy, a single figure was open to misinterpretation and they were wrongly used to assess the adequacy of an individual's diet. If establishing DRV's for energy, fats , fatty acids, sugars and starches it needs to be considered that at higher levels of consumption there is likely to be evidence of undesirable effects and for this purpose reasonable parameters or values need to be established. Heart of Mersey acknowledge that the current UK DRV's need to be reviewed. For the purpose of this consultation and given the importance of DRVs for a variety of applications, as stated above, where the evidence is insufficient, EFSA should adopt a precautionary approach and develop the best estimates based on the available evidence.

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Heart of Mersey	Conclusions and recommendations	Cis-monounsaturated fatty acids (cis-MUFA) Lines 69-71: Cis-MUFA are synthesised by the body, have no known role in preventing or promoting diet related diseases, and are therefore not required in the diet. The Panel therefore proposes not to set any DRV for cis-MUFA. Cis-polyunsaturated fatty acids (cis-PUFA) Lines 73 -76:In view of the different metabolic effects of the various dietary cis-PUFA, the Panel proposes not to formulate a DRV for the intake of total cis-PUFA. Also, the Panel proposes not to set specific values for the n-3 / n-6 ratio as available data are insufficient to recommend a ratio independent of absolute levels of intake. There is strong evidence to show that where monounsaturated and polyunsaturated fats are eaten in place of carbohydrates, they decrease levels of harmful LDL cholesterol. Yet we still have no strict guidelines regarding their intake. In the UK Cis- MUFA intake is recommended as 12% of energy and 6% of energy should be derived from cis- PUFA's. Diets rich in monounsaturated fats also lower LDL –cholesterol, reducing the risk of CHD.
Heart of Mersey	Conclusions and recommendations	Lines 63-65: The Panel recommends that SFA intake should be as low as possible within the context of a nutritionally adequate diet. Lines 1989-1991:There is no threshold of SFA intake below which no adverse effects are observed. Thus, no UL can be set. When translating nutritional information to the population, we need a recommended maximum intake of saturated fats or desirable population intake to support dietary goals/guidelines. If no upper limit is established this will lead to over consumption of saturated fat when considering the lipid profile of the diet COMA the former UK government committee on nutrition made recommendations in 1991 to reduce intake of total fat particularly saturated fat, so that consumption does not exceed 10 % of dietary energy. EFSA should initially set an interim target of 10% SFA intake which can subsequently be revised downwards once it has been met. HoM strongly suggests that this level may need to be reviewed due to the dose dependent relationship between intake of saturated fat and serum LDL cholesterol. HoM would support an intake 'as low as possible' within the context of a nutritionally balanced diet, ideally 7 E% in line with Japanese consumption.
Heart of Mersey	Conclusions and recommendations	n-3 polyunsaturated fatty acids (n-3 PUFA) Lines 115 -121: Taking into account that available data is insufficient to derive an AR, the Panel proposes to set an AI for adults of 250 mg for EPA plus DHA based on considerations of cardiovascular health. The Panel proposes an AI of 100 mg DHA for older infants (> 7 months of age) and young children below the age of 24 months. For the age period 2-18 years, the Panel proposes no AI for DHA plus EPA. However dietary advice for children should be consistent with advice for the adult population. The Panel considers that during pregnancy and lactation an adequate n-3 LC-PUFA supply consists of the AI for adults (250 mg DHA plus EPA) and 100-200 mg additional preformed DHA. HoM strongly supports the recommendations for the establishment of an AI for EPA plus DHA based on cardiovascular health for both children and adults. Consumption of omega 3 oils (average of 250mg/d for adults) is related to a 35% lower risk of CHD death.

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		Central and Eastern European countries with the biggest increases in dietary intake of ALA have seen the largest recent DECREASES in cardiovascular mortality (Zatonski et al, Eur J Epidemiol 2008;23(1):3-10.
Heart of Mersey	Conclusions and recommendations	Trans fatty acids (TFA) TFA are not synthesised by the human body, but are also not required in the diet. Therefore, no PRI, AR, or AI is set. Higher intakes of TFA have been consistently associated to an increased risk of CHD. There is a limit to which the intake of TFA can be lowered without compromising adequacy of intake of essential nutrients. Therefore, the Lines 2041-2: The Panel recommends that TFA intake should be as low as possible within the context of a nutritionally adequate diet. Trans fatty acids have a very negative impact on cardiovascular health. Recent large meta-analysis of randomised trials and prospective cohort studies found that replacing 1% of food energy from trans fats with plant based unsaturated fats reduced CHD risk by 12% [3]. Trans fatty acids can occur naturally in ruminant products but most are produced artificially (Industrial Trans Fats). Trans fatty acids have no nutritional benefit. HoM would strongly recommend that an EU population intake target for trans fatty acids is set and used to monitor the elimination of industrial TFAs from food production. This has been achieved in Denmark and is ongoing in Austria as demonstrated by the low average population trans fat intakes of 0.5-0.6%E. The rest of the EU deserves equal health benefits.
IMACE - International Margarine Association of the Countries of Europe	1. Introduction	Chapter Summary-Lines 77-128 IMACE reacts on the proposed DRVs for linoleic acid (LA) and alpha-linolenic acid (ALA). The EFSA panel recommends, based on the 'minimal level to prevent deficiency symptoms', AI levels of 4 E% for LA and 0.5 E% for ALA. LA and ALA deficiencies are virtually non-existent in the general population, whereas Cardiovascular Disease (CVD) is indisputably a major public health issue in Europe as it is the leading cause of mortality: 4.3 million deaths per year that make up 48% of all deaths in Europe (CVD statistics 2008). IMACE believes that EFSA should consider disease risk reduction in relation to the nutrient intake pattern, in line with current insights that dietary recommendations should also take prevention of morbidity and premature mortality via optimal nutrition into account. In fact, several other authoritative bodies do so: The US Institute of Medicine set Acceptable Macronutrient Distribution Ranges of 5-10 E% for LA and 0.6-1.2 E% for ALA (Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Institute of Medicine (IoM) 2002). The WHO judged the evidence that LA and ALA decrease the risk of CVD as 'convincing' and recommended 5-8 E% for n-6 fatty acids and 1-2 E% for n-3 fatty acids (Joint WHO/FAO expert consultation. Diet, Nutrition, and the prevention of chronic diseases. WHO Technical report series 916. Geneva 2003). The EC-sponsored Eurodiet report (2001) recommends intakes of 4-8 E% for LA and of 2 g for ALA, which is about 0.8 E% . Lines 151-159 Information on dietary cholesterol is a highly relevant marker for consumers to identify foods which are also high in saturated fats.Information on dietary cholesterol would enable consumers to make easier, quicker, and more informed food choices which fit in a healthy lifestyle. IMACE believes that the Panel should set a DRV for dietary cholesterol, which should be in line with

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		the DRV for saturated fats.
IMACE - International Margarine Association of the Countries of Europe	3. Dietary sources and intake data	Chapter 3-Lines 685-692: IMACE comments The figures indicated for cholesterol, clearly show that European adults tend to have a too high intake of dietary cholesterol compared to recommendations to limit the intake of dietary cholesterol below 300mg/d (cf. lines 939 to 942). As the Panel concluded that there is a positive relationship between the intake of dietary cholesterol with serum LDL concentrations, the fact that the average intake of dietary cholesterol is too high in European countries reinforces the need for clear and understandable information about dietary cholesterol. DRV for dietary cholesterol would enable people to control their dietary cholesterol intake and therefore maintain a healthy cholesterol blood level.
IMACE - International Margarine Association of the Countries of Europe	4. Overview of dietary reference values and recommendations	Chapter 4-Lines 939-942: IMACE comments There are additional sources which recommend to limit the intake of dietary cholesterol below 300mg/day i.e. ¿European guidelines on cardiovascular disease prevention in clinical practice – Third Joint Task force of European and other Societies on Cardiovascular disease prevention in clinical practice, European Heart Journal 2003; 24,1601-1610 ¿AHA Scientific statement – Diet and lifestyle recommendations revision 2006 –A scientific statement from the American Heart Association Nutrition Committee Circulation 2006; 114:82-96

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IMACE - International Margarine Association of the Countries of Europe	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Chapter 6-Lines 1891–1894:IMACE comments EFSA states that "There is [also] evidence from dietary intervention studies that decreasing the intakes of products rich in SFA by a replacement of products rich in n-6 PUFA (without changing total fat intake) reduced the number of cardiovascular events." This is strongly supported by a recent pooled analysis of cohort studies, which confirms a significant inverse relation between 'increased PUFA at the expense of SFA' and coronary heart disease risk throughout the normal population range of intake (Jakobsen et al, Am J Clin Nutr 2009;89:1425-32). The median total PUFA intake in the 11 populations included in this analysis varied between 2.3 E% and 9.0 E%, with most populations having an intake of around 5-6 E%. The highest (90th percentile) PUFA intake levels ranged from 3.7 E% to 10.4 E%, and were between 7 E% and 9 E% for most populations. Because LA makes up approximately 80 to 90% of total dietary PUFA, it can be derived that in these general populations, intakes of at least 6 E% for LA and of at least 1.0 E% are associated with the lowest risk of CHD. A DRV for ALA of 1 E% would also be in line with the 2 g/day as ALA that EFSA recently recommended to the Commission as labelling reference intake values (Question No EFSA-Q-2009-00548, adopted on 30 June 2009). Two g ALA per day in a 2000 kcal/d diet corresponds to ~0.9E%.
IMACE - International Margarine Association of the Countries of Europe	6.5. Trans fatty acids (TFA)	Chapter 6-Lines 1936-1959:IMACE comments IMACE welcomes the EFSA statement that "The available evidence indicates that TFA from ruminant sources have similar adverse effects on blood lipids and lipoproteins similar to those from industrial sources...The available evidence is insufficient to establish whether there is any difference between equivalent amounts of ruminants and industrially produced TFA and risk of CHD."
IMACE - International Margarine Association of the Countries of Europe	6.7. Cholesterol	Chapter 6-Lines 1964 to 1972: IMACE comments A DRV should be set also for dietary cholesterol. This is justified from a public health perspective given the fact that the negative effects of too high intakes of dietary cholesterol on health have clearly been demonstrated (cf. lines 1328 to 1340; 1701 to 1712; 1745 to 1751). In addition, IMACE sees an urgent need for a DRV to be set for dietary cholesterol in light of the Panel's conclusion that current average intake levels of dietary cholesterol among European adults are often well above the generally accepted and recommended intake limits (cf. lines 685 to 692 and lines 939 to 942). Furthermore, information on dietary cholesterol is a highly relevant marker for consumers to identify foods which are also high in saturated fats. From a consumer point of view, dietary cholesterol is far more easy to understand than the difference between healthy (unsaturated) and less healthy (saturated) fatty acids . Information on dietary cholesterol would enable consumers to make easier, quicker, and more informed food choices which fit in a healthy lifestyle. As a result, IMACE believes that the Panel should set a DRV for dietary cholesterol, which should be in line with the DRV for saturated fats – i.e. as low as possible, or at least in line with the generally accepted and recommended intake limits – i.e. max 300mg/day for adults.

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IMACE - International Margarine Association of the Countries of Europe	Conclusions and recommendations	Chapter Conclusions-Lines 2003-2035:IMACE comments The proposed average intake levels of 4E% for LA and 0.5 E% for ALA, are based on prevention of deficiency symptoms. This is in contrast with other international dietary recommendations that, taking prevention of CHD into account, advice substantially higher intake levels of LA and ALA for optimal health. From the available evidence, it can be derived that AI levels for preventing cardiovascular diseases should be at least 6 E% for LA and 1 E% for ALA. IMACE believes that with the currently proposed AI levels, EFSA does not seize the opportunity to help the European population achieving intakes of LA and ALA that have been shown to reduce the risk of CHD. If the EU implements these recommendations of the EFSA panel, evidence-based claims and other communications aimed at motivating consumers to increase intakes of LA and ALA will be extremely difficult to make. Chapter Conclusions-Lines 2047 to 2054: IMACE comments A DRV should be set also for dietary cholesterol as it is justified from a public health perspective given the fact that the negative effects of too high intakes of dietary cholesterol on health have clearly been demonstrated (cf. lines 1328 to 1340; 1701 to 1712; 1745 to 1751). There is an urgent need for a DRV to be set for dietary cholesterol in light of the Panel's conclusion that current average intake levels of dietary cholesterol among European adults are often well above the generally accepted and recommended intake limits (cf. lines 685 to 692 and lines 939 to 942). Furthermore, information on dietary cholesterol is a highly relevant marker for consumers to identify foods which are also high in saturated fats. Information on dietary cholesterol would enable consumers to make easier, quicker, and more informed food choices which fit in a healthy lifestyle. IMACE believes that the Panel should set a DRV for dietary cholesterol, which should be in line with the DRV for saturated fats – i.e. as low as possible, or at least in line with the generally accepted and recommended intake limits – i.e. max 300mg/day for adults.
Joint Dutch Product Bo	Conclusions and recommendations	1992-1993. The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oil and fruits and vegetable sectors in the Netherlands. We would like to submit comments to the summary but since this is not possible we submit our comments to the conclusions and recommendations chapter, under the same headings as in the summary Why are all the saturated fats treated as one group in the summary? The unsaturated fats are split up in separate groups, but the saturated fats are treated as one group. As stated in chapter 5.2.2 several saturated fats have different effects on cholesterol metabolism. In the Summary in line 66,67 the following is written: 'The Panel recommends that SFA intake should be as low as possible

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		within the context of a nutritionally adequate diet'. In the discussed scientific research in chapter 5 this recommendation is not supported. Furthermore, according to Table 5 (page 32), most Countries and also the WHO/FAO set the maximum SFA at 10 E%. In infants average intakes of SFA where between 11-13 E%. In adults, average SFA intakes vary between 9 to 17 E% and nearly 30% of the reported average intakes were 15 E% or higher (line 620-629). In addition: in several economically developed countries where the SFA is close to 10%, the capacity to decrease SFA much further is limited to major changes in dietary patterns, and is only likely to result in modest reductions in TC and LDL-C We therefore believe it is appropriate to set the recommendation for SFA at 10 E%.
Joint Dutch Product Bo	Conclusions and recommendations	line 1973 The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oils and fruits and vegetable sectors in the Netherlands. We would like to submit general comments and comments to the summary, but as this is not possible we submit these comments in the "conclusions and recommendations chapter. General remarks - The Dutch Product Boards are of the opinion that the conclusions in the summary do not reflect accurately the content of the report. More precise, the nuance in the report is lacking in the summary. Therefore, it is not immediately obvious on what basis the conclusions are drawn. Since the summary is generally the only part that policy makers read, it is important that the summary reflects the scientific state of the art, including the recent developments and nuances. - Recently, two WHO scientific updates were published in the European Journal of Clinical Nutrition (vol. 63, supplement 2s, pp S1-S75) and Annals of Nutrition and Metabolism (vol.55, no. 1-3: pp 5-300). It seems logical to take these two updates into account in the document.
Joint Dutch Product Bo	Conclusions and recommendations	line 1973, conclusions and recommendations. The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oil and fruits and vegetable sectors in the Netherlands. We would like to submit comments to the summary but since this is not possible we submit this comment to the conclusions and recommendations chapter. General remark: We would like to point out the following. Consumers do not eat saturated fats or unsaturated fats as such. They eat these nutrients in a matrix (food stuffs), as part of a balanced diet. In practice, the matrix influences the effects of the fatty acids, meaning that negative effects may not occur, or may be less pronounced, due to the presence of other nutrients in the food. In addition, basic food groups provide many positive nutrients such as vitamins, minerals and protein. Avoiding such foods

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		because of the presence of saturated fats or trans fats, may therefore not always be the preferred choice for consumers.
Joint Dutch Product Bo	Conclusions and recommendations	line 1982-1985 and line 2055: The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oil and fruits and vegetable sectors in the Netherlands. We would like to submit comments to the summary but since this is not possible we submit our comments to the conclusions and recommendations chapter, under the same headings as in the summary. What is the lower bound of the recommendation intake range of fat for children between 4-18 years? In line 50-55 no specific recommendation level is mentioned for children older than 4 years. In line 54 The Panel states that fat intakes below 25E% have been associated with low vitamin levels in some young children. So why then come to a lower bound of 20E% as stated in the table on line 2055 for children >4 years? It appears more prudent to recommend a total fat intake of at least 25E% for children.
Joint Dutch Product Bo	Conclusions and recommendations	Line 1986: The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oil and fruits and vegetable sectors in the Netherlands. We would like to submit a comment to the Annex on page 93. On page 93 (line 2915) the dietary reference value in the Netherlands is mentioned. However, these are the values from 2001, whereas the Dutch Health Council updated its advice in 2006. Therefore we recommend using the most recent dietary guidelines.

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Joint Dutch Product Bo	Conclusions and recommendations	Line 2010-20112, n-6 PUFA The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oil and fruits and vegetable sectors in the Netherlands. We would like to submit comments to the summary but since this is not possible we submit our comments to the conclusions and recommendations chapter, under the same headings as in the summary Why has the Panel set an AI for linoleic acid on 4 E% to prevent deficiencies as stated in line 89-91? This is in contrast with the WHO that set an AI of 2.5 E% LA to prevent deficiencies. In addition, why didn"t The Panel take into account the effect of n-6 PUFA on prevention of chronic diseases? This would be in line with the recommendation of the WHO, that judges the evidence that replacing SAFA by PUFA reduces the risk of CHD events as "convincing" and recommends a minimal intake level of PUFA of 6 E% to prevent chronic diseases.
Joint Dutch Product Bo	Conclusions and recommendations	line 2021-2023, n-3 PUFA The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oil and fruits and vegetable sectors in the Netherlands. We would like to submit comments to the summary but since this is not possible we submit our comments to the conclusions and recommendations chapter, under the same headings as in the summary Why has the Panel set the AI for a-linolenic acid on 0.5 E%? The WHO has set in her recent scientific update the AI of 0.5 E% of a-linolenic acid to prevent deficiency. Total n3-pufa (ALA+ EPA+ DHA) should be between 0,5-2 E% (of which n3 LCPUFA, based on a 2000 kcal diet should be 0,1-0,9 E%) as part of a healthy heart diet, possibly preventing some chronic diseases. The Dutch Health Council has set the AI for a-linolenic acid on 1 E%.
Joint Dutch Product Bo	Conclusions and recommendations	line 2039-2042: Trans fatty acids The Dutch Product Boards together represent the meat, eggs, dairy, fish, fats and oil and fruits and vegetable sectors in the Netherlands. We would like to submit comments to the summary but since this is not possible we submit our comments to the conclusions and recommendations chapter, under the same headings as in the summary We suggest adding to the statement of The Panel in the summary the following: The intake of TFA is close to the recommendation levels in most European countries, and are therefore not a public health issue anymore. The intake of total TFA is low because of the efforts made by the food industry in reducing the amount of industrial TFA in their products (and these efforts are ongoing). The level of ruminant TFA in meat (products) and dairy products is already naturally low.
Lipid Nutrition	1. Introduction	SUMMARY line 147-150 There is strong evidence that CLA reduces fat in humans and this can be deemed to prevent obesity or weight gain.

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Lipid Nutrition	2. Categories, structure and function	Line 583-586 Addition: Cis-9, trans-11 CLA and Trans-10, cis-12 CLA are also found in small quantities in human breastmilk in a 80/20-ratio. (Lipids. Vol.41, no 9(2006); Human Milk Fatty Acid Composition Varies Most in DHA). Delete: line 585 --> Trans-10, cis-12 CLA is mainly found in supplements and produced by industrial processing. Add: New line 585: Commercial available CLA for use in food supplements and foodstufs contains Cis-9, trans-11 CLA and Trans-10, cis-12 CLA in a 50/50-ratio.
Lipid Nutrition	3. Dietary sources and intake data	Between lines 684 and 685 There is a missing chapter on Intake data from CLA: New chapter 3.2.6 CLA Ritzenthaler et al. (2001) estimated the mean background dietary CLA intake (from all isomers) to be 212 and 151 mg/day for men and women, respectively. This study, with 51 men and 51 women between ages of 18 and 60, compared 3 day food duplicates with dietary records and food-frequency questionnaires. Earlier surveys, estimated intake to be 137 and 52 mg/day in college-aged males and females, respectively (Ritzenthaler et al., 1998), or 291 and 15 mg/day in lactating women with high- and low-dairy diets (Park et al., 1999). Herbel et al. (1998) reported 127 mg/day as the average daily CLA intake in a study with healthy young men and women. Thus, the mean daily dietary CLA intake from the background diet can be estimated at 212 and 151 mg/day for men and women, with subgroups consuming up to 300 mg/day. Commercial CLA-rich oil has been available on the EU market since 1995, mainly in food supplements. Typically these deliver a dose of up to 3 g of CLA per daily serving.
Lipid Nutrition	5.4. Inflammation and immne function	line 1430-1428 This evaluation is not correct ! This is quite the contrary, there are numerous human and animal studies which show clear effects of CLA on immune function. These include reduction in pro-inflammatory cytokines, increases in antibodies, reduction in cold symptoms, and reduction in allergy symptoms. (on request I can send an extensive overview of the relevent published literature ! -->contact: jaap.kluifhooft@lipidnutrition.com)

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Lipid Nutrition	5.7. Body weight control and energy balance	line 1606-1617 Remark/finetuning scientific evaluation: The Gaullier paper should not be used as a definitive trial to state that CLA causes fat loss from around the legs. That trial had a large number of women who typically gain fat from around the legs. This is why they observed fat mass from around that region. Also, several of the trials show a within group reduction in fat around the abdomen.
Lipid Nutrition	5.7. Body weight control and energy balance	line 1614 typo: "trans-10, cis-9 CLA" should read "trans-10, cis-12 CLA"
London Metropolitan University	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	We, the undersigned 22 scientific researchers and clinicians, specialising in omega-3 fatty acids, urge EFSA to withdraw and reconsider Para 6.4.2 in its entirety. The current text suffers from fundamental problems: 1. It includes, without qualification, the statement that "The human body can synthesize EPA and DHA from alpha-linolenic acid". In fact, the conversion rate is so low, especially for DHA, that consumers would receive little or none of the health benefits associated with DHA. There is much recent research on this point, summarised in the official ISSFAL position on conversion, published in 2008. 2. The AI of 250mg/d for combined EPA plus DHA is too low. Over the past 20 years, there have been 15 recommendations on EPA/DHA intakes by specialist organisations and committees. The average of these recommendations is 566mg/d. EFSA should reconsider its AI in the light of the much higher recommendations set by scientists who specialise in this field. 3. There is no mention of mental health at all in this section. In fact, there is a great deal of research documenting the benefits of LC n-3 PUFA on mental well-being throughout the life cycle, from foetal brain development to the amelioration of Alzheimer"s disease. The most recent major research review relevant to mental well being was published by the Food & Drug Administration earlier this year, "Summary of published research on the beneficial effects of fish consumption and omega-3 fatty acids for certain neurodevelopmental and caridovascular endpoints". EFSA should consider this large body of research evidence fully and carefully, then make recommendations appropriate for mental as well as physical health. In addition, earlier in section 6.4, the report declines to make any recommendation on the n-3/n-6 ratio. In fact, it is increasingly recognised that these fatty acids are physiological competitors. Therefore, the large and rising preponderance of n-6 fats in western diets is having a detrimental effect. EFSA should look at this question again. These are all basic scientific points. Therefore, EFSA should reconsider its conclusions and advice on omega-3 fatty acids afresh, right from the beginning.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Prof Michael Crawford Director, Institute of Brain Chemistry and Human Nutrition London Metropolitan University Prof Gordon Bell Institute of Aquaculture University of Stirling Dr Allain Amador Bueno University of Sao Paolo, Brazil Prof Stephen Cunnane Research for Centre on Aging University of Sherbrooke, Canada Peter Clough Technical Director Efamol Ltd Dr Pauline Emmett Centre for Child and Adolescent Health University of Bristol Prof Claudio Galli Professor of Pharmacology University of Milan Prof Jean Golding Emeritus, Paediatric & Perinatal Epidemiology University of Bristol Dr Laurence Harbige University of Greenwich Cmdr Joseph R Hibbeln Acting Chief, Section on Nutritional Neurochemistry US National Institutes of Health

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Prof Amanda Kirby Developmental Disorders University of Wales Prof William E M Lands Emeritus Professor of Biological Chemistry University of Michigan Dr Dianne LeFevre Psychiatrist Dr Robert Lister Institute of Brain Chemistry and Human Nutrition London Metropolitan University Prof Stephen Oppenheimer Nutritional Anthropology Oxford University Prof Margaret Rayman Nutritional Medicine University of Surrey Dr Alexandra Richardson Oxford University Director, Food and Behaviour Research Prof Clemens von Schacky Professor of Preventive Cardiology University of Munich Prof Andrew Sinclair Professor of Human Nutrition Deakin University, Australia Prof John Stein

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Professor of Neurophysiology Oxford University Dr Peter Sullivan Department of Paediatrics Oxford University Prof Jack Winkler Director, Nutrition Policy Unit London Metropolitan University
Martek Biosciences Corporation	2. Categories, structure and function	(Lines 453- 464) - Even though the Panel assumes that internal conversion of LA to AA (20:4n-6) is sufficient in most diets and proposes to not establish a DRV for AA, this scientific document should reflect the physiological importance of AA. AA is a substrate for production of eicosanoids, an essential component of cell membranes, and an important factor in cell signaling pathways. It is involved with regulation of gene expression and is important for neural development and function. AA is in all cell membranes and is found at particularly high levels in neural membranes, particularly those of the brain. This language should be consistently recognized throughout the Opinion including lines 92-94 of the Summary. (Institute of Medicine, Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids, The National Academies Press, Washington, DC 2005, pgs. 426-427.)
Martek Biosciences Corporation	2. Categories, structure and function	L471-477 – This section identifies the limited ability of alpha-linolenic acid (ALA) to serve as a source of DHA. A recent ISSFAL position paper by Brenna and co-workers confirms that conversion of ALA to DHA is less than 1% in adults, this reference may be a useful addition to the Opinion(Brenna JT, Salem N, et al. Prostaglandins, Leukotrienes and Essential Fatty Acids 80:85-91, 2009. See Summary Statement #2). Unfortunately, the limited conversion ALA to DHA is not sufficiently identified throughout the current draft opinion. Specifically, the Summary (L107) recognizes that the body converts ALA to DHA and EPA but fails to quantify the limited extent of conversion. We respectfully suggest that language from L474 be added to the opinion Summary, specifically, "The human body can synthesise EPA and DHA from a-linolenic acid, however, the conversion of ALA into DHA may be even less than 1%" at line 107. L480 – The Committee notes that "the developing brain accumulates large amounts of DHA both pre- and postnatally (until two years of age)…". We respectfully disagree, however, with the limitation of DHA accumulation only "until two years of age". Classic research by Martinez indicates that DHA accumulation by the brain postnatally "is still very significant until at least 2 years of age" [emphasis added], specifically, Martinez provides data for children up to 2.7 years(J Pediatr 120:S129-39, 1992 Pg. S132 Fig. 3A). More recent data from Carver and coworkers (Carver JD, et al. Brain Research Bulletin 56:79-85, 2001. Pg. 82 Fig. 1; Pg. 84 Table 2) indicates that levels of DHA in the cerebral cortex increases steadily up to the age of 18 years. Finally, it is well known that the brain growth spurt begins during the third trimester and continues throughout the first 3-4

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		years of life (Dobbing J and Sands J. Archives of Disease in Childhood, 48:757-767, 1973. Pg. 765), this important developmental period is recognized as a period of critical brain growth and neuronal development. Collectively, these data support recognition of an expanded range of DHA accumulation by the postnatal brain in the current Opinion or elimination of the "until two years of age" language without an effort to specify further.
Martek Biosciences Corporation	3. Dietary sources and intake data	Line 548 – The Panel recognizes meat as a source of AA (20:4n-6). This statement should also recognize the production of AA from fungal sources. Fungal AA is the predominant source of AA in infant formula.
Martek Biosciences Corporation	4. Overview of dietary reference values and recommendations	L866-867 – notes the U.S. IOM recommendation for DHA and EPA contribution toward reversing an n-3 fatty acid deficiency but fails to recognize the level of contribution specified by the IOM, i.e up to 10%. We respectfully request the following revised language be considered for L866-867, "Small amounts of EPA and DHA (up to 10%) can contribute towards reversing an n-3 fatty acid deficiency and can therefore contribute towards the AI for alpha-linolenic acid." L1012-1013 – We respectfully request the following revised language be considered for L866-867, "Small amounts of EPA and DHA (up to 10%) can contribute towards reversing an n-3 fatty acid deficiency and can therefore contribute towards the AI for alpha-linolenic acid."
Martek Biosciences Corporation	5.1. Dietary requirements	L1176-1180 – This section identifies the limited ability of alpha-linolenic acid (ALA) to serve as a source of DHA. A recent ISSFAL position paper by Brenna and co-workers confirms that conversion of ALA to DHA is less than 1% in adults, this reference may be a useful addition to the Opinion(Brenna JT, Salem N, et al. Prostaglandins, Leukotrienes and Essential Fatty Acids 80:85-91, 2009. See Summary Statement #2). L1199-L1207 – This section provides sound rationale for a DHA requirement during pregnancy and nursing. However, recent expert group recommendations and guidelines are not mentioned. Specifically, the Consensus recommendations on behalf of the European Commission research projects Perinatal Lipid Metabolism (PeriLip) and Early Nutrition Programming (EARNEST) could be recognized. In addition, the benefits to maternal and infant health noted by the PeriLip/EARNEST document should also be recognized, specifically, slightly longer pregnancy duration, reduced risk of preterm birth, and somewhat higher birth weight (Koletzko B, Cetin I, et al. Br J Nutr 98:873-877, 2007; Conclusions and Recommendations #2,6). L1220 – We respectfully request that "such small amounts of" be removed from this sentence. Given the very limited intake and availability of DHA, particularly from 6-24 months of age, classification of 100 mg as a small amount could be misleading as it suggests a goal readily accomplished as part of the normal diet. In fact, the most common source of DHA other than infant formula is fatty fish. Fish and seafood, however, are typically restricted by parents to at least 3 years of age due to allergy related concerns (ESPGHAN Committee on Nutrition, J Pedi Gastro Nutr 46:99-110, 2008. Pg. 104-105).

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Martek Biosciences Corporation	5.1. Dietary requirements	Line 1154 - In their Opinion, the Panel makes no recommendation for a DRV for ARA (20:4n-6). However, the Panel should make clear that the reasoning for this is based on information available from a plentiful, meat-based diet in healthy adults only. In general, research is lacking regarding an optimal intake of ARA for special populations. In addition, research does not indicate that there is not a need for ARA, especially for some populations. ARA is in all cell membranes and is found at particularly high levels in neural membranes, particularly those of the brain. Endogenous synthesis of ARA by the infant is insufficient to meet the demands of the growth and development. Tissue levels drop rapidly following birth unless dietary ARA is supplied in either human milk or a supplemented infant formula (Clandinin M, et al. Pediatr Res 1997;42:819-25, Table 8, p. 824). During the weaning period, the introduction of complementary feedings can vary greatly with regard to n-6 PUFA content and there may be many months of transition into the adult diet (C. Agostoni, et al. J Ped Gastr Nutr. 2008;46(1):99-110). ARA continues to be an important diet component during this transition and only a combination of ARA with DHA (22:6n-3) has shown neurocognitive benefits for infants. Importantly, all studies used to support the recent EFSA Article 14 opinion regarding DHA and visual development of infants provided DHA in combination with ARA. The developmental benefits of formula and complementary foods supplemented with both ARA and DHA continue well beyond the period of supplementation and extend into early childhood (Birch E, et al. Early Hum Dev. 2007;83(5):279-84). We respectfully request that the ARA be recognized as associated with neurodevelopmental outcomes.
Martek Biosciences Corporation	5.11. Nervous system function	L1817 – This sentence appears to contradict recommendations made by the Committee in the Conclusions of the current opinion. This sentence notes that optimal amounts of LC-PUFAs can not be specified for infants in the second six months of life, however, the Conclusions (L2029-2030) indicate a proposed "… AI of 100 mg DHA for older infants (> 7 months of age) and young children below the age of 24 months". We respectfully request that section 5.11 reflect the Panel's conclusion regarding an optimal level of DHA during the second six months of life.
Martek Biosciences Corporation	5.11. Nervous system function	Line 1804 – The current Opinion should reflect that only infant formulas which contain the combination of DHA and ARA show neurocognitive benefit and benefits that extend well beyond the period of supplementation (Birch E, et al. Early Hum Dev. 2007;83(5):279-84). In fact, all studies used to support the recent EFSA Article 14 opinion regarding DHA and visual development of infants provided DHA in combination with ARA. During the weaning period, the introduction of complementary feedings can vary greatly with regard to n-6 PUFA content and there may be many months of transition into the adult diet (C. Agostoni, et al. J Ped Gastr Nutr. 2008;46(1):99-110). We respectfully request that the Committee recognize that ARA may be limited during complementary feeding although an AI can not yet be defined. Line 1812 – The current Opinion should note that recommendations provided by the Committee are consistent with the EU Directive for Infant Formula and Follow-on Formula. The Opinion should be clear that the required combination of ARA with DHA applies to follow-on formula as well as infant formula.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Martek Biosciences Corporation	5.2. Serum lipids and lipoproteins	L1274-1279 – This section recognizes the role of EPA and DHA in triglyceride reduction but does not recognize the independent role of DHA in this regard. A recent analysis of 16 studies of algal DHA supplementation reports that "clinical trials with algal-DHA as a TG oil have demonstrated a marked reduction in serum TG levels (up to 26%) in normal individuals and in those with HTG or combined hyperlipidemia." (Ryan AS, et al. Am J Therapeutics 16:183-92. Table 2). We respectfully request that the independent role of DHA for TG reduction be recognized in this section. Additionally, recognition of the independent role of DHA for elevation of HDL is also requested (Ryan AS, et al. Am J Therapeutics 16:183-92. Table 3). L1279 – We respectfully request that the terminology "fish oil fatty acids" be replaced with EPA and/or DHA as it is more appropriate to recognize the beneficial nutrients as opposed to any one dietary source. These nutrients are not limited to fish oil but currently available from fish, marine microalgae and numerous fortified and enriched foods and beverages.
Martek Biosciences Corporation	5.3. Haemostatic function	L1377-L1386 – These lines recognize the role of EPA and DHA in hemostasis. It is important to note that changes in bleeding times resulting from decreased platelet aggregation as noted in L1380-L1382 are within a clinically normal range and considered a benefit as opposed to a safety issue in the general population (Lavie CJ, et al. J Am Coll Cardiol 54:585-594, 2009). L1399-L1400 – We respectfully request the following revised language be considered, "An exception may be the n-3 LCPUFA, which may decrease platelet aggregation in particular at intakes above 1 g but without clinically adverse changes in bleeding in the general healthy population."
Martek Biosciences Corporation	5.4. Inflammation and immne function	L1437 – We respectfully request that "fish oil" be removed as it could be misleading to suggest that only fish oil can provide beneficial n-3 LCPUFA. These nutrients are not limited to fish oil but currently available from fish, marine microalgae and numerous fortified and enriched foods and beverages.
Martek Biosciences Corporation	5.5. Blood pressure	L1464-L1473 - We respectfully request that the terminology "fish oil" be replaced with EPA and/or DHA since these nutrients are available from multiple sources in addition to fish oil such as DHA from marine microalgae. It seems more appropriate to recognize a particular intake level of the beneficial nutrients as opposed to any one dietary source. Studies of blood pressure in response to algal-DHA supplementation are available and suggest at least equal reductions in response to DHA as compared to EPA and DHA from fish oil (Ryan AS, et al. Am J Therapeutics 16:183-92. Table 3). L1486 – We respectively request "fish oil" be removed and n-3 LCPUFA rather than n-3 PUFA be used in this sentence. Authors provide data only for n-3 LCPUFA and blood pressure reduction therefore n-3 LCPUFA is a more appropriate term than n-3 PUFA which would typically include ALA. In addition, it could be misleading to suggest that only fish oil can provide beneficial n-3 LCPUFA. These nutrients are not limited to fish oil but currently available from fish, marine microalgae and numerous fortified and enriched foods and beverages.
Martek Biosciences Corporation	5.8. Cardiovascular disease	L1716 - We respectfully request that the term "fish oil" be replaced with EPA and DHA since these nutrients are available from multiple sources in addition to fish oil, such as marine microalgae, and it seems more appropriate to recognize a particular intake level of the beneficial nutrients as opposed to any one dietary source. Modifying the language in this section would also be consistent with that used in EFSA's scientific opinion regarding labelling reference intake values for n-3 and cardiovascular

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		disease prevention (The EFSA Journal, 1176:1-11, 2009) and with L1919-1924 of the current opinion.
Martek Biosciences Corporation	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	L1915 - This sentence recognizes the ability of the body to synthesize DHA and EPA from a-linolenic acid but does not identify the limited extent of this conversion. A recent ISSFAL position paper by Brenna and co-workers (Brenna JT, Salem N, et al. Prostaglandins, Leukotrienes and Essential Fatty Acids 80:85-91, 2009. See Summary Statement #2) confirms that conversion of ALA to DHA is less than 1% in adults. Unfortunately, the limited conversion ALA to DHA is not sufficiently identified throughout the current draft opinion. We respectfully suggest that language from L474 be added to this sentence, specifically, "The human body can synthesise EPA and DHA from a-linolenic acid, however, the conversion of ALA into DHA may be even less than 1%".
Martek Biosciences Corporation	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Line 1901 - Even though the Panel assumes that internal conversion of LA to ARA is sufficient in most diets and proposes to not establish a DRV for ARA (20:4n-6) this scientific document should reflect the physiological importance of ARA. ARA is a substrate for production of eicosanoids, an essential component of cell membranes, and an important factor in cell signaling pathways. It is involved with regulation of gene expression and is important for neural development and function. ARA is in all cell membranes and is found at particularly high levels in neural membranes, particularly those of the brain. (Institute of Medicine, Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids, The National Academies Press, Washington, DC 2005, pgs. 426-427). This scientific document should indicate the populations at risk for suboptimal ARA status including: vegans, particularly during the perinatal period; those with low intake of LA (18:2n-6); and, infants and toddlers during complementary feeding.
Martek Biosciences Corporation	Conclusions and recommendations	L2024 - This sentence recognizes the ability of the body to synthesize DHA and EPA from a-linolenic acid but does not identify the limited extent of this conversion. A recent ISSFAL position paper by Brenna and co-workers (Brenna JT, Salem N, et al. Prostaglandins, Leukotrienes and Essential Fatty Acids 80:85-91, 2009. See Summary Statement #2) confirms that conversion of ALA to DHA is less than 1% in adults. We respectfully suggest that language from L474 be added to this sentence, specifically, "The human body can synthesise EPA and DHA from a-linolenic acid, however, the conversion of ALA into DHA may be even less than 1%". L2029-2030 – Conclusions regarding a DHA AI for children > 7 months until the age of 24 months are not reflected in the opinion Summary. We respectfully request that the conclusions from L2020-2030 be added to the Summary.
Martek Biosciences Corporation	Conclusions and recommendations	Line 2013 - Even though the Panel assumes that internal conversion of LA to ARA is sufficient in most diets and proposes to not establish a DRV for ARA (20:4n-6) this scientific document should reflect the physiological importance of ARA. ARA is a substrate for production of eicosanoids, an essential component of cell membranes, and an important factor in cell signaling pathways. It is involved with regulation of gene expression and is important for neural development and function ARA is in all cell membranes and is found at particularly high levels in neural membranes, particularly those of the brain. (Institute of Medicine, Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids, The National Academies Press, Washington, DC 2005, pgs. 426-427). This scientific document should indicate the populations at risk for suboptimal ARA status including: vegans, particularly during the perinatal period; those with low intake of LA (18:2n-6); and, infants and toddlers during complementary feeding.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Center of Public Health Protection	1. Introduction	Line 349: It is more precisely to state - "Dietary fats mainly consist of triacylglycerols, which are...", since fat consists of heterogeneous mixture of different TG (ie not "triacylglycerol"). Ref.: 1) IUPAC. Joint Comm IUNS & IUPAC Commission on Food (2001) Lexicon of Lipid Nutrition (IUPAC Techn Rep) Pure Appl Chem 73: 685-744. 2) SM Grundy. Dietary Fat. In: Present Knowledge in Nutrition 7th ed, p.44 Line 380: It is more precisely to state - "Due to its physical properties, cholesterol, a steroid, is also included in dietary fats". (Cholesterol is not a fat, strictly categorizing). Ref.: 1) IoM (2005) DRI for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. The National Academies Press, Washington DC, p.424. 2) IUPAC. Joint Comm IUNS & IUPAC Commission on Food (2001) Lexicon of Lipid Nutrition (IUPAC Techn Rep) Pure Appl Chem 73: 685-744.
National Center of Public Health Protection	2. Categories, structure and function	Lines 444 and 445: Eicosanoid cascade include also Thromboxanes (cyclooxygenase pathway) - an important class of eicosanoids. Ref.: 1) IoM (2005) DRI for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. The National Academies Press, Washington DC, p. 434 2) IUPAC (2001) Joint Comm IUNS & IUPAC Commission on Food. Lexicon of Lipid Nutrition (IUPAC Techn Rep). Pure Appl Chem 73: 685-744 Lines 443 and 454: Here the abbreviation of Arachidonic acid (AA) (and also in lines 1813, 1815) is different from that in the other chapters - Lines 1155, 1158, 1160, 1161, 1271, 2055, 2246, where it is (ARA) - so an unification is necessary.
National Center of Public Health Protection	4. Overview of dietary reference values and recommendations	Additionally some technical aid: Line 862 : "".. a alpha-linolenic..." should become ".. an alpha-...."
National Center of Public Health Protection	5.6. Glucose tolerance and insulin sensitivity	Additionally some technical aid : Line 1523 : "..sourcers.." should become ".. sources"

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Center of Public Health Protection	5.8. Cardiovascular disease	Additionally some technical aid : Line 1629 : "A reviewe.." should become ".. review..."
National Center of Public Health Protection	6.1. Total fat	Additionally some technical aid : Line 1836 : .."..the available" should become ". The available.."
National Center of Public Health Protection	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	Additionally some technical aid : Line 1886 : "...to derive a, AR.." should become ".. an AR..."
National Center of Public Health Protection	Conclusions and recommendations	Additionally some technical aid : Line 2005 : "...to derive an LTI.." should become ".. a LTI.." Line 2055 : Summary ... Row "EPA + DHA" - third column "Children" "AI 7-24 mths.." should become " 7-24 months.."
National Center of Public Health Protection	References	Additionally some technical aid : Annex 3 : Table 6 : Line 2917 : Third row, First column : "SAFA" should become "SFA"

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Center of Public Health Protection	References	An unification is necessary for the presentation of references - eg: Lines 2086 and 2087: Int J Obes Relat Metab Disord 24: 1545-1552. and Lines 2207 and 2208: Amer.J.Clin.Nutr. 87, 1405-1413. ie - with or without dots in the titles of scientific journals; after the number of the respective volume - comma or :, etc. Unification concerns all the Section - "References".
National Heart Forum	1. Introduction	The National Heart Forum (NHF) welcomes the process of developing Dietary Reference Values (DRVs) for nutrients. We agree that DRVs can be used for a variety of purposes including diet assessment and planning, providing reference values in food labelling, in establishing food based dietary guidelines (FBDG) as well as nutrient profiles. We consider EFSA's work of essential and necessary for harmonising DRVs and FBDGs as much as possible across Europe. However, the European level guidelines, while useful, should not supersede existing dietary guidelines at the country level. EFSA should clarify the purpose of the European DRVs in relation to national dietary guidelines. Given the importance of DRVs for a wide variety of applications, we recommend that in instances where the evidence is insufficient, EFSA should adopt a precautionary approach and develop the best estimates based on the available evidence. We recommend that EFSA define a clear time-period over which the DRVs will apply eg 10 years. EFSA should also set time-scales for the evaluation of the effectiveness of the DRVs on improving the diet of the European population, after which they should be revised.
National Heart Forum	1. Introduction	We would like to know whether EFSA has consulted bodies that have developed DRVs in European countries such as the UK Scientific Advisory Committee on Nutrition, and recommend that it does so in the development of the European DRVs.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Heart Forum	2. Categories, structure and function	The National Heart Forum (NHF) welcomes the process of developing Dietary Reference Values (DRVs) for nutrients. We agree that DRVs can be used for a variety of purposes including diet assessment and planning, providing reference values in food labelling, in establishing food based dietary guidelines (FBDG) as well as nutrient profiles. We consider EFSA's work of essential and necessary for harmonising DRVs and FBDGs as much as possible across Europe. However, the European level guidelines, while useful, should not supersede existing dietary guidelines at the country level. EFSA should clarify the purpose of the European DRVs in relation to national dietary guidelines. Given the importance of DRVs for a wide variety of applications, we recommend that in instances where the evidence is insufficient, EFSA should adopt a precautionary approach and develop the best estimates based on the available evidence. We recommend that EFSA define a clear time-period over which the DRVs will apply eg 10 years. EFSA should also set time-scales for the evaluation of the effectiveness of the DRVs on improving the diet of the European population, after which they should be revised.
National Heart Forum	4. Overview of dietary reference values and recommendations	a) Lines 144-146 Trans fats: the current recommendation that TFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. A target will be needed on which to monitor progress and achievement towards attaining the lowest possible TFA intakes in the European population. b) A number of existing guidelines already recommend 1%E or less eg the WHO/FAO population nutrient intake goals and the German, Austrian, Swiss and French recommendations (line 1036). Such a target is achievable in practice, as demonstrated by the low average population trans fat intakes of 0.5-0.6%E which have been achieved in countries such as Denmark, Finland, Norway and Sweden [Lines 682-683]. c) Given the importance of DRVs for a variety of purposes, and EFSA's acknowledgement that trans fat intakes should be as low as possible, the National Heart Forum recommends that an EU population intake target of less than 1%E is set. Industry should use the mid-point value of 0.5%E for their GDAs. d) Lines 2041-2: "The Panel recommends that TFA intake should be as low as possible within the context of a nutritionally adequate diet." We agree with this statement, but recommend that an interim target of <1%E is set for the population to facilitate this process. A corresponding target of 0.5%E should be set for the food industry for the purposes of GDAs, to support the elimination of unnecessary industrially produced TFAs from the food supply.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Heart Forum	4. Overview of dietary reference values and recommendations	Lines 63-65 Saturated fats: the current recommendation that SFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of max 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. Lines 1989-1991: "There is no threshold of SFA intakes below which no adverse effects are observed. Thus no Upper Limit can be set." We agree. However, given the huge benefits to be had from reducing SFA intakes at the individual and population level, EFSA should set an interim target of <5%E intake. This target will help facilitate the evaluation and assessment of action to reduce population intakes, and it can subsequently be revised downwards once it has been met.
National Heart Forum	4. Overview of dietary reference values and recommendations	The National Heart Forum (NHF) welcomes the process of developing Dietary Reference Values (DRVs) for nutrients. We agree that DRVs can be used for a variety of purposes including diet assessment and planning, providing reference values in food labelling, in establishing food based dietary guidelines (FBDG) as well as nutrient profiles. We consider EFSA's work of essential and necessary for harmonising DRVs and FBDGs as much as possible across Europe. However, the European level guidelines, while useful, should not supersede existing dietary guidelines at the country level. EFSA should clarify the purpose of the European DRVs in relation to national dietary guidelines. Given the importance of DRVs for a wide variety of applications, we recommend that in instances where the evidence is insufficient, EFSA should adopt a precautionary approach and develop the best estimates based on the available evidence. We recommend that EFSA define a clear time-period over which the DRVs will apply eg 10 years. EFSA should also set time-scales for the evaluation of the effectiveness of the DRVs on improving the diet of the European population, after which they should be revised.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Heart Forum	5. Criteria (endpoints) on which to base the dietary reference values	Lines 63-65 Saturated fats: the current recommendation that SFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of max 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. Lines 1989-1991: "There is no threshold of SFA intakes below which no adverse effects are observed. Thus no Upper Limit can be set." We agree. However, given the huge benefits to be had from reducing SFA intakes at the individual and population level, EFSA should set an interim target of <5%E intake. This target will help facilitate the evaluation and assessment of action to reduce population intakes, and it can subsequently be revised downwards once it has been met.
National Heart Forum	6. Data on which to base dietary reference values	a) Lines 144-146 Trans fats: the current recommendation that TFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. A target will be needed on which to monitor progress and achievement towards attaining the lowest possible TFA intakes in the European population. b) A number of existing guidelines already recommend 1%E or less eg the WHO/FAO population nutrient intake goals and the German, Austrian, Swiss and French recommendations (line 1036). Such a target is achievable in practice, as demonstrated by the low average population trans fat intakes of 0.5-0.6%E which have been achieved in countries such as Denmark, Finland, Norway and Sweden [Lines 682-683]. c) Given the importance of DRVs for a variety of purposes, and EFSA's acknowledgement that trans fat intakes should be as low as possible, the National Heart Forum recommends that an EU population intake target of less than 1%E is set. Industry should use the mid-point value of 0.5%E for their GDAs. d) Lines 2041-2: "The Panel recommends that TFA intake should be as low as possible within the context of a nutritionally adequate diet." We agree with this statement, but recommend that an interim target of <1%E is set for the population to facilitate this process. A corresponding target of 0.5%E should be set for the food industry for the purposes of GDAs, to support the elimination of unnecessary industrially produced TFAs from the food supply.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Heart Forum	6. Data on which to base dietary reference values	Line 1992: "The panel therefore recommends that intakes should be as low as possible." We agree but recommend an interim target of <5%E intake is set to facilitate this process. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. We recommend this level owing to the significant reductions in population intake levels of saturated fat which have been achieved in Western European countries such as the UK, following the introduction of the initial 10%E targets. It is now time to revise the goal downwards to further improve population health.
National Heart Forum	6. Data on which to base dietary reference values	Lines 63-65 Saturated fats: the current recommendation that SFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of max 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. Lines 1989-1991: "There is no threshold of SFA intakes below which no adverse effects are observed. Thus no Upper Limit can be set." We agree. However, given the huge benefits to be had from reducing SFA intakes at the individual and population level, EFSA should set an interim target of <5%E intake. This target will help facilitate the evaluation and assessment of action to reduce population intakes, and it can subsequently be revised downwards once it has been met.
National Heart Forum	6. Data on which to base dietary reference values	Total fat [Lines 608 onwards]: We note the proposed recommendation of 20-35% Energy. However, we recommend that the range for total fat is limited to 20%-30%E for the following reasons: 1. reduced fat diets have a significant role in the prevention of weight gain [lines 1569-72; 1581-52], 2. prevention of weight gain is a key population goal for the European population 3. achievement of population level fat intake levels in the range 20-30%E is achievable in practice (line 1066) In addition, we recommend that the food industry should initially use the mid-point of 25%E as the GDA for adults and this should be reviewed after a period of time.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Heart Forum	6.1. Total fat	Total fat [Lines 608 onwards]: We note the proposed recommendation of 20-35% Energy. However, we recommend that the range for total fat is limited to 20%-30%E for the following reasons: 1. reduced fat diets have a significant role in the prevention of weight gain [lines 1569-72; 1581-52], 2. prevention of weight gain is a key population goal for the European population 3. achievement of population level fat intake levels in the range 20-30%E is achievable in practice (line 1066) In addition, we recommend that the food industry should initially use the mid-point of 25%E as the GDA for adults and this should be reviewed after a period of time.
National Heart Forum	6.2. Saturated fatty acids (SAT)	Line 1992: "The panel therefore recommends that intakes should be as low as possible." We agree but recommend an interim target of <5%E intake is set to facilitate this process. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. We recommend this level owing to the significant reductions in population intake levels of saturated fat which have been achieved in Western European countries such as the UK, following the introduction of the initial 10%E targets. It is now time to revise the goal downwards to further improve population health.
National Heart Forum	6.2. Saturated fatty acids (SAT)	Lines 63-65 Saturated fats: the current recommendation that SFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of max 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. Lines 1989-1991: "There is no threshold of SFA intakes below which no adverse effects are observed. Thus no Upper Limit can be set." We agree. However, given the huge benefits to be had from reducing SFA intakes at the individual and population level, EFSA should set an interim target of <5%E intake. This target will help facilitate the evaluation and assessment of action to reduce population intakes, and it can subsequently be revised downwards once it has been met.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Heart Forum	6.5. Trans fatty acids (TFA)	a) Lines 144-146 Trans fats: the current recommendation that TFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. A target will be needed on which to monitor progress and achievement towards attaining the lowest possible TFA intakes in the European population. b) A number of existing guidelines already recommend 1%E or less eg the WHO/FAO population nutrient intake goals and the German, Austrian, Swiss and French recommendations (line 1036). Such a target is achievable in practice, as demonstrated by the low average population trans fat intakes of 0.5-0.6%E which have been achieved in countries such as Denmark, Finland, Norway and Sweden [Lines 682-683]. c) Given the importance of DRVs for a variety of purposes, and EFSA's acknowledgement that trans fat intakes should be as low as possible, the National Heart Forum recommends that an EU population intake target of less than 1%E is set. Industry should use the mid-point value of 0.5%E for their GDAs. d) Lines 2041-2: "The Panel recommends that TFA intake should be as low as possible within the context of a nutritionally adequate diet." We agree with this statement, but recommend that an interim target of <1%E is set for the population to facilitate this process. A corresponding target of 0.5%E should be set for the food industry for the purposes of GDAs, to support the elimination of unnecessary industrially produced TFAs from the food supply.
National Heart Forum	Conclusions and recommendations	a) Lines 144-146 Trans fats: the current recommendation that TFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. A target will be needed on which to monitor progress and achievement towards attaining the lowest possible TFA intakes in the European population. b) A number of existing guidelines already recommend 1%E or less eg the WHO/FAO population nutrient intake goals and the German, Austrian, Swiss and French recommendations (line 1036). Such a target is achievable in practice, as demonstrated by the low average population trans fat intakes of 0.5-0.6%E which have been achieved in countries such as Denmark, Finland, Norway and Sweden [Lines 682-683]. c) Given the importance of DRVs for a variety of purposes, and EFSA's acknowledgement that trans fat intakes should be as low as possible, the National Heart Forum recommends that an EU population intake target of less than 1%E is set. Industry should use the mid-point value of 0.5%E for their GDAs. d) Lines 2041-2: "The Panel recommends that TFA intake should be as low as possible within the context of a nutritionally adequate diet." We agree with this statement, but recommend that an interim target of <1%E is set for the population to facilitate this process. A corresponding target of 0.5%E should be set for the food industry for the purposes of GDAs, to support the elimination of unnecessary industrially produced TFAs from the food supply.

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National Heart Forum	Conclusions and recommendations	Line 1992: "The panel therefore recommends that intakes should be as low as possible." We agree but recommend an interim target of <5%E intake is set to facilitate this process. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. We recommend this level owing to the significant reductions in population intake levels of saturated fat which have been achieved in Western European countries such as the UK, following the introduction of the initial 10%E targets. It is now time to revise the goal downwards to further improve population health.
National Heart Forum	Conclusions and recommendations	Lines 63-65 Saturated fats: the current recommendation that SFA intakes should be 'as low as possible' is not helpful to the use of DRVs for the assessment and planning of diets or the use of DRVs as basis for reference values food labeling. Targets will be key to the monitoring and assessment of efforts to reduce SFA intakes in the European population if this is a dietary goal. As noted in section 4.1.2 [Lines 758-780] the majority of existing guidelines in for example, Germany, Austria, Switzerland, US, UK and France, set SFA population targets of max 10%E or less. This target is achievable in practice, as evidenced by low intake values in South European countries [line 627], and the lower range level of less than 9%E recorded in Europe [Line626]. Given the importance of DRVs for a variety of purposes, we therefore recommend that based on the available evidence, a SFA target of <5%E is set for the European population. A food industry target of 5%E should be set for the purposes of GDAs for adults in the first instance. Lines 1989-1991: "There is no threshold of SFA intakes below which no adverse effects are observed. Thus no Upper Limit can be set." We agree. However, given the huge benefits to be had from reducing SFA intakes at the individual and population level, EFSA should set an interim target of <5%E intake. This target will help facilitate the evaluation and assessment of action to reduce population intakes, and it can subsequently be revised downwards once it has been met.
National Heart Forum	Conclusions and recommendations	Total fat [Lines 608 onwards]: We note the proposed recommendation of 20-35% Energy. However, we recommend that the range for total fat is limited to 20%-30%E for the following reasons: 1. reduced fat diets have a significant role in the prevention of weight gain [lines 1569-72; 1581-52], 2. prevention of weight gain is a key population goal for the European population 3. achievement of population level fat intake levels in the range 20-30%E is achievable in practice (line 1066) In addition, we recommend that the food industry should initially use the mid-point of 25%E as the GDA for adults and this should be reviewed after a period of time.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
National Nutrition Council	Conclusions and recommendations	We thank the panel for an enormous amount of work accomplished to the draft for dietary reference values for fat and carbohydrates and dietary fibre. Fats: 1. We suggest the recommendation for fat intake to be 25 – 35 E%. The suggested variation for fat intake (20-35 % of energy) in EFSA´s opinion is quite board. In Western countries it is extremely difficult to reach a recommended proportion of fatty acids in the diet, i.e. enough unsaturated fatty acids, when the intake of fat is below 25 % of energy. The current selection of fat containing foods in the EU countries makes this practically impossible. Furthermore, there does not seem to be additional benefit to limit the intake of fat below 25 % of energy. These issues are acknowledged also on page 24, lines 726-729 and 737-739. 2 Since the DRVs are meant to help EU countries draw national FBDGs, we strongly suggest that there would be an upper limit for saturated fatty acids including also trans fatty acids, e.g. 10 % of energy. We suggest this since it is widely used and there does not seem to be studies opposing this limit. Our suggestion to take into account both saturated fatty acids and trans fatty acids is in line with the definition given in the EU regulation (1924/2006) on nutrition and health claims. 3. By stating that cis-MUFA does not have a known role in preventing of promoting diet-related diseases, the EU countries are left with broad interpretation regarding the FBDGs. This is why some range for MUFAs should be given, either alone or together with PUFAs. According to Nordic nutrition recommendations, we suggest the range to be 10-15e% for cis-MUFA and 5-10E% for PUFA, or if the range given together for MUFA+PUFA: 20-25E% including, however, no less than two thirds of total fat. Could for example the population ranges in the EU countries form a basis for a range for MUFAs? Furthermore, the statement that cis-MUFAs are not needed in the diet seems quite awkward. Regarding dietary fats the diet cannot consist only of PUFAs and a minor amount of SFAs. 4. It is not clear how the panel ended up with AI of 0.5 E% for alpha-linolenic acid, 4 E% of linoleic acid and 250 mg for EPA plus DHA? Is there solid evidence for these estimates? Carbohydrates: 1. For diabetics it may be problematic to accept short-chain oligosaccharides as dietary fibre. 2. We strongly suggest to have a 10 E% limit for added sugars. This would be in line with the WHO Report (916) Diet, nutrition and the prevention of chronic diseases. By allowing the intake of sucrose up to 20 E% will cause problems regarding accomplishment of a well-balanced diet. Furthermore, we would like to point out that this statement is not in line with the draft for water and liquids which has a stricter opinion regarding sucrose intake. In addition, American Heart Association has stated

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		in its very recent scientific statement that attention should be paid to sugar intake, e.g. sugar sweetened beverages and recommends a limit for sugar to be 5 E%. Special comment: When launching the opinion on DRVs for nutrients EFSA has stated that they are used as a basis for reference values in food labelling. The Panel has come to a conclusion that the available data allow the setting of DRVs for quite few fat or carbohydrate components or, if values are given the range is very broad. In this situation the setting of labelling reference values will be difficult. However, the Panel has given earlier this year a scientific opinion (EFSA Journal (2009) 1008, 1-3) on the labelling reference values for energy, total fat, saturated fat, carbohydrate, sugars and salt which are included in a proposal for a Regulation on the provision of food information to the consumer. The basis for these reference values is contradictory with the opinion commented above. We feel that this situation is confusing and emphasize that the opinions of the Panel concerning these matters should be consistent.
National Nutrition Council	References	Lines 2486-2487 (Fats) Lines 1984-1985 Carbohydrates) There are new intake data from Finland: Paturi M, Tapanainen H, Reinivuo H, Pietinen P 2008.The national FINDIET 2007 survey (replaces Männistö et al 2003). AVAILABLE ON http://www.ktl.fi/attachments/suomi/julkaisut/julkaisusarja_b/2008/2008b23.pdf
none	1. Introduction	To Ms Haravgi-Nina Papadoulaki Spokesperson for Androulla Vassiliou, Commissioner for Health, EU Dear Ms Vassiliou The European Food Safety Authority (EFSA) issued on March 13, 2009 a draft for public consultation regarding dietary guidelines for Europe, consisting of two parts. One deals mainly with what type of fats one should eat, the other mainly with carbohydrates. In our opinion, these documents are not based on the current scientific knowledge of the role of fats and carbohydrates in health and disease. Instead, they represent the view of the lobbying organization International Life Sciences Institute (ILSI), formerly called Nutrition Foundation (see below). We are in particular concerned about the authors' review of the literature about saturated fat. Their references are selective and misleading and they have missed numerous studies having shown that saturated fat is harmless and even may be beneficial to health. Below we present the evidence for our objections.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		May we suggest that the present draft becomes revised by researchers independent of the food or drug industry. September 30, 2009 Yours sincerely Uffe Ravnskov, MD, PhD, independent researcher Magle Stora Kyrkogata 9 S 22350 Lund, Sweden ravnskov@tele2.se Göran Petersson, professor, Dept. of Chemical and Biological Engineering, Chalmers Institute, Göteborg, Sweden. goranp@chalmers.se Tore Schersten, MD, PhD, professor, previously Secretary of the Swedish Medical Research Council, Gammelvägen 3, Båstad, Sweden. torescher@hotmail.com Ralf Sundberg, MD, PhD, Slottssstaden Medical Group, Malmö, Sweden. ralfsundberg@telia.com
none	5.8. Cardiovascular disease	References 1. Reiser R: Saturated fat in the diet and serum cholesterol concentration: a critical examination of the literature. Am J Clin Nutr 1973;26:524-55. 2. Mensink RP, Katan MB: Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. Arterioscler Thromb Vasc Dis 1992;12:911-9. 3. Hegsted DM, Ausman LM, Johnson JA, Dallal GE: Dietary fat and serum lipids: an evaluation of the experimental data. Am J Clin Nutr 1993;57:875-83. 4. Woodside JV, Kromhout D: Fatty acids and CHD. Proc Nutr Soc 2005;64:554-64. 5. Kuller LH: Nutrition, lipids, and cardiovascular disease. Nutr Rev 2006;64:S15-26. 6. Lapointe A, Balk EM, Lichtenstein AH: Gender differences in plasma lipid response to dietary fat. Nutr Rev 2006;64:234-49 7. Ramsay LE, Yeo WW, Jackson PR: Dietary reduction of serum cholesterol concentration: time to think again. BMJ 1991;303:953-7. 8. Noakes M, Foster PR, Keogh JB, James AP, Mamo JC, Clifton PM: Comparison of isocaloric very low carbohydrate/high saturated fat and high carbohydrate/low saturated fat diets on body composition and cardiovascular risk. Nutr Metab 2006;3:7. 9. Meckling KA, O"Sullivan C, Saari D: Comparison of a low-fat diet to a lowcarbohydrate diet on weight loss, body

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ORGANISATION	CHAPTER TEXT	COMMENT TEXT
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ORGANISATION	CHAPTER TEXT	COMMENT TEXT
none	5.8. Cardiovascular disease	A relevant objection against such studies is that dietary information is inaccurate. A more reliable way to study previous intakes with disease is analyses of fat tissue, because intake of saturated fat during the last weeks or months is reflected by the levels of individual fatty acids in the fat tissue. The strongest associations are found between intake and concentrations of the short chain acids 12:0-15:0,52-56 and of the total numbers,57-60 but weakly or not at all of the longer ones, probably because a high intake of simple carbohydrates stimulates endogenous synthesis of the long chain saturated fatty acids.61 In three case-control studies of patients with myocardial infarction and healthy control individuals no difference was found as regards the content of the short-chain saturated fatty acids; in two studies it was even significantly lower in the patients (table 3).62-66 These studies concerned only patients with first myocardial infarction63-66 or patients who were not on a diet,62 and a diet-bias is therefore unlikely. Authors Cases/controls n Content in cases compared with controls 12:0 14:0 15:0 Kirkeby et al.62 27/68 No difference Wood et al.63 28/343 No difference Kark et al.64 180/492 No difference Clifton et al.65 79/167 Less** No difference Pedersen et al.66 100/98 No difference Less* Less** Table 3. Five case-control studies of the content of short-chain saturated fatty acids in the fat tissue of patients with myocardial infarction and of healthy control individuals. In many populations a major contribution of saturated fat comes from dairy products and all authoritative guidelines recommend a restriction of such food. However, in a meta-analysis of ten cohort studies including more than 400,000 individuals Elwood et al. found that compared with low-consumers the risks of myocardial infarction, ischaemic stroke and all cardiovascular events in high-consumers were 0.87 (0.74-1.03), 0.83 (0.77-0.90) and 0.84 (0.78-0.90) respectively.67 In a thorough review of the associations between dairy products and cardiovascular disease Tolstrup found no strong evidence in support either.68 All of these studies have been ignored by the authors of the draft.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
none	5.8. Cardiovascular disease	Cohort and case-control studies of saturated fat intake The diet of coronary patients and healthy individuals has been compared in numerous cohort and case-control studies. In a previous review of 28 cohorts in 21 studies patients with CHD had eaten significantly more saturated fat than the controls in three cohorts, but the differences were trivial, in one cohort they had eaten significantly less and in the other 24 cohorts no differences were seen.34 No difference was seen either in two recent, large cohort studies,39,40 or in the study referred to by the WHO guideline authors; in the latter the statistical significance disappeared after controlling for other dietary factors.41 Even more contradictory are the findings in stroke patients. In ten prospective cohort studies of healthy people the authors compared the intake of saturated fat in those who had stroke at follow-up with the intake of the others.42-51 With one exception49 all studies found that stroke patients had eaten less saturated fat than had the non-stroke individuals; in six of the studies the difference was statistically significant (table 2). n Ischemic haemorrhagic Total stroke Stemmerman et al.42 6832 none none Takeya et al.43 1366 7895 inverse* none none inverse* McGee et al.44 7084 inverse* Gillmann et al.45 832 inverse* Ross et al.46 18244 none Seino et al.47 2283 inverse* Iso et al.48 85761 inverse* He et al.49 43732 none none Iso et al.50 4775 inverse** Sauvaget et al.51 3731 none Table 2. Association between intake of saturated fat and stroke in ten cohort studies. * p<0.05; ** P<0.01

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
none	5.8. Cardiovascular disease	Effect of saturated fat intake on blood cholesterol Their most important argument is that saturated fat raises the concentration of cholesterol in the blood. This is no proof that saturated fat is harmful, and it isn't true either. The idea was originally put forward by Ancel Keys based on a number of laboratory experiments on healthy people whose diet was manipulated in may ways. However, already in 1973 the idea was questioned by Raymond Reiser. In a thorough review of 40 of these experiments he pointed at several types of methodological and interpretational errors.1 Instead of natural saturated fat many authors had used vegetable oils saturated by hydrogenation. This process results in the production of trans fatty acids, used for many years in the industrial production of margarine. These fatty acids indeed raise cholesterol, and several studies have also shown that an excess of dietary trans fat is associated with an increased risk of coronary heart disease. Another error in these experiments was that effects on blood cholesterol were attributed to saturated fat when it could be due to polyunsaturated fat as well. In spite of these flaws several authors maintain that saturated fat raises cholesterol, whereas monounsaturated and in particular polyunsaturated fat lower it, and some saturated fatty acids my be neutral.2-6 These conclusions have been based mainly on mathematical formulas using data from a large number of trials. But as almost all trial directors have made similar errors as those reviewed by Keys by changing the intake of several fats at the same time without controlling for intake of trans fat it is obviously difficult to rule out the effect of each type of fat. Even if saturated fat is hypercholesterolaemic the effect must be small. In a review of eight trials where the intake was reduced by 30-40 % the net reduction of cholesterol was only 0-4 %,7 and other studies have shown no effect at all. In experiments for instance, where carbohydrates were substituted with saturated fat, not even intakes between 20 % and 50 % of calories influenced total or LDL- cholesterol (table 1).8-17 These results are thus directly contrary to the draft statement that "there is a positive, dose-dependent relationship between the intake of a mixture of SFA and serum LDL cholesterol concentrations, when compared to carbohydrates."

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
none	5.8. Cardiovascular disease	Length of trial SFA; cal% Change of t-C Change of LDL-C Change of HDL-C Noakes et al8 12 w 18 None None None Meckling et al.9 10 w 20 None None Up Sondike et al.10 12 w 22 None None None Sharman et al.11 6 w 25 None None None Hays et al.12 52 w 50 None None None Westman et al.13 6 m + Down Down Foster et al.14 12 m + None None Up Yancy et al.15 24 w + Down None Up Seshadri et al.16 6 m + None None None Brehm et al.17 4 m + None None Up Table 1. Changes of blood lipids after a low-carbohydrate diet rich in saturated fat in ten trials. In all trials the concentration of triglycerides went down significantly. + means that the intake of saturated fat was unlimited. That other factors may override a possible hypercholesterolemic effect is obvious from studies of populations who live almost entirely on animal food, but have the lowest cholesterol ever measured in healthy people.18-20 In accordance, many cross-sectional studies of the dietary habits within a population have found no association between cholesterol and the intake of saturated fat.21-26 In the abovementioned low-carbohydrate trials (table 1) a high intake of saturated fat had no adverse effects on other lipids either. On the contrary HDL-cholesterol remained unchanged or went up and triglycerides went down significantly (table 1),8-17 whereas a reduction of the intake had the opposite effects.27-29 We are also surprised that Bresson et al have ignored one of the most interesting observations in this area. We refer to Ronald Krauss´ group and the fact that cardiovascular disease is stronger associated with small-size LDL than with other lipid fractions. Their crucial observation was that a high intake of saturated fat is followed by an increase of LDL size,27,30,31 thus the opposite of what should have been expected. Effects of saturated fat on the blood lipids is surrogate outcome, however. The crucial question is whether a high intake of saturated fat is deleterious to health and whether a reduction of the intake is beneficial.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
none	5.8. Cardiovascular disease	Saturated fat intake and atherosclerosis If high intakes of saturated fat should lead to atherosclerosis, people with high intakes should be more atherosclerotic than people with low intakes. No such association has been found in any study. In the International Atherosclerosis Project, fifteen populations were ranked by raised atherosclerosis and by selected diet components. Degree of atherosclerosis was associated with the total fat intake, but not with the intake of saturated fat.69 In three cohort studies of healthy individuals followed for several years, post-mortems of those who had died at follow-up found no association either between intake of saturated fat and degree of atherosclerosis-70-72 Angiographic follow-up studies have given disparate results. In a trial including 50 men with CHD, where a low-fat diet was compared with usual care, progress of the angiographic changes over 39 months was associated with intakes of palmitic and stearic acids.73 However, the group that ate the low-fat diet was also instructed to increase their intake of fish, fruit and vegetables, and intake of such food have been found inversely associated with the risk of CHD in almost all studies. In the MARGARIN study 81 hypercholesterolaemic individuals were followed for two years after having received dietary advice.74At follow-up associations between the changes of intima-media thickness of the coronary and femoral arteries, measured by ultrasound, and intake of saturated fat were not significant in multivariate regression analyses. When the patients were grouped into quintiles of change of saturated fat intake, a weak association was seen with the changes of the femoral, but not with the changes of the coronary arteries. However, a similar bias was introduced in that study also, because vascular changes were inversely associated with intake of fruit. As the effect of a reduced intake of saturated fat is said to be due to a lowering of LDL cholesterol it is also contradictory that LDL cholesterol was lowest in those whose intake of saturated fat had increased during the study period. In contrast, a highly significant inverse association was found between intake of saturated fat and progress of angiographic lesions in a 3-year follow-up study of 235 postmenopausal women with CHD.75 In the draft nothing is mentioned about these studies. The dietary trials The most important argument for causality is improvement or disappearance of the disease after decrease or discontinuation of the exposure to the suspected causal factor. To-day relevant data have been published from nine randomised, controlled trials where the only intervention was a change of dietary fat. Two meta-analyses of these trials found no significant effect, neither on cardiovascular or total mortality,34,76,77 and as mentioned above, most trials comparing high-carbohydrate-low-saturated fat diets with low-carbohydrate-high-saturated fat have found a better outcome as regards body weight an metabolic control in the latter ones. Most of these trials have been ignored by the draft authors. Instead they claim support from a review by Sacks and Katan78 of four allegedly successful dietary trials.79-82 None of them lowered mortality significantly; one of them, the Finnish Mental Hospital Trial79 was neither controlled or randomized; and in the and in the Dayton trial82 those who had lowered their intake of saturated fat were more atherosclerotic than the others. Besides, they had ignored four trials where the number of cardiovascular event had increased in the diet group.83-86

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
none	5.8. Cardiovascular disease	The influence of the food industry In 1941 the world of business intersected with the world of science through the Nutrition Foundation (NF) in the United States, a research body funded by the food industry. In the following years, sister foundations to NF, with names such as the British Nutrition Foundation, Swedish Nutrition Foundation, Nutrition Foundation of Italy, New Zealand Nutrition foundation etc. was started in most western countries . All these organizations promote industry interests and their goal is to increase the profit of the sponsoring industries. In most countries, the greater part of research on nutrition is financed by food industries, either directly or by proxies such as ILSI or the national Nutrition Foundation of that country. The problem with that is that most research on nutrition on health issues is performed in order to prove a health claim of a particular product from a sponsoring part. Recent research has shown that such sponsoring of research in the area of nutrition, increases the likelihood of being in favor of the product in question by a factor of ten. As a comparison, similar sponsoring of pharmaceutical products only doubles that kind of bias. As a result of this, what is regarded as science by the academic institutions in nutrition year by year, decade after decade, has diverged from medical science. Dietary advice from these institutions can no longer by regarded as health-promoting, rather the opposite. The expert group of EFSA, as well as national experts groups or that of WHO, share the same views of nutrition. These happen to be identical to the views of the food industry, which sponsored the research careers of these experts. In Sweden, there has been a debate on food and diet advice given by such expert groups. In this debate, qualified scientists have scrutinized the scientific basis of such advice in the Nordic Nutrition Recommendations, the advice on trans fats by the EFSA and the British SACN, the dietary advice for diabetics by the EASD, and claims by the Swedish Food authority on saturated fats. All were found to be utterly misleading because of selective citations (omitting relevant science), false citations (quoting studies that showed results opposite to the authors claims) and even referring to studies about different subjects. They illustrate that To mention an example, EFSA and SACN did not in their analyses of the risks of industrial trans fats mention the existence of a relevant study showing that consumption of margarine, rich in trans fats greatly increases the risk of heart disease. They could hardly have missed it, since a couple of years earlier this study was quoted by the Danish Ernaeringsrådet in their recommendation to ban industrial trans fats. The reports form EFSA and SACN were lame, and in the interest of ILSI, which works against a ban of such fats. As a matter of fact, a great number of the members of the EFSA expert panel work on behalf of ILSI, whereas the report to the SACN was prepared by a group from the University of Reading , whose research budget was sponsored by a manufacturer of industrial trans fats. The above illustrates that EFSA does not primarily serve its intended purpose of maintaining and protecting the health of European citizens, but rather the interests of the food industries behind ILSI, such as Coca-Cola, Unilever, McDonalds, Südzucker, Ajinomoto (producer of artificial sweeteners) to mention a few.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
NVB (Association of the Dutch Bakery Industry)	4. Overview of dietary reference values and recommendations	Comment on table 5, line 1035-1039 and other lines about the Dietary reference values of the Netherlands. On page 93 (line 2915) the dietary reference value in the Netherlands is mentioned. However, these are the values from 2001, whereas the Dutch Health Council updated its advice in 2006. Therefore we recommend using the most recent dietary guidelines.
NVB (Association of the Dutch Bakery Industry)	Conclusions and recommendations	Comment about line 56-67 in the Summary and line 1986-1993 in the Conclusions and recommendations. We would also like to react on the Summary, but because this isn"t possible we react on the Conclusions and recommendations. Please use this comment also for the Summary. We support the opinion of the Dutch Product Boards: Why are all the saturated fats treated as one group in the summary? The unsaturated fats are split up in separate groups, but the saturated fats are treated as one group. As stated in chapter 5.2.2 several saturated fats have different effects on cholesterol metabolism.
NVB (Association of the Dutch Bakery Industry)	Conclusions and recommendations	Comment on line 129-146 in the Summary and line 2036-2042 in the Conclusions and recommendations. We would also like to react on the Summary, but because this isn"t possible we react on the Conclusions and recommendations. Please use this comment also for the Summary. We support the opinion of the Dutch Product Boards: We suggest adding to the statement of The Panel in the summary the following: The intake of TFA is close to the recommendation levels in most European countries, and are therefore not a public health issue anymore. The intake of total TFA is low because of the efforts made by the food industry in reducing the amount of industrial TFA in their products (and these efforts are ongoing). The level of ruminant TFA in meat (products) and dairy products is already naturally low.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
NVB (Association of the Dutch Bakery Industry)	Conclusions and recommendations	Comment on line 66, 67 in the Summary and line 1992, 1993 in the Conclusions and recommendations. We would also like to react on the Summary, but because this isn"t possible we react on the Conclusions and recommendations. Please use this comment also for the Summary. We support the opinion of the Dutch Product Boards: In the Summary in line 66,67 the following is written: 'The Panel recommends that SFA intake should be as low as possible within the context of a nutritionally adequate diet'. In the discussed scientific research in chapter 5 this recommendation is not supported. Furthermore, according to Table 5 (page 32), most Countries and also the WHO/FAO set the maximum SFA at 10 E%. In infants average intakes of SFA where between 11-13 E%. In adults, average SFA intakes vary between 9 to 17 E% and nearly 30% of the reported average intakes were 15 E% or higher (line 620-629). In addition: in several economically developed countries where the SFA is close to 10%, the capacity to decrease SFA much further is limited to major changes in dietary patterns, and is only likely to result in modest reductions in TC and LDL-C We therefore believe it is appropriate to set the recommendation for SFA at 10 E%.
NVB (Association of the Dutch Bakery Industry)	Conclusions and recommendations	We support the opinion of the Dutch Product Boards: In conclusion, we would like to point out the following. Consumers do not eat saturated fats or unsaturated fats as such. They eat these nutrients in a matrix (food stuffs), as part of a balanced diet. In practice, the matrix influences the effects of the fatty acids, meaning that negative effects may not occur, or may be less pronounced, due to the presence of other nutrients in the food.
NVB (Association of the Dutch Bakery Industry)	Conclusions and recommendations	We would also like to react on the Summary, but because this isn"t possible we react on the Conclusions and recommendations. Please use this comment also for the Summary. NVB is supporting the opinion of the Dutch Product Boards that the conclusions in the summary do not reflect accurately the content of the report. More precise, the nuance in the report is lacking in the summary. Therefore, it is not immediately obvious on what basis the conclusions are drawn. Since the summary is generally the only part that policy makers read, it is important that the summary reflects the scientific state of the art, including the recent developments and nuances.
NVB (Association of the Dutch Bakery Industry)	References	Recently, two WHO scientific updates were published in the European Journal of Clinical Nutrition (vol. 63, supplement 2s, pp S1-S75) and Annals of Nutrition and Metabolism (vol.55, no. 1-3: pp 5-300). It seems logical to take these two updates into account in the document.
Ocean Nutrition Canada	Conclusions and recommendations	We applaud the Panel's proposal to establish a DRV of 250mg for EPA + DHA. This will help to broaden recognition of the value EPA+DHA with consumers across Europe. However, while an intake of 250mg/day provides measurable benefits, we believe this level doesn't deliver optimal benefits for the general population. Consideration of a higher level is warranted. 250mg/day EPA+DHA should be considered a minimal intake, rather than a target intake. We encourage the Panel to establish a higher target intake level based upon available

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		cardiovascular clinical data. The Panel's opinion on intake levels for EPA+DHA included the work of Mozaffarian and Rimm (JAMA 296:1885-1896, 2006) who concluded that the risk of CHD death was not further attenuated above an intake of 250mg/day n-3 LCPUFAs. Given the multitude of assumptions on which the authors dose-response assessment was based, we don't believe that 250mg/day is a level above which there are no additional benefits. For example; 1. Of the 20 studies included in the dose-response assessment, 6 studies included insufficient data to derive a robust estimation of n-3 LCPUFA intake. Therefore the estimated intakes may be associated with considerable error. 2. Protective effects of n-3 LCPUFAs against CHD death are not seen in studies with the lowest intake/reference group already consuming a high amount of n-3 LCPUFAs. These studies probably lack sensitivity and are misleading. It appears from the dose-response figure in Mozaffarian and Rimm (2006) that the plateau effect is being caused by 4 data points representing intakes in excess of 2,000 mg/day. Had the studies in which the reference intake group was consuming in excess of 250mg/d of the n-3 LCPUFAs been excluded, an inverse and linear dose-response relationship between n-3 LCPUFA intake and risk of CHD death may have been evident up to intakes of approximately 1,000mg/day. 3. An assumption inherent in the combining of data from subjects with and without a history of CHD is that the dose required for reducing risk of CHD death is the same. This may or may not be true. The most relevant studies are those in subjects free of CHD upon entry (Harris et al. Curr Atheroscler Rep 10:503-509, 2008). We believe the Panel's conclusion that intakes in excess of 250mg/day offer no additional protection against CHD death is challenged by the following: 1. A significant inverse trend was noted between n-3 LCPUFA intake and risk of fatal CHD above an intake of 250 mg/d of EPA+DHA (Dolecek et al. World Rev Nutr Diet 66:205-216, 1991; Yuan et al. Am J Epidemiol 154:809-816, 2001; Mozaffarian et al. Circulation 107:1372-1377, 2003). 2. A recent meta-analysis of 6 US epidemiologic studies (Harris et al. Curr Atheroscler Rep 10:503-509, 2008) noted a significant inverse dose-response between intake of the n-3 LCPUFAs beyond 250mg/d and risk of CHD death in subjects previously free of CHD. 3. In 3 meta-analyses, incremental decreases in risk of CHD death have been reported with fish intakes greater than 1-170-gram portion per week (an amount cited by Mozaffarian and Rimm (2006) to be approximately equivalent to an intake of 250 mg/day of the n-3 LCPUFAs) (He et al. Circulation 109:2705-2711, 2004; Whelton et al. Am J Cardiol 93:1119-1123, 2004; König et al. Am J Prev Med 29:335-346, 2005). Taking into account these observations as well as emerging data that risk of non-fatal myocardial infarction may be reduced with n-3 LCPUFA intakes in excess of 250-500mg/d (He et al. Circulation 109:2705-2711, 2004; Iso et al. Circulation 113:195-202, 2006), the Panel's conclusion can be modified. We recommend that the consumption of 250 mg/day of EPA+DHA should be considered a minimum recommended intake.

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PIE - Platform for Ingredients in Europe	2. Categories, structure and function	2.1.3.1. n-6 polyunsaturated fatty acids (n-6 PUFA) We agree with the statement that only linoleic acid (LA) is essential, but that arachidonic acid (ARA) as such is not necessary in the diet is questionable. In fact the metabolism of LA into ARA, as well as into gamma linoleic acid (GLA) is shown to decrease with age, which also influences the metabolism of omega-3 fatty acids into eicosapentaenoic acid (EPA). References: - Angela Liou, Y., Innis, S. M., 2009. Dietary linoleic acid has no effect on arachidonic acid, but increases n-6 eicosadienoic acid, and lowers dihomo-gamma-linolenic and eicosapentaenoic acid in plasma of adult men. Prostaglandins Leukot Essent Fatty Acids. 80, 201-6. - Choi, Y. S., et al., 1988. Age-related changes in lipid metabolism in rats: the consequence of moderate food restriction. Biochim Biophys Acta. 963, 237-42. - Choi, Y. S., Sugano, M., 1988. Effects of dietary alpha- and gamma-linolenic acid on lipid metabolism in young and adult rats. Ann Nutr Metab. 32, 169-76. - Hrelia, S., et al., 1990. Delta-6-desaturation of linoleic and alpha-linolenic acids in aged rats: a kinetic analysis. Biochem Int. 22, 659-67. 2.1.3.1. n-6 polyunsaturated fatty acids (n-6 PUFA) We agree with the statement that only linoleic acid (LA) and alfa-linoleic acid (ALA) are essential. But it is also important to acknowledge that the 'conversion' from ALA into EPA and DHA is clearly limited in humans; i.e. intake of LA, and ALA could not be sufficient to eliminate the need for intake of DHA, and EPA via the diet. Then based on the essence of ALA as such an advised intake (AI) for ALA of 0.5 E%/day may need more consideration. ALA is considered to be implicated in the reduction of cardiovascular disease (CVD) risk, and this fact did lead to the WHO/FAO to advise an intake of 1.0 E%/day. We would recommend EFSA not to divert from that. 2.1.4. Trans fatty acids (TFA) It is stated that Trans fatty acids (TFA) are not synthesized by the human body. The human body produces rumenic acid (i.e. Conjugated Linoleic Acid (cis-9, trans-12)), which can be found in breast milk. Although it may be a product of the conversion of vaccenic acid (trans-9 octadecenoic acid) from (dairy) food, the statement denying human production of TFA can be controversial. It is unclear whether the intake of TFA includes or excludes the level of rumenic acid and vaccenic acid; e.g. if it refers to chemically defined TFA or to TFA as defined by the Codex alimentarius, which excludes bovine TFA (merely rumenic acid, and vaccenic acid). Whilst the level of vaccenic acid can be substantial, a clear definition of TFA should be included.

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PIE - Platform for Ingredients in Europe	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	6.4. cis-polyunsaturated fatty acids (cis- PUFA) There is a need to keep a balance in the metabolism of omega-3 and omega-6. Indeed it is also well known that an unbalance between omega-6/omega-3 can determine skin reactions (e.g. eczema) and lung problems in babies. Thus we suggest EFSA to provide some recommendations based on the best scientific data available. References: - Alm, B., et al., 2009. Early introduction of fish decreases the risk of eczema in infants. Arch Dis Child. 94, 11-5. - Koch, C., et al., 2008. Docosahexaenoic acid (DHA) supplementation in atopic eczema: a randomized, double-blind, controlled trial. Br J Dermatol. 158, 786-92. - Miyake, Y., et al., 2008. Relationship between dietary fat and fish intake and the prevalence of atopic eczema in pregnant Japanese females: baseline data from the Osaka Maternal and Child Health Study. Asia Pac J Clin Nutr. 17, 612-9. - Oddy, W. H., et al., 2006. Atopy, eczema and breast milk fatty acids in a high-risk cohort of children followed from birth to 5 yr. Pediatr Allergy Immunol. 17, 4-10. 6.4.1. n-6 polyunsaturated fatty acids (n-6 PUFA) We believe that an advised intake (AI) for LA of 4 E% may need more consideration. LA is considered to imply a reduction of CVD risk. As such the WHO/FAO advice is an intake of 5-8 E%/day. We would recommend EFSA not to divert from that.
PIE - Platform for Ingredients in Europe	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	6.4.2. n-3 polyunsaturated fatty acids (n-3 PUFA) This EFSA Opinion makes clear that currently available evidence indicates that consumption of preformed EPA+DHA substantially decreases the risk of mortality from coronary heart disease and sudden cardiac death. PIE welcomes the recognition of the role these nutrients can play in addressing the nutritional aspects associated with cardiovascular diseases, the leading cause of mortality within Europe(1). The EFSA opinion identifies that the consumption of EPA+DHA required gaining these beneficial effects, lies in the range 250 mg – 500 mg daily, and proposes to set an Adequate Intake (AI) at 250 mg for adults. There is a large amount of data from both observational and intervention studies on the link between EPA+DHA consumption and reduced risk of cardiovascular diseases, and it is for this reason that meta-analyses are required to evaluate the totality of evidence. Despite the uncertainties and variabilities within the meta-analyses, the data clearly show a dramatic reduction in risk as intake increases from 0 towards 250 mg/day. However, the overall analysis of data and conclusions from several studies, suggest that the maximum benefit is reached between 250 mg/g and 500 mg/d. It is for this reason that a review in 2008 by ILSI North America supported a DRI for

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		EPA+DHA between 250 and 500 mg/d, and agreed with international recommendations that have been set around 500 mg/d for the reduction in risk of coronary heart disease(2). Although PIE welcomes the proposed AI, it is our belief that setting the level at the lowest end of the range within which greatest benefit lies, will result in a reduction in benefit for the overall population, or lack of significant benefit for specific groups. There is strong evidence that shows benefit at 500 mg/d regarding reduced risk of cardiovascular diseases. For example, the meta-analysis of Harris et al.(3) ,discussed in the EFSA opinion, examined six epidemiological studies and illustrated a beneficial trend up to 500 mg/d of EPA+DHA. Moreover, in a recently published and comprehensive review of evidence, it was concluded that the daily target intake of EPA+DHA should be at least 500 mg/day for healthy individuals, and 800 to 1000 mg/day for individuals with pre-existing cardiovascular disease(4). Although an intake of 250 mg/d provides a substantial benefit for primary prevention, it may not confer optimal health. It is on this basis that PIE hopes the opinion is only an interim value and that in the near future, a further assessment of new evidence will be made, such that a dietary reference value of 500 mg that might provide for optimal health of the EU population can be established. References: (1) Health Statistics, Key data on health 2002. European Communities 2002. ISBN 92-894-3730-8. (2) Harris WS, Mozaffarian D,Lefevre M, Toner CD, Colombo J, Cunnane JC, Holden JM, Klurfeld DM, Morris MC, Whelan J, 2009 Towards Establishing Dietary Reference Intakes for Eicosapentaenoic and Docosahexaenoic Acids. J. Nutr. 139: 804S–819S. (3) Harris WS, Kris-Etherton PM, Harris KA, 2008. Intakes of long-chain omega-3 fatty acid associated with reduced risk for death from coronary heart disease in healthy adults. Curr Atheroscler Rep. 10(6), 503-9 (4) Lavie CJ, Milani RV, Mehra MR, Ventura HO, 2009. Omega-3 Polyunsaturated Fatty Acids and Cardiovascular Diseases J Am Coll Cardiol ;54:585–94.
PIE - Platform for Ingredients in Europe	6.5. Trans fatty acids (TFA)	Natural levels of TFA can be substantial. Considering e.g. levels of natural TFA in breast milk, levels of 6% of the total fat may occur (Precht and Molkentin, 1999). In that sense clarity concerning TFA, and the advised limits needs refining. References: - Precht, D., Molkentin, J., 1999. C18:1, C18:2 and C18:3 trans and cis fatty acid isomers including conjugated cis delta 9, trans delta 11 linoleic acid (CLA) as well as total fat composition of German human milk lipids. Nahrung. 43, 233-44.

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Product Board for Margarine, Fats and Oils	2. Categories, structure and function	The text in line 454 is confusing: The sentence (454) 'Strictly speaking, only linoleic acid is essential, as the body can synthesize arachidonic acid from linoleic acid.' is (partly) inconsistent with the sentence in line 461 'The conversion of linoleic acid is very limited.'. We suggest to change line 454 in: 'Although linoleic acid is essential, the synthesis of AA from linoleic acid is very limited, making an additional intake of ARA, or GLA appropriate.' Furthermore, the text in line 463 states that delta-5 desaturase activity is decreased in elderly women. In addition to that, there is evidence that (mainly) delta-6 desaturase activity decreases with age (Angela Liou and Innis, 2009; Choi and Sugano, 1988; Hrelia et al., 1990).
Product Board for Margarine, Fats and Oils	4. Overview of dietary reference values and recommendations	Saturated fat: In the Summary in line 66,67 the following is written: 'The Panel recommends that SFA intake should be as low as possible within the context of a nutritionally adequate diet'. In the discussed scientific research in chapter 5 this recommendation is not supported. Furthermore, according to Table 5 (page 32), most countries and also the WHO/FAO do set maximum of SFA at 10 E%. In adults, average SFA intakes vary between less than 9 to nearly 17 E% and nearly 30% of the reported average intakes were 15 E% or higher (line 620-629). In addition, in several economically developed countries where the SAFA has fallen close to 10%, the capacity to decrease SFA much further is limited without major changes in dietary patterns, and is only likely to result in modest reductions in cholesterol levels. We therefore believe it is appropriate to set a goal for SFA at 10 E%. In line 776 and in table 6 (line 2915) the dietary reference value in the Netherlands is mentioned. However, these are the values from 2001, whereas the Dutch Health Council updated its advice in 2006. Therefore we recommend to use the most recent dietary guidelines.
Product Board for Margarine, Fats and Oils	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	n-3 PUFA Why has the Panel set the AI for a-linolenic acid on 0.5 E%, whereas again a higher intake is connected with the prevention of CVD. Cardiovascular Disease (CVD) is indisputably a major public health issue in Europe as it is the leading cause of mortality: 4.3 million deaths per year that make up 48% of all deaths in Europe (CVD statistics 2008). The WHO has set in her recent scientific update the AI of 0.5 E% of a-linolenic acid to prevent deficiency and between 0,5-2 E% (n-3 fatty acids including 0,1-0,9 E% n-3 LC PUFA) as part of a healthy heart diet probably preventing chronic diseases. A DRV for ALA of 1 E% would also be in line with the 2 g/day as ALA that EFSA recently recommended to the Commission as labelling reference intake values (Question No EFSA-Q-2009-00548, adopted on 30 June 2009). Two g ALA per day in a 2000 kcal/d diet corresponds to ~0.9E%. The Dutch Health Council have set the AI for a-linolenic acid on 1 E%. We suggest to set the AI for a-linoleic acid on at least 1 E% for preventing cardiovascular diseases. n-6 PUFA Why has The Panel set the AI for linoleic acid on 4 E%, whereas recent scientific evidence suggests an even higher intake based on protective effects of linoleic acid on CHD as is reviewed by Harris et al. and published this year in Circulation (vol 119. no. 6, pp 902-907)? We propose to take this review also into account in the document. The reduction in cardiovascular risk by replacement of SAFA by n-6 PUFA (lines 1891-1894) is also supported by a recent pooled analysis of cohort studies (Jakobsen

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		et al, Am J Clin Nutr 2009;89:1425-32). In the recent scientific update of the WHO, the WHO recommends an intake of PUFA acid between 6-11 E% as part of a healthy heart diet to prevent chronic diseases. Under the condition that our suggestion's AI for a-linolenic acid on 1 E% and The Panel's AI for long chain n-3 fatty acids on 0,1 E% is taken into consideration, it can be derived that the recommendation level for n-6 PUFA should be at least 4,9 E%. We suggest to set the AI for n-6 PUFA on at least 6 E% for preventing cardiovascular diseases.
Product Board for Margarine, Fats and Oils	Conclusions and recommendations	General remarks - The Product Board for Margarine, Fats and Oils is of the opinion that the conclusions in the summary do not in all cases accurately reflect the content of the report. More precise, the nuance in the report is lacking in the summary. Therefore, it is not immediately obvious on what basis the conclusions are drawn. Since the summary is generally the part that policy makers will read, it is important that the summary reflects the scientific state of the art, including the recent developments and nuances. - Recently, two WHO scientific updates have been published in the European Journal of Clinical Nutrition (vol. 63, supplement 2s, pp S1-S75) and Annals of Nutrition and Metabolism (vol.55, no. 1-3: pp 5-300). It seems logical to take these two updates into account in the document. Total fat What is the lower bound of the recommendation intake range of fat for children between 4-18 years? In line 50-55 no specific recommendation level is mentioned for children older than 4 years. In addition, in line 54 The Panel states that fat intakes below 25E% have been associated with low vitamin levels in some young children. Why then come to a lower bound of 20E% as stated in the table on line 2055 for children >4 years? It appears more prudent to recommend a total fat intake of at least 25E%. Transfats We would emphasize that The Panel states in the summary that the intake of TFA is close to the recommendation levels in most European countries TFA are not a public health issue anymore. The intake of total TFA is low because of the efforts made by the food industry in reducing the amount of industrial TFA in their products (and are still doing so). We welcome and agree with the conclusion of the EFSA that there is insufficient evidence to establish whether there is a difference between ruminant and industrial TFA consumed in equal amounts on the risk of Cardiovascular Disease (CVD). However, Additionally, The Panel states that TFA are not synthesized by the body (line 130, 1937, 2037), but this is not correct. CLA and vaccenic acid can be produced in small amounts in our body. We suggest to delete this sentence.
Safefood	4. Overview of dietary reference values and recommendations	Safefood is a North-South Body promoting food safety and healthy eating on the island of Ireland. Our remit is for both research (inc surveillance) and communication. From both a monitoring and communications point of view Safefood has a general concern around the lack of specific DRVs for saturated fat, monounsaturated fats, polyunsaturated fats (PUFA), N-6 PUFAs and trans fats. The lack of clear targets for these nutrients could make communications to consumers on these issues more challenging. It may also mean that development of indicators, against which to measure improved population dietary

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		intakes, are more difficult to identify.
Scientific & Regulatory Affairs / Danone Research	1. Introduction	Line 128 n-6:n-3 fatty acid ratio: Some dietary recommendations include guidelines for the n-6:n-3 ratio in the diet, as this may contribute to maintaining cardiovascular health. Recent recommendations suggest lowering the ratio preferably by a combination of an n-3 increase and an n-6 decrease. Indeed, in the studies by Sanders and Griffin (Griffin et al., 2006; Sanders et al., 2006), it appeared that in the context of a total PUFA intake equivalent to 6% of energy, decreasing the ratio by increasing the intake of very long chain n-3 fatty acids to approximately 1-1,5g/d resulted in potentially beneficial effects with regard to cardiovascular risk. In contrast, Stanley et al, 2007 concluded in their review that the n-6:n-3 fatty acid ratio is not a useful concept and that it draws attention away from increasing absolute intakes of long chain n-3 fatty acids which have been shown to have beneficial effects on cardiovascular health. Independently of the debate on the ratio, we would at least suggest an overall recommendation to increase absolute intake of n-3 and reasonably limit that of n-6.
Scientific & Regulatory Affairs / Danone Research	1. Introduction	LINE 146 If the limited data suggest that the effects of ruminant and industrial TFA on blood lipid profiles are similar when consumed in similar quantities, it is important to mention that very few people consume the high levels of ruminant TFA used in these studies and that observational studies do not support adverse CHD effects of ruminant TFA in amounts actually consumed (Mozaffarian et al., 2009). This is reinforced by the recent WHO scientific update on TFA (Uauy et al., 2009). This is also the conclusion of AFSSA (French food safety agency) in its 2009 report: TFA from natural origin do not present a risk in terms of cardiovascular disease as they are consumed at very low level (0,5 to 0,9% of the total energy intake). The EFSA recommendation concerning the dietary reference value for TFAs should then deal only with industrially derived TFA. Trans fat from natural origin should not be included.

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Scientific & Regulatory Affairs / Danone Research	1. Introduction	LINE 67 (Part 2 of comment) More generally, it should be noted that : - the evidence of the role of SFA in Coronary Heart Disease is not conclusive (Mente et al., 2009); Indeed, some studies show that in some cases a greater saturated fat intake is associated with less progression of coronary atherosclerosis, whereas carbohydrate intake is associated with a greater progression (Mozaffarian et al., 2004; Griel et al., 2006). In addition the WHI study (Howard et al, 2006) indicates that a decrease of fat intake (leading to an intake of 9,5% SFA) does not significantly reduce the risk of stroke, coronary heart disease, or cerebrovascular disease in postmenopausal women. - SFA have different physiological functions depending on their chain length, justifying the previous conclusion that SFA should not be evaluated as one single group. (Sengupta 2006, Hashim, 1960, Tsuji, 2001, Yu et al, 1995, Kelly, 2001, Temme et al, 1997, Salter et al, 1998, Billet MA 2000, Casey, 1995, Rioux, 2002, Peitzsch, 1993, Borgese, 1996. Dabadie, 2005). Moreover, recommending SFA intake to be "as low as possible" could result in overly strict guidelines as this would likely be understood to mean "zero". A low intake of SFA would result in an excessive consumption of MUFA and PUFA, unbalancing the diet, thereby doing more harm than good. In conclusion, the scientific data shows that certain types of saturated fat do not have negative but positive effects. As such, considering SFAs as a single group does not seem justified and doing so could actually have a negative impact on health. We would suggest taking into account the different physiological functions of SFA in order to evaluate the DRV.
Scientific & Regulatory Affairs / Danone Research	1. Introduction	Line 67 In our view, this recommendation does not reflect the recent scientific evidence on saturated fatty acids. Very recently (Sept 2009), during the International Conference on Saturated Fat in Copenhagen, organized by the European Dairy Association (EDA) in collaboration with the Danish Dairy Board, several international experts agreed that there is no conclusive evidence with regards to negative health effects of saturated fatty acids from milk fat. The scientists stated that there is no reason for considering saturated fatty acids as a single group anymore, and that more research is needed in order to make well-founded policy recommendations with regard to the intake of saturated fatty acids: - Prof. Bruce German (University of California) told the attendants that evidence from the past five years has changed the view and understanding of the effects of fat on cholesterol metabolism. For instance, dietary cholesterol does not affect blood cholesterol. Scientific evidence does not support the assumption that saturated fat intake should be as low as possible as this is often understood to mean "zero". Moreover, Prof. German suggested that, in personalized diets, appropriate doses of saturated fats are likely to have a beneficial impact. - French Professor Philippe Legrand (University of Rennes) indicated that based on the latest science there is no reason to consider saturated fatty acids as a single group anymore in terms of structure, metabolism, functions and deleterious effects. Only three of the many different saturated fatty acids found in milk fat should now be considered as atherogenic. Some

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		saturated fatty acids in milk fat might even have beneficial effects on the cholesterol metabolism. For him, the saturated fatty acids in dairy products have an interesting composition. He pleaded for more precise studies to investigate further on a possible dose-effect and to put the different saturated fatty acids into perspective. - Prof Werner Buck, EDA President: 'Saturated fatty acids should be considered individually and not as a whole group due to their different physiological effects. We are glad that recent scientific findings support our belief by clearly indicating that specific actions of some saturated fatty acids are even beneficial for human health.'
Scientific & Regulatory Affairs / Danone Research	1. Introduction	Line 86 However nutritional recommendation should not stress a n-6 PUFA over consumption, and promote instead a good balance between n-3 PUFA and n-6 PUFA. The relative intake of n-6 to n-3 PUFA is indeed clearly emerging as a new factor in the development of adipose tissue (Ailhaud et al., 2008). Line 97 There has been evidence on negative effects on health of excessive intakes of n-6 PUFA and lipid peroxidation (Elmadfa and Kornsteiner, 2009). It could also contribute to excessive adipose tissue development (Ailhaud, 2006; Lecerf, 2009). Therefore, an upper limit should be considered in order to protect consumer health
Scientific & Regulatory Affairs / Danone Research	2. Categories, structure and function	¿ Line 414 to 424 As for PUFA, additional information about structure and functions of SFA should be added. SFA are components of reserve triglycerides, glycerophospholipids and sphingolipids (membrane structure, myeline…). SFA cannot be considered as a whole, in terms of structure, metabolism and cellular functions. They have to be classified regarding their chain length: Structure and function of short and medium chain fatty acids Short and medium chain SFA have a specific metabolism. As reported by Bach and Babayan (1982), triglycerides made of C6:0, C8:0, C10:0 and C12:0 (MCTs) have unique physical, chemical, and structural characteristics and their modifications (structured lipids) make special lipids tools for solving certain medical problems. They are indeed hydrolyzed both faster and more completely than long chain triglycerides (LCTs). The products of this hydrolysis are absorbed as fast as glucose. MCTs are oxidized rapidly in the organism and they have a very low tendency to deposit as body fat. As reported by Sengupta et al. (2006), short chain butyric acid is likely to have a protective function against colon cancer (inhibition of tumor proliferation, apoptosis induction). Short and medium chain SFA have an hypocholesterolemic effect at physiological dose. This effect of diets high in C8:0 and C10:0 was shown in humans by Hashim (1960). Medium chain SFA have also a beneficial role in adiposis. The human study of Tsuji et al. (2001) suggests weight loss with a diet high in medium chain fatty acids. C6:0, C8:0 and C10:0 have a role in weight reduction, reduced fat deposition, decrease of VLDL production, hypocholesterolemic effect and antiviral role (Rioux et al., 2007; Legrand, 2008). Structure and function of long chain fatty acids Long chain SFA are converted, in part, by ¿9-desaturation in monounsaturated fatty acids, but with significantly different effectiveness, increasing with the length of the chain. Stearic acid is the best substrate of ¿9-desaturase; and its conversion to

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		oleic acid is important (Legrand, 2002; Legrand, 2008). The long chain stearic acid has no negative effects on cholesterol level (Yu et al.; 1995) and, as presented by Kelly (2001), it has a beneficial effect on thrombogenic and atherogenic risk factors in males. Myristic acid has a positive action through an increase of HDL-cholesterol when consume at usual level (Temme et al., 1997; Salter et al., 1998; Billet MA, 2000). Some SFA regulate specifically the activity of proteins by acylation (myristoylation, palmitoylation). Some studies show that, for example, myristic acid plays a key role through its ability to acylate proteins, a reaction which is called N-terminal myristoylation. Various examples of important cellular regulations where the intervention of myristic acid is proven have been described (Casey, 1995; Rioux, 2002; Peitzsch, 1993; Borgese, 1996). Myristic acid also has a function in the biosynthesis of EPA and DHA (Dabadie et al., 2005; Rioux et al., 2005) and of sphyngolipids. Trans fatty acids ¿ Line 572 Partially hydrogenated vegetable oils can contain_1–65% of TFAs, of which isomers of elaidic acid (trans-9 and trans-10 18:1) are the 2 most common isomers. On the other hand, dairy products contain smaller amounts of TFAs (1–8% of total fatty acids in milk fat), and the main isomer is vaccenic acid (trans-11 18:1). Humans can utilize vaccenic acid, in the endogenous synthesis of rumenic acid (cis-9, trans-11 18:2), a fatty acid that may not have a negative effect on biomarkers of CVD risk (17–19). These 2 sources of TFAs differ in their TFA isomer distribution and contribution to dietary intake, and, as a consequence, they also may have different biological effects (Chardigny et al., 2008)
Scientific & Regulatory Affairs / Danone Research	Conclusions and recommendations	2055 SUMMARY OF DRVS FOR FATS (Table) Adults SFA Not in excess of 10-12% within the context of a nutritionally adequate diet. TFA from industrial origin As low as possible

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Scientific & Regulatory Affairs / Danone Research	Conclusions and recommendations	Lines 1986 The conclusion and recommendation on SFA should better reflect the content of Section 6.2, specifically lines 1862 to 1868 and also take into account the following: SFAs have different physiological functions depending on their chain length. (Sengupta 2006, Hashim, 1960, Tsuji, 2001, Yu et al, 1995, Kelly, 2001, Temme et al, 1997, Salter et al, 1998, Billet MA 2000, Casey, 1995, Rioux, 2002, Peitzsch, 1993, Borgese, 1996. Dabadie, 2005). Recent results show that certain types of SFA have positive effects on health, especially cardiovascular health (individual statements by B. German, P. Legrand and W. Buck; International Conference on Saturated Fat. Copenhagen. 2009). As such they should not be evaluated as one single group. Recommending an SFA intake 'as low as possible' may result in an excessive consumption of MUFA and PUFA (especially for n-6 fatty acids (Lecerf, 2008; Ailhaud, 2006), unbalancing the diet, thereby doing more harm than good. We suggest to set a threshold in line with guidelines from European countries, the USA and the WHO corresponding to a maximum level of 10-12% of the total daily energy intake Line 2002 : n-6:n-3 fatty acid ratio Independently of the debate on the ratio, we would at least suggest an overall recommendation to increase absolute intake of n-3 and reasonably limit that of n-6. Line 2042 Evidence from studies distinguishing the ruminant and industrial origin of TFAs generally do not support an adverse effect of ruminant TFA (in contrast to industrial TFA) on the risk of CHD (Mozaffarian et al., 2009; Uauy et al., 2009; AFSSA - French food safety agency). Ruminant TFAs cannot be removed entirely from the diet, as they are naturally present. On the other hand the presence in food of TFAs resulting from the partial hydrogenation of oils can be controlled: indeed the use of industrial TFA containing foods should be avoided by restaurants and food manufacturers and their consumption avoided by consumers. We would therefore agree with the EFSA recommendation of a DRV for trans fatty acids to be as low as possible if limited to those of industrial origin.
Scientific & Regulatory Affairs / Danone Research	References	AFSSA (Agence Française de Sécurité Sanitaire des Aliments) (2009) Avis de l'Agence française de sécurité sanitaire des aliments sur l'estimation des apports en acides gras trans de la population française (Request 2007-SA-220) Ailhaud G, Massiera F, Weill P, Legrand P, Alessandri JM, Guesnet P, 2006. Temporal changes in dietary fats: role of n-6 polyunsaturated fatty acids in excessive adipose tissue development and relationship to obesity. Prog Lipid Res. May;45(3):203-36. Epub 2006 Feb 10. Billett MA, Bruce JS, White DA, Bennett AJ, Salter AM., 2000. Interactive effects of dietary cholesterol and different saturated fatty acids on lipoprotein metabolism in the hamster. Br J Nutr. 2000 Oct;84(4):439-47. Borgese N, Aggujaro D, Carrera P, Pietrini G, Bassetti M. A role for N-myristoylation in protein targeting: NADH-cytochrome b5 reductase requires myristic acid for association with outer mitochondrial but not ER membranes. J Cell Biol. 1996 Dec;135(6 Pt 1):1501-13

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		Calder PC, 2004. n-3 Fatty acids and cardiovascular disease: evidence explained and mechanisms explored. Clin. Sci. 107, 1-11. Casey PJ. Protein lipidation in cell signaling. Science. 1995 Apr 14;268(5208):221-5. Chardigny J-M, Destaillats F, et al. 2008. Do trans fatty acids from industrially produced sources and from natural sources have the same effect on cardiovascular disease risk factors in healthy subjects? Results of the trans Fatty Acids Collaboration (TRANSFACT) study. American Journal of Clinical Nutrition. 87:558-566. Dabadie H, Peuchant E, Bernard M, LeRuyet P, Mendy F, 2005. Moderate intake of myristic acid in sn-2 position has beneficial lipidic effects and enhances DHA of cholesteryl esters in an interventional study. J Nutr Biochem. 2005 Jun;16(6):375-82 Griel AE, Kris-Etherton PM. Beyond saturated fat: the importance of the dietary fatty acid profile on cardiovascular disease. Nutr Rev. 2006 May;64(5 Pt 1):257-62. Griffin MD, Sanders TA, Davies IG, Morgan LM, Millward DJ, Lewis F, Slaughter S, Cooper JA, Miller GJ & Griffin BA (2006) The effects of altering the ratio of dietary n-6/n-3 fatty acids on insulin sensitivity, lipoprotein size and postprandial lipemia in men and postmenopausal women aged 45 to 70 years: The OPTILIP Study. Am J Clin Nutr 84, 1290–1298. Hashim SA, Arteaga A, Van Itallie TB, 1960. Effect of a saturated medium-chain triglyceride on serum-lipids in man. Lancet. 1960 May 21;1(7134):1105-8. Kelly FD, Sinclair AJ, Mann NJ, Turner AH, Abedin L, Li D. A stearic acid-rich diet improves thrombogenic and atherogenic risk factor profiles in healthy males. Eur J Clin Nutr. 2001 Feb;55(2):88-96. Kris-Etherton PM, Harris WS & Appel LJAmerican Heart Association. Nutrition Committee. 2002 Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation, 106, 2747-2757. Lecerf JM. Acides gras et maladies cardiovasculaires. Sciences des Aliments 2008. 28:53-67. Legrand P, Catheline D, Rioux V, Durand G, 2002. Lauric acid is desaturated to 12:1n-3 by hepatocytes and rat liver homogenates. Lipids. 2002 Jun;37(6):569-72. Mente A et al. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. Arch Intern Med 2009;169: 659-669 Mozaffarian D, Rimm EB, Herrington DM. Dietary fats, carbohydrate, and progression of coronary atherosclerosis in postmenopausal women. Am J Clin Nutr. 2004; 80 :1175–1184. Mozaffarian D, Aro A, Willett WC 2009 Health effects of trans-fatty acids: experimental and observational evidence. Eur J Clin Nutr. 63 Suppl 2:S5-21. Peitzsch RM, McLaughlin S. Binding of acylated peptides and fatty acids to phospholipid vesicles: pertinence to myristoylated proteins. Biochemistry. 1993 Oct 5;32 (39):10436-43. Ravnskov U, 1998. The questionable role of saturated and polyunsaturated fatty acids in cardiovascular disease. J Clin Epidemiol. 1998 Jun;51(6):461-4; discussion 465

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Scientific & Regulatory Affairs / Danone Research	References	Rioux V, Galat A, Jan G, Vinci F, D"Andrea S, Legrand P. Exogenous myristic acid acylates proteins in cultured rat hepatocytes.J Nutr Biochem. 2002 Feb;13(2):66-74. Salter AM, Mangiapane EH, Bennett AJ, Bruce JS, Billett MA, Anderton KL, Marenah CB, Lawson N, White DA., 1998. The effect of different dietary fatty acids on lipoprotein metabolism: concentration-dependent effects of diets enriched in oleic, myristic, palmitic and stearic acids. Br J Nutr. 1998 Feb;79(2):195-202 Sanders TA, Lewis F, Slaughter S, Griffin BA, Griffin M, Davies I, Millward DJ, Cooper JA & Miller GJ (2006) Effect of varying the ratio of n-6 to n-3 fatty acids by increasing the dietary intake of a-linolenic acid, eicosapentaenoic acid and docosahexaenoic acid, or both on fibrinogen and clotting factors VII and XII in persons aged 45–70 y: The OPTILIP Study. Am J Clin Nutr 84, 513–522. Sengupta S, Muir JG, Gibson PR, 2006. Does butyrate protect from colorectal cancer ? J Gastroenterol Hepatol. 2006 Jan;21(1 Pt 2):209-18. Review. Stanley JC, Elsom RL, Calder PC, Griffin BA, Harris WS, Jebb SA, Lovegrove JA, Moore CS, Riemersma RA, Sanders TAB, 2007. UK Food Standards Agency Workshop Report : the effects of the dietary n-6:n-3 fatty acid ratio on cardiovascular health. British J Nutr 98, 1305-1310. Temme EH, Mensink RP, Hornstra G., 1997. Effects of medium chain fatty acids (MCFA), myristic acid, and oleic acid on serum lipoproteins in healthy subjects. J Lipid Res. 1997 Sep;38(9):1746-54. Tsuji H, Kasai M, Takeuchi H, Nakamura M, Okazaki M, Kondo K. Dietary medium-chain triacylglycerols suppress accumulation of body fat in a double-blind, controlled trial in healthy men and women. J Nutr. 2001 Nov; 131(11):2853-9.
Scientific Advisory Committee on Nutrition	1. Introduction	Summary- n-6 PUFA Line 78; include ‘it’ in the sentence Summary- TFA Line 137; comma should be full stop Summary-CLA Line 148; there is more data on CLA and oxidative damage than is covered here. It may be worth looking again at the evidence in relation to safety and upper limits. Introduction The opinion lacks information on the methodology employed to identify the relevant evidence. It is recommended that this should be included together with assessments of quality and any data analysis used to inform the DRVs for fat.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Scientific Advisory Committee on Nutrition	2. Categories, structure and function	Section 2.1.3.1- n-6 polyunsaturated fatty acids (n-6 PUFA) There is no clear indication in this section that DHA is much more difficult to synthesise than AA which requires peroxisome transport etc. There is good evidence to support differential AA/DHA synthesis in humans. This has important implications for any dietary recommendation and should be made explicit.
Scientific Advisory Committee on Nutrition	3. Dietary sources and intake data	Section 3.2 Intake data It is important to acknowledge the deficiencies in the intake data where it is used to make recommendations: • Supplement use is not taken into account. Supplement use may make an important contribution to total intake of important PUFA/LCPUFA (e.g. marine oil supplement use in member states with low intakes of fish). This is not considered in the report. • There is a rapidly increasing trend toward manipulation and modification of the nutrient composition of foods with many novel foods having the potential to have a large impact on the overall intake of highly bioactive nutrients. This complexity may not be captured by the intake data used in this analysis. • The methods used to assess dietary intake are known to result in a significant underestimate of intake (e.g. as verified by doubly labelled water); underestimates of 25% are not unusual. This should be acknowledged in the report. Also, what would be the implications of such underestimation for this report?

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Scientific Advisory Committee on Nutrition	4. Overview of dietary reference values and recommendations	The logic of using absolute amounts for EPA/DHA DRVs and % of energy for everything else is not well explained. It is also worth noting that if fats are expressed as a % of energy then the distribution is not normal because the energy requirement is skewed. What effect would this have on the recommendations? There is no mention in the report of positional isomers of fatty acids within triacylgrycerol; the same overall intake of fatty acids could have different health consequences depending on the position on the triacylglycerol moiety. Lines 479-482 state that "The developing brain accumulates large amounts of DHA both pre- and postnatally", see also line 1199. The figure used for accumulation of DHA in the brain is incorrect. Also, the story is more complicated than as presented (see for example European Journal of Clinical Nutrition. 2004 Dec;58(12):1559-70.). Line 704; 'unbeneficial' should be ' detrimental' Line 1035; this summary table is very useful. Given the importance of pregnancy and lactation in relation to fats, it would be useful to summarise the pregnancy/lactation recommendations, already in raw form in the appendices, in the same way. Section 4.1.4.1 PUFAs (n-6 PUFAs) Line 854; should define 'triene/tertaene' Section 4.1.4.2 PUFAs (n-3 PUFAs) The Scientific Advisory Committee on Nutrition (SACN) recommended intake of EPA and DHA is 450mg/day which is the equivalent of two portions of fish per week, one of which should be oily. This based on the evaluation of evidence, in terms of cardiovascular disease risk, as detailed in the SACN report "Advice on fish consumption: benefits & risks". We note that EFSA's DRV's for n-3 PUFA's are set lower than this, making it possible for white fish to be considered "oily". Therefore, we urge EFSA revisit the evidence it has based its recommendations on. http://www.sacn.gov.uk/reports_position_statements/reports/advice_on_fish_consumption_benefits__risks.html Line 866; It is not clear what is meant here. The logic of retroconversion of DHA to EPA should also be made explicit. 4.2- children Line 943 'children' should be 'children and infants'
Scientific Advisory Committee on	5.8. Cardiovascular disease	Lines 1629-1630; 'decreasing intakes … at the expense of'?

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Nutrition		
Scientific Advisory Committee on Nutrition	6.1. Total fat	Line 1830; 'in itself' should be 'in themselves'
Scientific Advisory Committee on Nutrition	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	6.4.2 n-3 PUFA It is considered that EFSA's DRV for n-3 PUFA's of 250mg/day does not reflect the evidence available relating to cardiovascular disease. A level closer to the SACN recommendation of 450mg/day would be more appropriate. This is based on the balance of the scientific evidence from RCTs and observational studies and on two portions of fish, one oily (one portion is 2.8g DHA/EPA/week) and one white (one portion average 0.4g/DHA/EPA week). This is a weekly total of 3.2g/week which equates to 450mg/day.
Scientific Advisory Committee on Nutrition	Conclusions and recommendations	Conclusions and recommendations- saturated fats The lack of definite information about saturated fat levels is a major concern given the national guidelines presently existing throughout Europe (e.g. UK Committee on Medical Aspects of Food Policy, COMA, DH 1994) and its impact on public health. Trans Fats EFSA have not set a DRV for trans fats, however it would be useful to have a figure to inform health policy. In light of the health sensitivities around trans fats SACN assessed the previous recommendations set by COMA in 1994 and upheld the COMA recommendation that the average trans fatty acid intake should not exceed 2% food energy, as there is currently no firm scientific basis for revision. The review was published in 2007 and can be found at: http://www.sacn.gov.uk/reports_position_statements/position_statements/update_on_trans_fatty_acids_and_health_-_december_2007.html) The review included a re-estimation of trans fats intake for adults aged 19-64 years using consumption data from the UK National Diet and Nutrition Survey for adults in 2000/01 and the new trans fat values provided by industry. A new value for mean trans fat intake for all adults aged 19-64 years was estimated at 1.0% of food energy. This is lower than the original NDNS estimate of mean trans fat intake in this age group - 1.2% food energy. It was not possible to take account of all the reductions in trans fat levels so this figure is an overestimate of actual intake.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
The Omega-3 Centre	1. Introduction	1. Shorter chain omega-3s versus long chain omega-3s The DRVs for omega-3s must discriminate between the physiologically active long chain omega-3s (EPA, DHA) and the shorter chain omega-3s (alpha-linolenic acid (ALA)). Whilst ALA is an essential fatty acid, it is poorly converted into DHA (around 1% in infants and considerably lower in adults). In a recent review on ALA and conversion to omega-3 long chain polyunsaturated fatty acids in humans, the authors concluded "present evidence indicates that n-3 LCPUFA status can be improved by increasing their intake or by decreasing LA intake, and a combination of the two is likely to be most effective". Based on this evidence, it is unclear why the EFSA Draft scientific opinion, Line 107 states without qualification, "The human body can synthesize EPA and DHA from alpha-linolenic acid". The Omega-3 Centre recommends that the EFSA develop DRVs for omega-3s that distinguish between the shorter chain omega-3 (ALA) needs, and long chain omega-3s (DHA, EPA and DPA) needs. This is important to ensure consumers are not misled or confused about how to meet their omega-3 needs – they need both shorter chain and long-chain omega-3s (LC O3s) for cardiovascular health. In most western countries, it is the long-chain omega-3s that are consumed inadequately: • Australia - population intakes in 1995 (the most recent national nutrition survey) were significantly lower that the NHMRC Suggested Dietary Targets for adult women and men (430mg/day and 610mg/day respectively) and there was a great difference between the mean and median intakes which is likely to reflect a low consumption of fish by the majority. In children, the majority are below the Suggested Dietary Targets (around 87-90% of children do not meet the SDTs for their age group) • USA – average intake of EPA and DHA is between 100 and 200mg/day requiring a four-fold increase in fish/seafood consumption to meet recommendations for intake • United Kingdom – average intake has been estimated to be 120mg for men based on The Dietary and Nutritional Survey of British Adults in 1990. The O3C recommends labelling information on food and beverage products that assists consumers in increasing their daily long chain omega-3 (LC O3s) recommendations for heart health.
The Omega-3 Centre	1. Introduction	Executive Summary and recommendations The Omega-3 Centre endorses the requirement for Population Reference Intakes for fatty acids for the European population, including long chain polyunsaturated fatty acids. The various health benefits of consuming long chain omega-3s are well-documented and indicate their importance in cardiovascular health. It is essential that the dietary reference values for long chain omega-3s: • Distinguish between the shorter chain omega-3 (ALA) and long chain omega-3s to achieve optimal health benefits from

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		increased intakes of long chain omega-3s • Are consistent with current recommendations for long chain omega-3s and cardiovascular health of 500mg/day DHA & EPA • Provide scientifically validated reference values for the development of content claims to increase consumer understanding of useful sources of long-chain omega 3s and thereby lead to health benefits from increased intakes of these beneficial fatty acids in the European diet. Key Recommendations The Omega-3 Centre recommends that the EFSA develop DRVs for omega-3s that distinguish between the shorter chain omega-3 (ALA) needs and the long chain omega-3s (DHA, EPA and DPA). The Omega-3 Centre recommends labelling information on food and beverage products that assists consumers in increasing their daily long chain omega-3 recommendations for heart health. The Omega-3 Centre endorses the proposed EFSA Recommended Intakes of an additional 100-200mg DHA per day for pregnancy and lactation. The Omega-3 Centre endorses the "dietary advice for children of 1-2 fatty fish meals/week or at-least 250mg EPA & DHA per day". The Omega-3 Centre recommends DRVs are set for long chain omega-3s at a level that will lead to a public health benefit by encouraging adequate levels of enrichment of foods/beverages to increase the population's long chain omega-3 intake. The Omega-3 Centre recommends an increase of the proposed AI to 500mg in order to be compatible with the recent evidence based recommendations for long chain omega-3s and cardiovascular health The O3C recommends that EFSA undertake dietary modelling based on current dietary patterns to establish minimum content levels for long chain omega-3s that would lead to beneficial intake levels. The O3C recommends assessment of the impact on industry stakeholders in development of content criteria claims

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
The Omega-3 Centre	4. Overview of dietary reference values and recommendations	3. Long chain omega-3s, RIs in pregnancy and lactation and recommendations for children The Omega-3 Centre endorses the proposed EFSA Recommended Intakes of an additional 100-200mg DHA per day for pregnancy and lactation as this is consistent with European consensus evidence-based guidelines that pregnant women should aim to achieve a dietary intake of LC-03s that supplies a DHA intake of at least 200mg/day (Koletzko, B et al The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations J.Perinat.Med.36(2008) 5-14). In addition, The Omega-3 Centre endorses the "dietary advice for children of 1-2 fatty fish meals/week or at-least 250mg EPA & DHA per day".
The Omega-3 Centre	5. Criteria (endpoints) on which to base the dietary reference values	2. Long chain omega-3s and cardiovascular health The various health benefits of consuming the long chain omega-3s (LC O3s), particularly EPA and DHA have been well-documented in the adult population for cardiovascular health. Specifically, EPA and DHA can reduce the risk of arrhythmias, decrease triglyceride levels, slow the growth rate of atherosclerotic plaques, and reduce blood pressure slightly (Brownawell AM, Harris WS, Hibbeln JR et al. Nutrition Reviews 67(7):391-397). In the revision of nutrient reference values in Australia and New Zealand as endorsed by the NHMRC (2006), the essential roles of DHA and EPA were recognised and included: • DHA's important role as a structural membrane lipid, particularly in nerve tissue and the retina • Cardiovascular benefits of long chain omega-3s • Anti-inflammatory benefits of long chain omega-3s. The Adequate Intakes (AIs) were based on the median intakes assessed in the National Nutrition Survey of Australia in 1995 and reflect low intakes within the Australian population and are not considered helpful in determining optimal intakes for health. The Suggested Dietary Targets (SDTs) were a new concept (in 2006) for Australian and New Zealand nutrient reference values. The SDTs were based on the 90th percentile of intake as this provided potential benefit whilst being a safe level: NHMRC Nutrient Reference Values (2006) recommend Suggested Dietary Targets (SDTs) of 430mg/day and 610mg/day of EPA, DPA and DHA for females and males over the age of 14 years, respectively for cardiovascular health (NHMRC. Nutrient Reference Values for Australia and New Zealand. Canberra. Commonwealth of Australia 2006). These levels are consistent with the National Heart Foundation of Australia (NHFA) Position Statement, Fish, fish oils and omega-3 polyunsaturated fatty acids (2008) - which recommends 500mg daily of DHA and EPA to lower risk of cardiovascular disease through a combination of the following:

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		• Two or three serves (150g serve) of oily fish per week • Fish oil capsules or liquid • Food and drinks enriched with marine omega-3s These Australian guidelines (NHMRC SDTs and NHFA) are consistent with the American Heart Association (AHA) guidelines that state: "Evidence from prospective secondary prevention studies suggests that EPA+DHA supplementation ranging from 0.5 to 1.8 g/d (either as fatty fish or supplements) significantly reduces subsequent cardiac and all-cause mortality. For linolenic acid, total intakes of 1.5 to 3 g/d seem to be beneficial". Based on the evidence the AHA Dietary Guidelines recommend including at least two servings of fish per week (particularly fatty fish). In addition, the data support inclusion of vegetable oils (eg, soybean, canola, walnut, flaxseed) and food sources (eg, walnuts, flaxseeds) high in linolenic acid in a healthy diet for the general population (American Heart Association 2008). A more recent review (2009) of long chain omega-3s and cardiovascular protection, in the American College of Cardiology journal concludes "based on considerable evidence, the target EPA + DHA consumption should be at least 500 mg/day for individuals without overt CV diseases, and at least 800-1000 mg/day for individuals with known CHD and HF" (Lavie CJ, Milani RV, Mehra MR, Ventura HO. J Am Coll Cardiol 2009 Aug 11; 54(7):585-94). In summary, there is increasing evidence to recommend a Suggested Dietary Target of 500mg/day for long chain omega-3s (EPA + DHA) for cardiovascular benefit. This recommended level is not consistent with the EFSA's proposed AI of 250mg/day for EPA & DHA for cardiovascular benefits (Lines 116-118). The Omega-3 Centre recommends an increase of the proposed AI to 500mg in order to be compatible with the recent evidence based recommendations for long chain omega-3s and cardiovascular health
The Omega-3 Centre	5. Criteria (endpoints) on which to base the dietary reference values	4. Content Claims Content claims on food labels such as "source of omega-3s", "good source of omega-3s" are a simple and effective means of communicating the nutritional benefits of a food or beverage at point-of-sale. It is important therefore that the DRVs are set at adequate levels to ensure omega-3 content claims are validated scientifically and will have the desired public health benefit – increased long chain omega-3 intake (DHA, EPA) with attendant cardiovascular health benefits. In Australia, Food Standards Australia New Zealand (FSANZ) has recommended the inclusion of a General Level Health Claim: "EPA and DHA contributes to heart health" in their most recent consultation paper (P293, Nutrition, Health & Related Claims Consultation Paper for First Review 20 March 2009). FSANZ proposed a minimum content of 50mg DHA and EPA per serving of food which the O3C supports as this reflects 10% of the 500mg daily intake target recommended by the National

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		Heart Foundation of Australia for achieving a heart health benefit. The O3C recommends DRVs are set for long chain omega-3s at a level that will lead to a public health benefit by encouraging adequate levels of enrichment of foods/beverages to increase the population's long chain omega-3 intake. Setting the level too low will mean many food products and beverages can claim to be sources of long chain omega-3 when their contribution to total intake would be negligible. Given the low mean and even lower median population intake of long chain omega-3s, it would seem prudent to have content claim criteria set at levels that will make a difference to intake levels and thereby improve public health outcomes. The O3C recommends that EFSA undertake dietary modelling based on current dietary patterns to establish minimum content levels for long chain omega-3s that would lead to beneficial intake levels. The O3C recommends assessment of the impact on industry stakeholders in development of content criteria claims in terms of product development and innovation. For example, what levels of long chain omega-3 enrichment are feasible in specific products from both a sensory and cost-effective perspective?
Unilever	Conclusions and recommendations	Lines 2010-2012 and 2021-2023. -> Unilever reacts on the proposed DRVs for linoleic acid (LA) and alpha-linolenic acid (ALA). The EFSA panel recommends, based on the 'minimal level to prevent deficiency symptoms', AI levels of 4 E% for LA and 0.5 E% for ALA. LA and ALA deficiencies are virtually non-existent in the general population, whereas Cardiovascular Disease (CVD) is indisputably a major public health issue in Europe as it is the leading cause of mortality: 4.3 million deaths per year that make up 48% of all deaths in Europe (CVD statistics 2008). -> Unilever believes that the panel should use its own 'criterion of adequacy': 'disease risk reduction in relation to the nutrient intake pattern', in line with current insights that dietary recommendations should also take prevention of morbidity and premature mortality via optimal nutrition into account. In fact, several other authoritative bodies do so: The US Institute of Medicine set Acceptable Macronutrient Distribution Ranges of 5-10 E% for LA and 0.6-1.2 E% for ALA (Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Institute of Medicine (IoM) 2002). The WHO judged the evidence that LA and ALA decrease the risk of CVD as 'convincing' and recommended 5-8 E% for n-6 fatty acids and 1-2 E% for n-3 fatty acids (Joint WHO/FAO expert consultation. Diet, Nutrition, and the prevention of chronic diseases. WHO Technical report series 916. Geneva 2003). The EC-sponsored Eurodiet report (2001) recommends intakes of 4-8 E% for LA and of 2 g for ALA, which is about 0.8 E% . - >This EFSA draft scientific opinion states (lines 1891–1894) that "There is [also] evidence from dietary intervention studies that decreasing the intakes of products rich in SFA by a replacement of products rich in n-6 PUFA (without changing total fat intake) reduced the number of cardiovascular events." This is strongly supported by a recent pooled analysis of cohort studies, which confirms a significant inverse relation between 'increased PUFA at the expense of SFA' and coronary heart disease risk throughout the normal population range of intake (Jakobsen et al, Am J Clin Nutr 2009;89:1425-32). The median total PUFA

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		intake in the 11 populations included in this analysis varied between 2.3 E% and 9.0 E%, with most populations having an intake of around 5-6 E%. The highest (90th percentile) PUFA intake levels ranged from 3.7 E% to 10.4 E%, and were between 7 E% and 9 E% for most populations. Because LA makes up approximately 80 to 90% of total dietary PUFA, it can be derived that in these general populations, intakes of at least 6 E% for LA and of at least 1.0 E% are associated with the lowest risk of CHD. -> A DRV for ALA of 1 E% would also be in line with the 2 g/day as ALA that EFSA recently recommended to the Commission as labelling reference intake values (Question No EFSA-Q-2009-00548, adopted on 30 June 2009). Two g ALA per day in a 2000 kcal/d diet corresponds to ~0.9E%. -> CONCLUSION: The proposed AI levels of 4E% for LA and 0.5 E% for ALA, are based on prevention of deficiency symptoms. This is in contrast with other international dietary recommendations that, taking prevention of CHD into account, advice substantially higher intake levels of LA and ALA for optimal health. From the available evidence, it can be derived that AI levels for preventing cardiovascular diseases should be at least 6 E% for LA and 1 E% for ALA. Unilever believes that with the currently proposed AI levels, EFSA does not seize the opportunity to help the European population achieving intakes of LA and ALA that have been shown to reduce the risk of CHD. If the EU implements these recommendations of the EFSA panel, evidence-based claims and other communications aimed at motivating consumers to increase intakes of LA and ALA will be extremely difficult to make.
University of Aberdeen	1. Introduction	These comments cover the multiple sections. Web site did not seem to respond to individual submissions. Dietary reference values for fat It is important to acknowledge the deficiencies in the intake data where it is used to make recommendations: • Supplement use is not taken into account. Supplement use may make an important contribution to total intake of important PUFA/LCPUFA (e.g. marine oil supplement use in member states with low intakes of fish). This is not considered in the report. • There is a rapidly increasing trend toward manipulation and modification of the nutrient composition of foods with many novel foods having the potential to have a large impact on the overall intake of highly bioactive nutrients. This complexity may not be captured by the intake data used in this analysis. • The methods used to assess dietary intake are known to result in a significant underestimate of intake (e.g. as verified by doubly labelled water); underestimates of 25% are not unusual. This should be acknowledged in the report. Also, what would be the implications of such underestimation for this report? Section 2.1.3.1: No clear indication here that DHA is much more difficult to synthesise than AA – requiring peroxisome transport etc. There is good evidence to support differential AA/DHA synthesis in humans. This has important implications for any dietary recommendation and should be made explicit. Section 4: The logic of using absolute amounts for EPA/DHA DRVs and % of energy for everything else is not well explained. It is also worth noting that if fats are expressed as a % of energy then the distribution is not normal as the energy requirement is skewed. What effect would this have on the recommendations?

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		There is no mention in the report of positional isomers of fatty acids within triacylgrycerol; the same overall intake of fatty acids could have different health consequences depending on the position on the triacylglycerol moiety. Lines 479-482 state that "The developing brain accumulates large amounts of DHA both pre- and postnatally", see also line 1199. The figure used for accumulation of DHA in the brain is incorrect. Also, the story is more complicated than as presented (see for example European Journal of Clinical Nutrition. 2004 Dec;58(12):1559-70.). line 78; 'it' missing Line 137; coma should be full stop Line 704; 'unbeneficial' should be ' detrimental' Line 854; should define 'triene/tertaene' Line 943 'children' should be 'children and infants' Lines 1629-1630; 'decreasing intakes … at the expense of'? Line 1830; 'in itself' should be 'in themselves' Line 866; Not clear what is meant here. Should also be explicit about the logic of retroconversion of DHA to EPA. Line 148; There is more data on CLA and oxidative damage than is covered here. It may be worth looking again at the evidence in relation to safety/upper limit. Line 1035; this summary table is very useful. Given the importance of pregnancy and lactation in relation to fats it would be useful to summarise the pregnancy/lactation recommendations, already in raw form in the appendices, in the same way.
University of Aberdeen	3. Dietary sources and intake data	Dietary reference values for fat It is important to acknowledge the deficiencies in the intake data where it is used to make recommendations: • Supplement use is not taken into account. Supplement use may make an important contribution to total intake of important PUFA/LCPUFA (e.g. marine oil supplement use in member states with low intakes of fish). This is not considered in the report. • There is a rapidly increasing trend toward manipulation and modification of the nutrient composition of foods with many novel foods having the potential to have a large impact on the overall intake of highly bioactive nutrients. This complexity may not be captured by the intake data used in this analysis. • The methods used to assess dietary intake are known to result in a significant underestimate of intake (e.g. as verified by doubly labelled water); underestimates of 25% are not unusual. This should be acknowledged in the report. Also, what would be the implications of such underestimation for this report?
University Pablo Olavide	5.2. Serum lipids and lipoproteins	- 5.2.3. Page 38, lines 1253-1257. There exist several studies showing a clear effect of Cis-MUFA on serum lipid and lipoprotein profile. For example: • Pérez- Jiménez F., López-Miranda J, Mata P. Protective effect of dietary monounsaturated fat on arteriosclerosis: beyond cholesterol. Atherosclerosis 2002, 163: 385-398. • Mensink FH, Katan MB. Effect of a diet enriched with monounsaturated or polyunsaturated fatty acids on levels of low

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		density and high density lipoprotein cholesterol in healthy women and men. New Engl J Med 1989, 321: 436-41. • Mata P, Alvarez-Sala L, Rubio MJ, Nuño J, De Oya M. Effects of long term monounsaturated - vs polyunsaturated-enriched diets on lipoproteins in healthy men and women. Am J Clin Nutr 1992, 55: 846-50. • Gardner CD, Kraemer HC. Monounsaturated versus polyunsaturated dietary fat and serum lipid. Arterioscler Throm Vasc Biol 1995, 15: 1917-27. • López S, Bermúdez B, Pacheco YM, López-Lluch G, Moreda W, Villar J, Abia R, Muriana FJ. Dietary oleic and palmitic acids modulate the ratio of triacylglycerols to cholesterol in postprandial triacylglycerol-rich lipoproteins in men and cell viability and cycling in human monocytes. J Nutr. 2007 Sep;137(9):1999-2005. • Sánchez-Muniz FJ, Bastida S, Gutiérrez-García O, Carbajal A.Olive oil-diet improves the simvastatin effects with respect to sunflower oil-diet in men with increased cardiovascular risk: a preliminary study. Nutr Hosp. 2009 May-Jun;24(3):333-9. • Moreno JA, Pérez-Jiménez F, Moreno-Luna R, Pérez-Martínez P, Fuentes-Jiménez F, Marín C, Portugal H, Lairon D, López-Miranda J. The effect of apoE genotype and sex on ApoE plasma concentration is determined by dietary fat in healthy subjects. Br J Nutr. 2009 Jun;101(12):1745-52.
University Pablo Olavide	5.4. Inflammation and immne function	5.4.1. Page 42, line 1410 and 5.4.4. Page 42, lines 1435-1436. The studies published by Fuentes F et al. (Fuentes F, López-Miranda J, Pérez-Martínez P, Jiménez Y, Marín C, Gómez P, Fernández JM, Caballero J, Delgado-Lista J, Pérez-Jiménez F. Chronic effects of a high-fat diet enriched with virgin olive oil and a low-fat diet enriched with alpha-linolenic acid on postprandial endothelial function in healthy men. Br J Nutr. 2008 Jul;100(1):159-65.), Pacheco YM et al (A meal rich in oleic acid beneficially modulates postprandial sICAM-1 and sVCAM-1 in normotensive and hypertensive hypertriglyceridemic subjects. Pacheco YM, López S, Bermúdez B, Abia R, Villar J, Muriana FJ. J Nutr Biochem. 2008 Mar;19(3):200-5) and Jiménez-Gomez Y et al (Jiménez-Gómez Y, López-Miranda J, Blanco-Colio LM, Marín C, Pérez-Martínez P, Ruano J, Paniagua JA, Rodríguez F, Egido J, Pérez-Jiménez F. Olive oil and walnut breakfasts reduce the postprandial inflammatory response in mononuclear cells compared with a butter breakfast in healthy men. Atherosclerosis. 2009, 204: 70-6) show that a Mediterranean diet rich in MUFA plays a key role in postpandrial endothelial function and inflammatory biomarkers.
University Pablo Olavide	5.4. Inflammation and immne function	5.4.1. Page 42, line 1410 and 5.4.4. Page 42, lines 1435-1436. The studies published by Fuentes F et al. (Fuentes F, López-Miranda J, Pérez-Martínez P, Jiménez Y, Marín C, Gómez P, Fernández JM, Caballero J, Delgado-Lista J, Pérez-Jiménez F. Chronic effects of a high-fat diet enriched with virgin olive oil and a low-fat diet enriched with alpha-linolenic acid on postprandial endothelial function in healthy men. Br J Nutr. 2008 Jul;100(1):159-65.), Pacheco YM et al (A meal rich in oleic acid beneficially modulates postprandial sICAM-1 and sVCAM-1 in normotensive and hypertensive hypertriglyceridemic subjects. Pacheco YM, López S, Bermúdez B, Abia R, Villar J, Muriana FJ. J Nutr Biochem. 2008 Mar;19(3):200-5) and Jiménez-Gomez Y et al (Jiménez-Gómez Y, López-Miranda J, Blanco-Colio LM, Marín C, Pérez-Martínez P, Ruano J, Paniagua JA, Rodríguez F, Egido J, Pérez-Jiménez F. Olive oil and walnut breakfasts reduce the postprandial inflammatory response in mononuclear cells compared with a butter breakfast in healthy men. Atherosclerosis. 2009, 204: 70-6) show that a Mediterranean diet rich in MUFA plays a key role in postpandrial endothelial function and inflammatory biomarkers.
University Pablo Olavide	5.6. Glucose tolerance and insulin sensitivity	- 5.6.2. Page 44, lines 1499-1507, 5.6.5 Page 45, lines 1551-1552, 5.9.1. Page 50, lines 1724-1733 and 5.9.4. Page 50, lines 1753-1755. There exist several studies showing that Cis-MUFA improves insulin resistance and glucose homeostasis:

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
		• Bos MB, de Vries JH, Feskens EJ, van Dijk SJ, Hoelen DW, Siebelink E, Heijligenberg R, de Groot LC. Effect of a high monounsaturated fatty acids diet and a Mediterranean diet on serum lipids and insulin sensitivity in adults with mild abdominal obesity. Nutr Metab Cardiovasc Dis. 2009 Aug 17. • Paniagua JA, de la Sacristana AG, Sánchez E, Romero I, Vidal-Puig A, Berral FJ, Escribano A, Moyano MJ, Peréz-Martinez P, López-Miranda J, Pérez-Jiménez F. A MUFA-rich diet improves posprandial glucose, lipid and GLP-1 responses in insulin-resistant subjects. J Am Coll Nutr. 2007 Oct;26(5):434-44. • Paniagua JA, Gallego de la Sacristana A, Romero I, Vidal-Puig A, Latre JM, Sanchez E, Perez-Martinez P, Lopez-Miranda J, Perez-Jimenez F. Monounsaturated fat-rich diet prevents central body fat distribution and decreases postprandial adiponectin expression induced by a carbohydrate-rich diet in insulin-resistant subjects. Diabetes Care. 2007 Jul; 30(7):1717-23. • Low CC, Grossman EB, Gumbiner B. Potentiation of effects of weight loss by monounsaturated fatty acids in obese NIDDM patients. Diabetes. 1996 May; 45(5):569-75. • Berglund L, Lefevre M, Ginsberg HN, Kris-Etherton PM, Elmer PJ, Stewart PW, Ershow A, Pearson TA, Dennis BH, Roheim PS, Ramakrishnan R, Reed R, Stewart K, Phillips KM; DELTA Investigators. Comparison of monounsaturated fat with carbohydrates as a replacement for saturated fat in subjects with a high metabolic risk profile: studies in the fasting and postprandial states. Am J Clin Nutr. 2007 Dec; 86(6):1611-20. • Julios U. Fat modification in the diabetes diet. Exp Clin Endocrinol Diabetes. 2003 Apr; 111(2):60-5. • Ros E. Dietary cis-monounsaturated fatty acids and metabolic control in type 2 diabetes. Am J Clin Nutr. 2003 Sep; 78(3 Suppl):617S-625S. • Salas J, López Miranda J, Jansen S, Zambrana JL, Castro P, Paniagua JA, Blanco A, López Segura F, Jiménez Perepérez JA, Pérez Jiménez F. The diet rich in monounsaturated fat modifies in a beneficial way carbohydrate metabolism and arterial pressure. Med Clin (Barc). 1999 Dec 11;113(20):765-9
University Pablo Olavide	5.7. Body weight control and energy balance	- 5.7.2. Page 46, lines 1585-1593. The writing of the statement is confusing and difficult to understand. Thus, it should be clarified.
University Pablo Olavide	6.3. Cis-monounsaturated fatty acids (Cis-MUFA)	We consider that the following statement "Cis-MUFA are synthesised by the body, have no known role in preventing or promoting diet-related diseases, and therefore not required in the diet" written in lines 69-70, 1876-1877 and 1995-1996, should be eliminated or modified. The reason is that the mentioned statement is completely different of a previous EFSA opinion from July 2005 (Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to nutrition claims concerning omega-3 fatty acids, monounsaturated fat, polyunsaturated fat and unsaturated fat; Request Nº EFSA-Q-2004-107). In this request it is textually written "Substitution of saturated fatty acids (SFA) in the diet by an equal amount of MUFA reduces low density lipoprotein (LDL) cholesterol; elevated plasma LDL-cholesterol has been causally linked to coronary heart disease. Because SFA intakes of many EU populations exceed levels (about 10% energy) widely recommended for maintenance of lower levels of plasma LDL-cholesterol, MUFA consumption plays an important nutritional role in limiting SFA intake".

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
VBZ (Association of the Dutch Bakery and Confectionary Industry)	4. Overview of dietary reference values and recommendations	Comment on table 5, line 1035-1039 and other lines about the Dietary reference values of the Netherlands. On page 93 (line 2915) the dietary reference value in the Netherlands is mentioned. However, these are the values from 2001, whereas the Dutch Health Council updated its advice in 2006. Therefore we recommend using the most recent dietary guidelines.
VBZ (Association of the Dutch Bakery and Confectionary Industry)	Conclusions and recommendations	Comment about line 56-67 in the Summary and line 1986-1993 in the Conclusions and recommendations. We would also like to react on the summary, but because this isn"t possible we react on the conclusions and recommendations. Please use this comment also for the summary. We support the opinion of the Dutch Product Boards: Why are all the saturated fats treated as one group in the summary? The unsaturated fats are split up in separate groups, but the saturated fats are treated as one group. As stated in chapter 5.2.2 several saturated fats have different effects on cholesterol metabolism.
VBZ (Association of the Dutch Bakery and Confectionary Industry)	Conclusions and recommendations	Comment about line 66,67 in the Summary and line 1992-1993 in the Conclusions and recommendations. We would also like to react on the Summary, but because this isn"t possible we react on the Conclusions and recommendations. Please use this comment also for the Summary. We support the opinion of the Dutch Product Boards: In the Summary in line 66,67 the following is written: 'The Panel recommends that SFA intake should be as low as possible within the context of a nutritionally adequate diet'. In the discussed scientific research in chapter 5 this recommendation is not supported. Furthermore, according to Table 5 (page 32), most Countries and also the WHO/FAO set the maximum SFA at 10 E%. In infants average intakes of SFA where between 11-13 E%. In adults, average SFA intakes vary between 9 to 17 E% and nearly 30% of the reported average intakes were 15 E% or higher (line 620-629). In addition: in several economically developed countries where the SFA is close to 10%, the capacity to decrease SFA much further is limited to major changes in dietary patterns, and is only likely to result in modest reductions in TC and LDL-C We therefore believe it is appropriate to set the recommendation for SFA at 10 E%.

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VBZ (Association of the Dutch Bakery and Confectionary Industry)	Conclusions and recommendations	Comment on line 129-146 in the Summary and line 2036-2042 in the Conclusions and recommendations. We would also like to react on the Summary, but because this isn"t possible we react on the Conclusions and recommendations. Please use this comment also for the Summary. We support the opinion of the Dutch Product Boards: We suggest adding to the statement of The Panel in the summary the following: The intake of TFA is close to the recommendation levels in most European countries, and are therefore not a public health issue anymore. The intake of total TFA is low because of the efforts made by the food industry in reducing the amount of industrial TFA in their products (and these efforts are ongoing). The level of ruminant TFA in meat (products) and dairy products is already naturally low.
VBZ (Association of the Dutch Bakery and Confectionary Industry)	Conclusions and recommendations	We support the opinion of the Dutch Product Boards: In conclusion, we would like to point out the following. Consumers do not eat saturated fats or unsaturated fats as such. They eat these nutrients in a matrix (food stuffs), as part of a balanced diet. In practice, the matrix influences the effects of the fatty acids, meaning that negative effects may not occur, or may be less pronounced, due to the presence of other nutrients in the food.
VBZ (Association of the Dutch Bakery and Confectionary Industry)	Conclusions and recommendations	We would also like to react on the summary, but because this isn"t possible we react on the conclusions and recommendations. Please use this comment also for the summary. VBZ is supporting the opinion of the Dutch Product Boards that the conclusions in the summary do not reflect accurately the content of the report. More precise, the nuance in the report is lacking in the summary. Therefore, it is not immediately obvious on what basis the conclusions are drawn. Since the summary is generally the only part that policy makers read, it is important that the summary reflects the scientific state of the art, including the recent developments and nuances.
VBZ (Association of the Dutch Bakery and Confectionary Industry)	References	Recently, two WHO scientific updates were published in the European Journal of Clinical Nutrition (vol. 63, supplement 2s, pp S1-S75) and Annals of Nutrition and Metabolism (vol.55, no. 1-3: pp 5-300). It seems logical to take these two updates into account in the document.
VU University Amsterdam	5.2. Serum lipids and lipoproteins	Lines 1337-1338: The numbers have been interchanged. 0.036 should be 0.061 and 0.061 should be 0.036
VU University Amsterdam	6.4. Cis-polyunsaturated fatty acids (Cis-PUFA)	This is a valuable overview of the literature. However, the recommendation for linoleic acid is puzzling and will not help to promote the health of Europeans. Line 1897 states: "The Panel proposes to set an AI for linoleic acid of 4 E%, based on the lowest estimated mean intakes of the various population groups from a number of European countries, where overt linoleic deficiency symptoms are not present." This comparison of population groups is not useful for deriving the Adequate Intake for the prevention of linoleic acid

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		deficiency. For such prevention, 1 E% is already sufficient, as shown in the studies cited in the report. However, it seems more prudent to base the AI on the prevention of coronary heart disease. The clinical trials which showed that dietary linoleic acid prevents coronary heart disease employed intakes in the range of 9 to 21 E%, with a mean of 14 E%. This would therefore be the most rational AI value. As 14 E% is impractably high EFSA would be justified to set the recommendation somewhat lower, e.g. at 8-10 E%. But setting the AI at 4 E% will send a signal that this is a healthy intake, while in fact the country with this intake – Finland – historically has a high rate of coronary heart disease. The low intake of linoleic acid and high intake of saturated fat in Finland is a major cause of this [Pietinen P et al. Changes in diet in Finland from 1972 to 1992: impact on coronary heart disease risk. Prev Med. 1996 ;25(3):243-50] . The present EFSA AI may increase instead of decrease coronary heart disease in the EU. Prof. dr Martijn B. Katan I have no conflicts of interest regarding this report. Neither I nor my family members have any consultancies, grants, stocks, or other financial interests in food, drug or medical companies.