Would you be so kind as to find herewith our comments on the developments of
the Draft Report 'Diet, Nutrition, and the prevention of Chronic Diseases'
which are concerning sodium or salt. They amount to 5 pages as requested.

As the chapter or annexe on iodine deficiency disorders (IDD) is still
missing, we are not in a position to express our views with this respect. We
expect that, later on, we shall be consulted on it, and more especially on
universal salt iodisation which is recommended by WHO.

With our best regards.

Bernard Moinier

COMMENTS ON THE DRAFT REPORT
DIET, NUTRITION AND THE PREVENTION OF CHRONIC DISEASES
BY ESPA

Page 15
Foetal development and the maternal environment
Infancy and childhood

Under both of these items a development about iodine deficiency disorders (IDD) and their prevention is missing although the enormous and escalating social costs make it a compelling case for public health policy.

Pages 19 + 22
"Guidelines should try to ensure that the overall benefit to the majority of the population substantially outweighs any potential adverse effects to the rest of the population"

This sound remark is also valid for salt restriction policy. It does not make sense to recommend that sodium dietary intake should be < 2 g/day (NaCl 5 g/day) whereas there is no convincing or probable justification for such a low level in the literature. According to the draft report, convincing means "evidence based on epidemiological studies showing consistent association between the exposed and the disease, with little or no evidence to the contrary". This wording remains a dead letter for sodium and high blood pressure or related diseases.

Page 32, table 6

The same remark prevails for the table where "high salt intake" is listed among increased risk factors for cardio-vascular diseases. Moreover, what is high sodium intake? More than 200 mmol/day (NaCl 12 g/day)? A clear-cut definition should be given, and a span would presumably be more appropriate.

Page 36, table 7

Idem

Pages 38-39

The prevention of dental caries should mention salt fluoridation. At least the following sentence would be inserted: “Salt fluoridation should be widely encouraged for its systemic action”.

Page 43

“High sodium intake” deserves the same remarks as before.

Page 48
“Low sodium foods”

Low sodium foods are widely available, and there is no need to restrict the consumer choice to dietetic food or to invite the food industry to “lower the sodium content of regularly consumed foods like bread or cereal”. The food industry adjust salt according to technological, sensory and preservative reasons in processed food.

Annex 4

Pages 12-13
NHANES I Study

There is a long development to assimilate the study by Alderman et al.[(1)] to a non-relevant one because of methodological flaws. The relationship of sodium intake to cardio-vascular disease and all cause mortality was duly investigated. Sodium intake proved to be inversely related to cardio-vascular disease mortality. Why to refer to Poulter correspondence[(2)] where he suggests the investigators misinterpret their findings without echoing author’s reply[(3)] who endorses his call for further data to confirm the inverse association of sodium to mortality? It would have been also advisable to comment on the analysis of prediction factors of cardiovascular events performed by Tunstall-Pedoe[(4)]. Urinary sodium was identified as non significant or poorly related in a large cohort of 5754 men and 5875 women.

Pages 39-41
Minerals: blood pressure and cardio-vascular diseases
Sodium

The development relating to sodium deserves some criticism because of selected references and/or one-sided interpretations. This is obvious, first, with Intersalt, which is described as “the most comprehensive epidemiological evidence” of a direct correlation between sodium intake and the prevalence of hypertension[(5)]. It had been designed to evidence a linear relationship between blood pressure and hypertension occurrence on the one hand and dietary sodium consumption on the other hand. However, there was no such direct correlation. The estimated effect of salt on blood pressure depends on statistical adjustments. The Intersalt investigators have favoured results obtained by combining data from 52 centres, irrespective of the presence of subjects with lower blood pressure in 4 centres with extremely low salt consumption. The claimed correlation was lost when reanalysed by only pooling the 48 high salt centres (un-acculturated populations excluded). The downwards slope among the 48 centres reflects a negative relationship between blood pressure and salt intake, which contradicts the “salt hypothesis”.

A disputable post-hoc analysis showed that dietary sodium intake was significantly related to the slope of blood pressure with age.

It is not so surprising that a number of reviewers like Freedman[6] have underlined that, even when revisited, the Intersalt data were not supporting the salt hypothesis which was the priority of the study. And since that time, the publication of new data relating to sodium dietary effect has continuously eroded agreement by the relevant experts in high blood pressure research about the role of sodium.

Migration studies are to correlate blood pressure and lifestyle factors (blood pressure raising effects of urbanisation). The study completed in Kenya[7] is inconsistent with another one relating to Kuna Indians[8]. They do not develop high blood pressure when moving to Panama City, their dietary salt intake averaging 13 g/day.

"An overview of observational data in populations"[9] is presented as a further evidence of alleged benefits of curtailing salt intake. Interventional studies generally provide a firmer rationale than observational studies for recommendations. However, modifying salt intake results generally in altered intake of other nutrients which may have independent effects on blood pressure and other cardiovascular risk factors. Therefore meta-analysis of such studies should be carefully performed in pooling trials with well designed protocols, significant number of subjects, and appropriate duration. The meta-analysis by Law has been disregarded by Swales [10] and other members of the scientific community for its inaccuracy. Using inadequate data, or analysing them with flawed assumptions produces inherently unreliable conclusions.

Why to refer only to the most dispraised meta-analysis and never mention the more recent ones by Midgley[11] or by Graudal[12]? The former is actually mentioned in the reference list but without being referred to in the sodium related chapter… Are only Law and Cutler worth of their salt? Is that because Midgley and Graudal have reached just opposite conclusions that their meta-analyses are ignored? Although the interpretation of their respective findings differ, their conclusions both confirm a negligible effect of sodium restriction in the general population: systolic blood pressure lowered by $\simeq$1 mm Hg when salt intake is reduced by ± 30%.

This is also a matter of fact when referring to reviews based on literature investigation. Further to MEDLINE compilation, the main conclusions drawn by Fodor are crystal-clear: "Restriction of salt intake for the normotensive population is not recommended at present, because of insufficient evidence demonstrating that this would lead to a reduced incidence of hypertension… For hypertensive patients, particularly those over the age of 44 years, it is recommended that the intake of dietary sodium be moderately restricted to a target range of 90-130 mmol/day[13]. Such are the options for Canada where approximately 1/5 of the population has high blood pressure.

The situation in Finland as studied by Tuomilehto[14] deserves consideration for the presentation of its results. The major flaws are as follows:

- the average urinary sodium excretion in this population sample is very high suggesting that 50% ingest more than 12 g/day
- there is no relationship between urinary sodium and blood pressure: why do the authors not comment on it?
- the association between urinary sodium and cardiovascular events exists only in overweight people: BMI of the investigated individuals exceeds average.

Such data are not convincing for the general population. Lowering overweight contributes to suppress salt sensitivity[15]. In this study, changing from high- to low-salt diet induced significant blood pressure decline in obese subjects, but not in the non-obese controls. Furthermore, after a subgroup of obese subjects had achieved weight loss, sodium sensitivity disappeared. There are now consistent findings showing that salt sensitivity is not an immutable trait. It seems to be influenced by the overall quality of the diet. It can be mitigated, even eliminated, simply by adjustments to improve it. Over years, studies have evidenced that a global dietary approach had a greater influence on blood pressure in a given population than focussing on one single nutrient.

The DASH diet trial[16], alias DASH II, has been disconnected from DASH I[17]. Why? Both were used to suggest that a dietary manipulation, and, in the second, combined with a salt reduction of about 3 g/day may be justified. The lay press has extensively covered the publication of the second as if it was ending a long controversy by the final identification of the culprit: salt. Focussing on this aspect to the exclusion of other physiological effects was disappointing.

The DASH investigators have not tested the effects of weight loss. Why? Whelton has presented evidence from the TONE study that combining salt restriction and weight loss was more successful[18]. Another study[19] showed that a modest weight loss is likely to lower the need for antihypertensive medication. It is suggested to reflect an improvement in insulin sensitivity and a decrease in sympathetic nervous system activity. It occurs independently of salt restriction.

DASH investigators failed to conclude that the DASH diet (fruits, vegetables, and low fat dairy products) was the nutritional priority to lowering blood pressure, and not sodium restriction. Focussing mainly on sodium restriction is to weaken the salt hypothesis in as much as DASH II deserves other critical comments summarised by Kurtzman[20]. The population was not reflecting the general population due to a majority of overweight and hypertensive African-Americans. The anti-salt protagonists were disappointed to find that reducing dietary sodium to more than half produced a blood pressure effect only in hypertensive African-Americans women… The experiment lasted only 30 days. Would many people benefit from eating an unpalatable diet over years? Would low salt diet be safe on long term? At last, a general remark. Despite increasing obesity, the average population is living longer than ever while there is a fall in cardiovascular events, even in countries with high salt intake like Sweden or Japan. The debate about salt intake is now a remote one.

In the draft report mention is made that “clinical trials have also demonstrated the sustained blood pressure lowering effects of sodium restriction in infancy” (2 studies) “and in elderly” (2 studies). The issue should be more carefully documented. Rumours have emerged that long term effects of neonatal sodium restriction were not as favourable as expected due to a serious adverse impact of salt deprivation on the development of the central nervous system. A recent study[21] outlined that sodium deficiency in early life – like iodine deficiency – might have detrimental consequences. Failure to provide a sufficient amount of salt in the first two weeks of postnatal life would predispose children to poor motor and neuropsychological development at 10-13 years of age.

Adverse effects in the elderly are well characterised thanks to a number of studies having identified

- an alteration of cognitive functions
- an increase in LDL cholesterol
- anorexia owing to unpalatable diet, and nutrient deficiencies.

"Based on the observational and trial data so far available, it would be justified to recommend a daily salt intake of less than 5 g/day". This conclusion sounds rather strange for people who are familiar with the salt and health issue. Dietary salt intake is less than it has been previously believed. Intersalt has shown that the average sodium intake is about 150 mmol/day. This suggests that 95% of individuals are likely to ingest between 100 and 200 mmol/day (NaCl 5.8-11.9 g/day). To get this amount reduced should require a hard evidence which is neither provided in the draft report nor in the literature.

The salt debate has important implications for Health policy since salt is an efficient carrier for iodine and fluoride. Considering sodium restriction, the late Swales[22] has defined a set of criteria for assessing the validity of a specific recommendation with this respect. "Any decision to recommend reduction in salt intake should reflect analysis of all the scientific evidence available".

Pages 58-59 + 64 + 65
DASH diets

Confer previous comments.

The absence of any evidence that persons consuming a diet limited in sodium are living better and longer should prevent from political extrapolations on which would be forged a "scientific consensus".

Annex 7
Osteoporosis Pages 17-18 + 23

"The evidence that sodium is important in the aetiology of osteoporosis or that sodium restriction may be a beneficial strategy for fracture prevention is inconclusive".

Other reviews should be mentioned to support this remark. The possible aetiologic role of dietary salt in osteoporosis has been investigated by Cohen and Roe[23]. There is no sound evidence that the consumption of salt at the present average level of 9 g/day constitutes a risk factor for osteoporosis. Therefore a reduction to 5 g/day should not be recommended. The second review[24] was aimed at summarising the evidence of the hypothesised relationship, and discussing the possible mechanisms. They concluded as follows: "The relationship between salt intake and osteoporosis is still controversial. A possible relation between salt intake and facture risk should be addressed in future studies".

An interesting question which remains pending is whether the long-term consumption of relatively small amounts of fluoride, such as those facilitated by fluoridised salt (or fluoride-rich mineral water) may participate in the prevention of osteoporosis. In the reverse, it is unfit to assimilate "high sodium intake" to increased fracture risk in the table on page 23.

(1) Alderman et al, Dietary sodium intake and mortality, : the National Health and Nutrition Examination Survey (NHANES I), *Lancet 1998*; 1:781-785

(2) Poulter, *Lancet 1998*, 352 :987

(3) Alderman, *Lancet 1998* ; 352 :988

(4) Tunstall-Pedoe, Comparison of the prediction of 27 different factors of coronary heat disease and death in men and women of the Scottish heart health study : cohort study *BMJ 1997*; 315:722-729

(5) *BMJ 1988* ; 297 :319-328

(6) Freedman et al., Salt and blood pressure: conventional wisdom reconsidered. *Internat J Epidemiol on-line*

(7) Poulter et al., *BMJ 1990* ; 300 :967-972

(8) Hollenberg et al., Aging, acculturation, salt intake and HBP in the Kuna of Panama, *Hypertens 1997*; 29/2:171-176

(9) Law et al., By how much does salt reduction lower blood pressure. III: analysis of data from trials of salt reduction, *BMJ 1991*; 302:819-824

(10) "Despite of the existence of more rigorous and up-to-date reviews, the meta-analysis by Law et al. continues to be cited more frequently than any other. The most likely explanation is that, despite its manifest flaws, its conclusions are more congenital than those reached by the more recent unsupportive meta-analyses". *Am J Hypertens* 2000; 13:2-7

(11) Midgley et al., Effects of reduced dietary sodium on blood pressure: A meta-analysis of randomised controlled trials, *JAMA 1996*; 275:1590-1597

(12) Graudal et al., Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterols and triglicerides, *JAMA 1998*; 279:1383-1391

(13) *CMAJ 1999* ; 160 (9 Supp) :529 ss

(14) Urinary sodium excretion and cardiovascular mortality in Finland : a prospective study, *Lancet 2001*; 357:848-851

(15) Rocchini et al. The effects of weight loss on the sensitivity of blood pressure to sodium in obese adolescents, *N Engl J Med 1989*; 9:329-335

(16) Sacks et al. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension. *N Engl J Med 2001*; 344:3-10

(17) Appel et al. A clinical trial of the effects of dietary patterns of blood pressure. *N Engl J Med 1997*; 336:117-1124

(18) Whelton et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomised control trial of non-pharmacological interventions in the elderly. *JAMA 1998*; 279:839-846

(19) Mertens et al. Overweight, obesity, and blood pressure: the effects of modest weight reduction. *Obes Res 2000*; 8:270-278

(20) Kurtzman et al. *Am J Kidney Dis 2001*; 37:636-637

(21) Al-Dahhan et al. Effects of salt supplementation of new born premature infants on neuro-developmental outcome at 10-13 years. *Arch Dis Child Fetal Neonatal Ed 2002*; 86:F 120-123

(22) Population advice on salt restriction: the social issue. *Am J Hypertens 2000*; 13:2-7

(23) Cohen and Roe. Review of risk factors in osteoporosis with particular reference to a possible aetiological role of dietary salt. *Food Chem Toxicology 2000*; 38:237-253

(24) Burger et al. Osteoporosis and salt intake *Nutr Metab Cardiovasc Dis 2000*; 10:46-53