The following additional information is provided to complement the document "*A critical appraisal of, and commentary on, 50 Reasons to oppose fluoridation.*"

Laboratory and animal experiments – statements 12, 13, 14, 15, 17, 18, 20, 21, 27).

The following points should be noted in relation to some of the assertions made in the statements listed above:

- Emsley *et al*., (1981) (cited in the '*50 Reasons*' document) review amide-fluoride systems. The authors conclude that the assertion that fluoride causes genetic damage, birth defects and cancer cannot be established from the chemistry of the ion, which they say is stable in aqueous solution. Emsley *et al.*, (1981) also report that fluoride is an essential element in low concentrations for various chemical reactions including an intermediate step in reactions involving amides.
- Many nutrients and chemicals are known to alter enzyme activity. Observations of such interactions in test tube studies provide a very low level of evidence in themselves and cannot be extrapolated to the real-life interactions in living tissue. As McDonagh *et al*., (2000) have commented "*exposure in in vitro (laboratory studies) is very different to those in vivo (real life situations). In cell culture experiments cells are exposed directly to a fluoride solution containing highly reactive unbound ions. This is very different to exposure in the body…*" On the question of toxicology studies McDonagh *et al*., (2000) note that "*the history of health technology development shows that there have been numerous new interventions that were promising (or harmful) in animal and laboratory studies that turned out to be ineffective (or safe) when tested in humans. One example would be the drug omeprazole (Losec) which caused gastric tumours in pre-clinical animal studies. However, such tumours have not been documented in humans, even in patients with conditions that require continuous treatment for many years. In general, when human data are available, animal or laboratory data provide far less reliable estimates of effect and, as such, do not bear significant weight on decisions about interventions.*"
- Lepo *et al*., (2000) reviewed the fluoride literature to assist the understanding of the potential environmental and human health impacts of fluoridation of water. The authors noted that in *in vitro* laboratory experiments the concentration of

fluoride at which enzyme inhibition occurs is quite often of the order of 100 to 1,000 times greater than the concentration at which inhibition occurs in humans and such experimental inhibition is not physiologically meaningful. Normal fluoride soft-tissue levels are in the micromolar range whereas enzyme inhibition typically requires millimolar concentrations.

- The DHSS report (1991) on the benefits and risks of fluoride (cited in the '*50 Reasons*' document) includes the following text in relation to the mutagenicity of fluoride: "*the most consistent finding is that fluoride has not been shown to be mutagenic in standard tests in bacteria (Ames Test)*" (DHSS 1991).

- A report by Jackson *et al*., (2002) "*Chemistry and Bioavailability Aspects of Fluoride in drinking Water*" discusses the chemistry of water fluoridation, possible interactions between fluoride and other elements in water and any effects on bioavailability. The authors conclude that the effect of major cations (positively charged ions) calcium and magnesium and sodium on the bioavailability of fluoride is very small.
- Jackson *et al*., (2002) also reported that fluoride at a concentration of 1mg/l has essentially no interaction with other chemical species in water and negligible impact on corrosivity of water through the distribution system.

- Two studies were conducted by Jackson *et al*., (1997) to assess the potential for adverse physiologic and genotoxic effects of long-term fluoride ingestion in adults residing in three communities with varying water fluoride levels (0.2 ppm, 1.0 ppm, and 4.0 ppm). All were long-time (≥ 30 years) residents of their respective communities. The investigation provided evidence that the long-term ingestion of water containing 0.2 ppm, 1.0 pmm or 4.0 ppm fluoride did not have any clinically important physiologic or genotoxic effects in healthy adults.
- Kaminsky *et al*., (1990) have also concluded that there is no evidence that fluoride is genotoxic except in some *in vitro* assays at cyotoxic concentrations.
- The study by Mihashi and Tsutsui (1996) (cited in the '*50 Reasons*' document) involved treating Rat Vertebral Body-Derived cells (RVBd) with sodium fluoride at 0.5-2.0 mM for 24 hours.

- In the study by Freni (1994) (cited in the '*50 Reasons*' document) the water was fluoridated to 3 ppm or more which is considerably higher than the optimum level recommended for water fluoridation. This study also compared county birth data with county fluoride levels and attempted to show an association between high fluoride levels in drinking water and lower birth rates (Freni 1994). The study used population means rather than data on individual women. Whether or not the fluoride effect on the fertility rate found at the county level also applies to individual women was not investigated. Population data does not adjust for confounding factors such as age of the subjects. The potential influence of confounding factors must also be considered. A large variation exists in this age range, which more than likely had a large influence on the findings of the study.
- In the study conducted by Chinoy *et al*., (1994) (cited in the '*50 Reasons*' document) the effects of 25, 50 and 250 mM sodium fluoride on human spermatozoa was investigated *in vitro* at intervals of 5, 10 and 20 minutes. It was reported that sodium fluoride did not affect the extracellular pH of the sperm "*except that a slight acidification was caused by the 250mM dose only*". The doses of fluoride administered to the human spermatozoa were much higher than that provided by public water fluoridation. They were also administered *in vitro* which makes it more difficult to correlate the findings to the *in vivo* situation.
- A Working Group appointed by the Medical Research Council (2002) did not consider that the available evidence supported claims that fluoridated water affects the reproductive system and consequently they did not recommend any further research in this area, noting, "*the plausibility of fluoride affecting the reproductive capacity of humans at the intakes experienced from fluoridated drinking water is low*".

- Alzheimer's disease is a degenerative condition resulting in dementia, occurring mainly in the elderly. Aluminium has been suggested as a possible cause of, or risk factor for, Alzheimer's disease due to its presence in the brain tissue of Alzheimer's disease patients (specifically beta-amyloid plaques and neurofibrillary tangles). The proposed link between dietary aluminium intake and Alzheimer's disease is still the subject of considerable debate. If absorption of aluminium is reduced by ingestion of fluoride, this condition should be less

common in communities with fluoridated drinking water (Foster, 1993; Kraus and Forbes, 1992). The Medical Research Council (2002) note that "*the possible link between aluminium uptake and Alzheimer's disease is by no means established*."

- A number of areas addressed in the paper by Struneka and Patocka (1999) (cited in the '*50 Reasons*' document) are widely accepted as aluminium toxicity e.g. aluminium related bone disease, dialysis encephalopathy and microcytic anaemia. However, these elevated levels of aluminium only occurred in patients on dialysis (either from dialysis fluid or because of aluminium containing phosphate binders).

- In the study by Mullinex *et al*., (1995) (cited in the '*50 Reasons*' document) rats were fed fluoride at levels up to 125 times greater than that found in optimally fluoridated water. The study attempted to demonstrate that rats fed extremely high levels of fluoride (75 ppm to 125 ppm in drinking water) showed behaviour-specific changes related to cognitive deficits. In addition, the experiment also studied the offspring of rats who were injected two to three times a day with fluoride during their pregnancies in an effort to show that prenatal exposure resulted in hyperactivity in male offspring. The external validity of these findings are highly questionable due to the doses administered and the fact that the body weight and gastrointestinal systems of rats are not directly comparable with those of humans.
- Two reviewers (Ross and Daston 1995) of the study by Mullinex *et al*., (1995) have suggested that the observations made can be readily explained by mechanisms that do not involve neurotoxicity. They found inadequacies in experimental design that may have led to invalid conclusions. For example, the results of the experiment were not confirmed by the use of control groups which are an essential feature of test validation and experimental design. In summary the scientists stated, "*we do not believe the study by Mullenix et al. 1995 can be interpreted in any way as indicating the potential for NaF (sodium fluoride) to be a neurotoxicant*." Another reviewer (Whitford 1996) has noted that "*it seems more likely that the unusually high brain fluoride concentrations reported in Mullenix et al. were the result of some analytical error*."
- Information on fluoride and the pineal gland is limited and further targeted research may be warranted (Luke 2001). The Medical Research Council (2002)

has concluded that such research " *is presently of low priority unless and until critical literature reviews are undertaken that demonstrate specific research needs*."

Unsupported statements/assertions – statements 1, 11, 16, 33, 34, 36, 37, 40, 41, 42, 43, 46, 47, 48, 49, 50 (NOTE: these statements have no supporting references to peer reviewed biomedical literature and/or represent opinions expressed by the author or the opinions of others with no references to the peer reviewed biomedical literature and/or contain references to the administration or organization of regulatory agencies in United States and/or refer to the history or sociology of the debate over water fluoridation in the United States).

The following points should be noted in relation to some of the assertions made in the statements listed above:

- Several large community-based epidemiological studies found no increased renal disease associated with long-term exposure to drinking water with fluoride concentrations of up to 8mg/l (DHSS 1991, NRC 1993).

- Urbansky and Schock (2000) investigated possible complexation of lead by fluoride and hexafluorosilicate and found that the lead fluoride complexes accounted for less than 1% of the total dissolved lead. They concluded that "*no credible evidence exists to show that water fluoridation, at a concentration of 1mg/l fluoride, has any quantitative effects on the solubility, bioavailability, bioaccumulation or reactivity of lead or lead compounds*". The authors also reported that fluoride at a concentration of 1mg/l will have essentially no interaction with other chemical species in water and negligible impact on corrosivity of water towards the distribution system. The Medical Research Council (2002) note that aluminium and fluoride are mutually antagonistic in competing for absorption in the gut. Therefore, the more fluoride in the diet, the less aluminium is absorbed. At the same time, ingestion of aluminium counteracts dental fluorosis, reducing fluoride stores in teeth and bones. This effect has been demonstrated in experimental animals and humans (Foster, 1993; quoting Navia 1970). The authors of the report thus concluded that "*fluoride will reduce rather than increase any toxic potential from aluminium in food or water*".

- Buzalef *et al*., (2001) note that factors such as malnutrition (Rugg-Gunn *et al*., 1997), altitude or renal dysfunction can produce enamel changes that resemble enamel fluorosis even in the absence of significant exposure to fluoride.
- The Oral Health in America 2000 proposals (cited in the '*50 Reasons*' document) highlight the social impact of dental disease in children and note that pain and suffering due to untreated dental disease can lead to disruption of family life, and problems in eating, speaking and enjoyment of social or school activities.
- One of the objectives of the York systematic review on water fluoridation (McDonagh *et al*., 2000) was to examine whether water fluoridation results in a reduction of caries across social groups and between geographical locations, bringing equity. No longitudinal studies were found by the York review to address this issue. It was thus decided to include cross-sectional studies only from the U.K as it would be difficult to compare measures of social class from different countries. The authors reported that some evidence exists that water fluoridation reduces the inequalities in dental health across social classes in 5- and 12-year-olds, using the dmft/DMFT outcome measure. This effect was not seen in the proportion of caries-free children among 5-year-olds. The small quantity of studies, differences between these studies and their low quality rating suggests caution in interpreting these results (McDonagh *et al*., 2000).
- The data contained in the Children's Oral Health in Ireland Report 2002 (Whelton *et al*., 2004) generally supports the published literature, which asserts that the oral health of the less well off is worse than that of the rest of the population. In this report, possession of a medical card was used as a surrogate for disadvantage in the Republic Of Ireland. For the vast majority of the age groups in the study, ownership of a medical card by the parents or guardians is an indication of low income. The mean number of decayed (visual and cavitated), missing and filled teeth (vdmft, primary teeth 5-year-olds; VDMFT, permanent teeth 8-, 12- and 15-year-olds) among child and adolescent dependents of medical card holders in the Republic of Ireland as a whole was 1.9 in full-fluoridated areas. For the less deprived, dependents of non-medical card holders the vdmft/VDMFT was 1.1 in full-fluoridated areas. In non-fluoridated areas, the vdmft/VDMFT for child and adolescent dependents of medical card holders was 2.6 and for dependents of non-medical card holders in non-fluoridated areas, it was 2.1. Child and adolescent

dependents of medical card holders in full-fluoridated areas have a vdmft/VDMFT of 1.9 versus 2.6 in non-fluoridated areas.

- The preliminary results of the National Survey of Children's Oral Health 2002 (Whelton et al 2004) were published in 2004. The decay experience (DMFT) among 12-year-olds in the fluoridated Republic of Ireland (RoI) was 1.1 compared to 1.3 in non-fluoridated communities in the Republic and 1.5 in the non-fluoridated communities of Northern Ireland (NI). For 15-year-olds, the DMFT was 2.1 in the fluoridated communities of RoI, 3.2 in the non-fluoridated communities of the RoI and 3.6 in the non-fluoridated communities of NI. 23% of 8-year-olds and 39% of 15-year-olds have enamel fluorosis in the RoI.

- Fluoride levels in Irish public water supplies are very closely monitored on daily, monthly and quarterly examinations. A sensitive method for monitoring the total amount of fluoride ingested or absorbed is to monitor the levels of enamel fluorosis. The levels of enamel fluorosis in children and adolescents in Ireland have been assiduously monitored since the early 1980's (O'Mullane et al 1986, Whelton et al 1998, 2004). Using Dean's index, these studies have shown a slight increase in the prevalence of the questionable, very mild and mild grades of fluorosis. The risk factors for enamel fluorosis have been identified and strategies recommended for reducing the prevalence of enamel fluorosis in the Republic of Ireland (Department of Health 2002, www.fluoridationforum.ie).

- Acute fluoride toxicity occurring from the ingestion of optimally fluoridated water is impossible (Whitford 1996). The amount of fluoride necessary to cause death for a human adult (70 kg man) has been estimated to be 5-10 grams of sodium fluoride, ingested at one time (Hodge *et al*., 1965). In terms of fluoride ion, this corresponds to an ingested dose range of between 32-64 mgF/kg of body weight (Whitford 1996). This is more than 9,655-19,310 times as much fluoride as is consumed at one time in a single 8-ounce glass of optimally fluoridated water. Dietary fluoride intake by adults in optimally fluoridated (1 ppm) areas averages 1.4 to 3.4 mg/day, and in non-fluoridated areas averages 0.3 to 1.0 mg/day (Institute of Medicine, Food and Nutrition Board (1997).

- Heath *et al*., (2001) investigated the amounts of fluoride ion ingested following use of a variety of topical fluoride materials commercially available. Fluoride mouthrinses appeared to provide the highest salivary retention rates per dose of all forms of topical fluoride. Ingestion rates from concentrated gels were acceptable when effective evacuation methods were applied. None of the concentrated gels used resulted in elevations in total blood fluoride levels of concern in adults.
- Generally, the use of fluoride supplements on a community basis has ceased in Ireland. On an individual basis they are used as follows:

  High risk individuals

  Over 3 years of age

  Low fluoride area

  Chewed/ sucked slowly

  Using an appropriate dosing schedule

- The U.S. Food and Drug Administration has established "market baskets" which reflect the actual 14-day consumption of various food items by an average individual in different age groups, from six-month-old children to adults. In a nationwide study of market baskets from areas with varying levels of fluoride in water supplies, it was determined that little or no change in food fluoride content has occurred as a result of the fluoridation of U.S. water supplies (Pendrys *et al*., 1990, Olsen 1986).

- The statement in the '*50 Reasons*' document that the "*optimal fluoridation level is still 1 part per million, the same level deemed optimal in 1945*" is incorrect.
- Hong-Kong reduced its water fluoride levels to 0.5ppm in the mid 1990s (Burt 1999). In Canada the optimum level of fluoride in the water supplies was lowered from 1.0 - 1.2 mg/L to 0.8 - 1.0 mg/L (http://www.hc-sc.gc.ca./waterquality).
- The Forum on Fluoridation in Ireland (Department of Health and Children 2002) have advised that, in light of changed circumstances in Ireland and the best available scientific evidence, the Fluoridation of Water Supplies Regulations in Ireland should be amended to redefine the optimal level of fluoride in drinking water from the present level (0.8 to 1ppm) to between 0.6 and 0.8 ppm, with a target value of 0.7 ppm.

- The question of the possible impact of public water fluoridation on the risk of bone fractures has been addressed in the "Systematic Review of Public Water Fluoridation" (McDonagh *et al*., 2000). Using a qualitative method of analysis (*i.e*. visually examining forest plots), McDonagh *et al*., (2000) found no clear association of hip fracture with water fluoridation. The evidence on other fractures follows a similar trend. Overall, the findings of studies of bone fracture effects showed small variations around the 'no effect' mark.

- The monitoring of drinking water in Ireland, general legislation concerning fluoride, fluoride and the aquatic environment, the manufacture of hydrofluorosilicic acid (HSFA), quality control of HFSA, heavy metals concentrations in HFSA, and the treatment of drinking water and technical guidelines are dealt with in detail in Chapters 9 and 10 and Appendices 9, 10, 11, 12, 13, 14 and 15 of the Report of the Forum on Fluoridation (Department of Health and Children 2002) (www.fluoridationforum.ie).
- The chemical used to fluoridate public water supplies in the Republic of Ireland is hydrofluorosilicic acid. This product must meet the specification for chemicals used for the treatment of water intended for human consumption by the European Committee for Standardisation, CEN (1998). The product used in Ireland is produced as a primary product specifically for the fluoridation of water supplies in Ireland and in Spain. Hydrofluorosilicic acid is manufactured from compounds and minerals containing both fluoride and silica (e.g. fluorite, apatite) and an acid (usually sulphuric acid). The process of producing hydrofluorosilicic acid is a "wet chemical" process involving the reaction of sulphuric acid with rock compounds. The resulting gases are passed through a water medium until the concentration reaches 25 – 30%, which is then filtered.
- Because of the nature of the raw materials it is recognised in the CEN specification that limits should apply for impurities and any toxic substances present in the final product. For the purpose of the present specification, "toxic substances'' are those defined in the EU Directive 80/778/ EEC of 15th of July 1980. They include such substances as Antimony, Arsenic, Cadmium, Chromium, Lead, Mercury, Nickel and Selenium. Furthermore, the recently adopted water

Framework Directive 2000/60 /EC and the Water Quality (Dangerous Substances) Regulations, 2001 provide for stringent regulation of all these substances (Department of the Environment and Local Government (2000, 2001). The standards are consistent with the recommendations of SCTEE, (EU Advisory Scientific Committee on Toxicity, Ecotoxicity and the Environment). The quality of drinking water in the EU is subject to very stringent regulation and monitoring.

- The Forum on Fluoridation in Ireland (www.fluoridationforum.ie 2002) have investigated the metals content of a small number of samples of the raw fluoridation additive, HFSA. Three random samples of HFSA as used in Ireland were analysed for a range of eight heavy metals. On the completion of the analyses a risk assessment was prepared. This assessment demonstrated that, at the concentrations of the respective metals which would result in drinking water after the additive had been diluted to the upper limit of 1 parts per million fluoride, the residual metals concentrations would be a tiny fraction of the guideline values recommended by the World Health Organisation. For example, the average test result in three samples of HFSA from Spain (data from Dublin regional public analyst) contained 1.1 mg/kg arsenic. After a dilution factor of 352,000 used in ensuring 1 ppm fluoride in water by volume, the concentration of arsenic in water due to HFS acid after fluoridation was 0.0000031. The W.H.O drinking water guideline for the metal is 0.01 mg/l. This means that an adult would need to consume 288,000 litres of water per week to exceed J.E.F.C.A. Safety Levels (PWT) (A). (J.E.C.F.A. FAO Joint Expert Committee on Food Additives) (Department of Health and Children 2002). This situation is unlikely to arise.
- The chemicals used for water fluoridation in Ireland are manufactured to exacting quality standards. Within the EU, drinking water, whether fluoridated or non-fluoridated, is subject to the same stringent regulatory framework for water quality. It must be emphasised that the Drinking Water Directives (as with other community legislation) are adopted only on the basis of meticulous consideration by the EU Commission and Council, by the European Parliament and by appropriate technical experts from the member states. Furthermore, in framing proposals to be scrutinised thus, the Commission is guided by an expert group – the Scientific Committee on Toxicity and Ecotoxicity and the Environment

(SCTEE) – and also takes into account the medical opinions of the World Health Organisation. The SCTEE committee is completely independent of water fluoridation programmes (www.fluoridationforum.ie).

- Council Directive 98/83/EC (European Committee for Standardization 1998) is based on the quality of water intended for human consumption. This new Directive was drawn up in order to adapt the previous Directive of 1980 to scientific and technological progress (www.fluoridationforum.ie). The main thrust of the Commission Directive includes reviewing parametric values, and where necessary strengthening them in accordance with the latest available scientific knowledge (WHO guidelines, Scientific Committee on Toxicology and Ecotoxicology) (http://www.lenntech.com/drinking-water-standards.htm). The 1980 EU Directive specifies the Community Limit for fluoride in drinking water as 1.5 mg/l. The 1998 EU Regulations maintained the same limit and this is not without significance. In Ireland the 1988 Regulations specified a limit of 1mg/l F, in line with the upper limit in the National Fluoridation Act. The stricter standard of 1mg/l F is also specified in the 2000 Drinking Water Regulations (European Communities Regulations 2000). However, the latter contains the quality comment: 'the parametric value is 1 mg/l for fluoridated supplies. In the case of supplies with naturally occurring fluoride the parametric value is 1.5 mg/l F.' This a practical recognition of the fact that in some areas the natural levels of fluoride must be accepted up to the limit in the Directive. (Department of Health and Children 2002,www.fluoridationforum.ie).

- Proponents of water fluoridation recognise the importance of continuing scientific research. For example, the National Institute of Dental and Craniofacial Research (NIDCR) hosted a research workshop to identify needs for international collaborative research on fluoride (Clarkson *et al*., 2000). The workshop was co-sponsored with 10 partners including the Centre for Disease Control and Prevention (CDC) and the International Association for Dental Research (IADR) and was attended by approximately 80 experts in fluoride research including government, industry and academia. Based on findings presented by the speakers and discussed extensively at the workshop, the participants agreed an international research agenda on fluorides.

- There is no universal and widely accepted definition of the precautionary principle. Sandin (1999), for example, has reported 19 different definitions of the principle. One legal analysis has further identified 14 different formulations of the principle in treaties and non-treaty declarations (Vanderzwagg 1999 cited in Foster *et al*., 2000).
- In an attempt to clarify the meaning and applicability of the precautionary principle, the European Commission (EC 2000) issued a guidance document in February 2000. The Commission argued that measures based on the precautionary principle should comply with the basic principles for all other legislation and should incorporate the basic principles of risk management. Measures taken should be:
  1) Proportional to the chosen level of protection. Measures based on the precautionary principle must not be disproportionate to the desired level of protection and must not aim at zero risk.
  2) Non-discriminatory in their application
  3) Consistent with measures already adopted in similar circumstances or using similar approaches
  4) Based on the examination of the potential benefits and costs of action or lack of action
  5) Subject to review in the light of new scientific data
  6) Indicate responsibility for producing the scientific evidence necessary for a more comprehensive risk assessment.
- Whilst the Commission has provided some clarification in affirming that the precautionary principle must be seen as part of risk management rather than as an overarching principle and that application of the principle requires consideration of both the costs and benefits of action or lack of action, a number of problems remain. Some non-governmental and environmental proponents of the precautionary principle have strongly opposed both of these aspects of the EC interpretation of the principle, once again highlighting the lack of consensus on the meaning of the principle (see Lyons *et al*., 2000). Moreover the Communication speaks in general terms about ‘factors’ that should be considered leaving broad ambiguity on the precise meaning and requirements of the

precautionary principle (Marchant 2001). The Commission further stressed that their Communication was not intended to be the ‘final word’ on the precautionary principle, rather it was intended to open up the debate and provide the basis for discussions in the Council and European Parliament.

- In order to be of any use to policy makers the precautionary principle, and its applications, must be precise and detailed within a well-defined framework. Unless and until the principle has been clarified, it remains unworkable and fails to provide practical decision-making criteria for policy-makers.

The effectiveness of water fluoridation – statements 2, 3, 4, 5, 6, 35, 38, 39

The following points should be noted in relation to some of the assertions made in the statements listed above:

- Mc Neil (1957) and McClure (1970) have noted that the initial decision made by the US Public Health Service to endorse fluoridation (alluded to in the '*50 Reasons*' document) was influenced by several factors, including:
    a. The epidemiological studies carried out by Dean in the 1930s and 1940s and, in particular, Dean's 21 cities study published in 1942. This study examined the relationship between the caries experience of 7,257 12- to 14-year old children from 21 cities in four states in the US and the naturally occurring fluoride content of the water supply.
    b. Studies on the general health of populations residing in naturally fluoridated regions carried out by the USPHS
    c. The first Grand Rapids report of 1949.
- The issue of the effectiveness of water fluoridation in Ireland has been addressed in the report of the Forum on Water Fluoridation published in September 2002 (www.fluoridationforum.ie, Department of Health 2002) to which the reader is referred.
- More recently the results of the National Surveys of Children's Dental Health in both the Republic of Ireland and Northern Ireland have been published (Whelton *et al*., 2004).
- The data from the WHO Oral Health Country/Area Profile Programme (WHO) (cited in the '*50 Reasons*' document) should be interpreted cautiously. For many countries the caries levels quoted are based on local studies (reports of studies of national random samples not always being available). Countries being compared did not use the same research protocol, hence examiners in different countries were not governed by the same agreed clinical criteria. In comparing the oral health status of different populations in different countries, variations in the diagnostic methods used during the course of oral health surveys will obviously affect the results. Confounding factors also have to be considered when interpreting studies on dental caries and include age, gender, social class, ethnicity, country, tooth type (primary or permanent), use of

fluoride, method of measurement of caries (clinical exam, radiographs, or both), and training and calibration of examiners (McDonagh *et al*., 2000). Such confounders have not been acknowledged in the '*50 Reasons*' document. Furthermore the only 'explanatory' variable mentioned in the data provided is the fluoridation status of each country. Such an analysis is superficial and inadequate as inter-country comparisons of trends in oral health cannot be made on the basis of water fluoridation status alone, devoid of consideration of other pertinent contributory factors. The superficial comparisons that have been made between countries on the basis of mean DMFT at age 12 are unwarranted as they fail to acknowledge the diverse factors mentioned above which may have influenced trends in dental caries.

- The studies by Seppa *et al*., (2000a & b) in Finland and Kunzel *et al*., (2000) in Germany are two of the studies cited in the '*50 Reasons*' document as evidence that 'dental decay has not increased but has actually decreased' with the cessation of water fluoridation. However, the details of these studies, in particular their external validity, are neither presented nor discussed. As single studies are specific to time, sample, and context it follows that the results of a particular study may not be applicable to other populations, settings, treatment variables and measurement variables.
- The study by Seppa *et al*., (2000a & b), examined caries trends between 1992 - 1998 in two 'low fluoride' Finnish towns (Kupio and Jyvaskyla). Kupio, a town with 83,000 inhabitants, had been fluoridated (1.0mg/l) since 1959. Water fluoridation ceased in Kuopio in 1992. Jyvaskyla had historically been used as a reference town for Kupio in dental caries surveys. The results of observations made in 1998 coupled with earlier findings in 1995 suggested that, following the discontinuation of water fluoridation in Kupio, caries did not increase amongst 12 year olds. In 12 year olds there was a decrease in the percentage of subjects with no carious legions (caries free) but the mean DMFS value did not differ consistently from those in Jyvaskyla. It could be speculated that an increased use of other preventive measures in Kupio after 1992 compensated for the cessation of water fluoridation. However, Seppa *et al*., note that the number of fluoride and sealant applications actually decreased markedly in Kupio from 1993 to 1998, probably due to a policy

change towards targeted prevention on the basis of individual needs. (Seppa *et al*., 2000a & b).

- For some time local surveys had suggested that the effect of water fluoridation on caries was decreasing in Kupio (Seppa *et al*., 2000a & b). In 1973, for example, 13-15 year olds living in Kupio had 40% lower average DMFS scores than those living in Jyvaskyla, but in a similar survey 9 years later, no difference could be found. The small percentage of the Finnish population (0.02%) covered by the Kuopio fluoridation scheme would also have rendered negligible the diffusion effect of water fluoridation. Seppa *et al*., 2000 note that in interpreting their results consideration must be given to the fact that most of the processed food and drinks consumed in Kuopio come from low-fluoride areas (Seppa *et al.*, 2000a & b). Given the almost complete convergence of caries experience between fluoridated Kuopio and other non-fluoridated parts of Finland and the absence of the diffusion effect of water fluoridation, the finding that there was no indication of an increasing trend of caries following the cessation of water fluoridation was not unexpected.
- Caution should be exercised in the interpretation of this study and in assessing the degree to which its results can be generalised to other countries. A number of commentators have noted the inappropriateness of extrapolating data obtained from Nordic countries to other countries (Forss 1999, Seppa 2001). Forss (1999), for example, has noted that to focus on prevention programmes in Nordic countries is '*a most restricted vision*'. Furthermore she notes that '*it must therefore be emphasised that it would be dangerous to generalize the results of studies on the efficiency of fluoride programs. Data valid in one part of the world may not be applicable or relevant in other parts*.'
- The favourable socio-economic position of the Nordic countries should be noted. The UN Human Development Report (2004) uses as its main measure of social progress the Human Development Index (HDI) in comparing 162 states. (UN Human Development Report, 2004). Norway is at the top of the table with a HDI rank of 1. Sweden is ranked in 2nd position, Finland 13th, Denmark 17th and Ireland is ranked in 10th position. Despite Ireland's favourable overall ranking, the UN Report notes that proportionately more people live in poverty in Ireland than in any other industrialised nation outside

the US. In terms of poverty, the report ranks Ireland 16th out of 17 Western countries with 15.3% of the population living in poverty. Only the US with 15.8% in poverty is worse than Ireland. By comparison Sweden is at the top of the table with just 6.5% in poverty, Norway 7.1%, Denmark 9.1%, and Finland has 8.4% of the population living in poverty. In addition the report also shows that Ireland spends less on health than any other Western nation. Expenditure on health in Ireland is 6.5% of GDP, compared with Norway (8.1%), Sweden (8.8%), Denmark (8.5%) and Finland (7%).

- The dietary and oral hygiene habits of the respective populations also merit attention. Data from the National Health and Lifestyles Surveys in Ireland, (Friel et al, 1999, 2003), which give an overview of dietary practices internationally, are relevant in this context. Of all countries surveyed the percentage of students who reported eating sweets or chocolate every day were consistently the highest in Northern Ireland (73-81%), Scotland (71-78%) and Ireland (71-80%). The lowest percentages were consistently recorded in Denmark (19-31%), Sweden (14-31%) and Norway (13-30%). Of all countries surveyed the lowest percentages were recorded in Finland (12-24%). Similar trends were observed with respect to the consumption of soft drinks, again with Finland (6-22%) reporting the lowest consumption and Northern Ireland (69-75%), Ireland (51-75%) and Scotland (60-77%) reporting the highest consumption.
- Local studies of particular population groups in the UK and Ireland have also shown that sugars account for between 25% and 29% of pre-school children's daily food energy, with extrinsic sugars accounting for between 12% and 19%. In school children sugars account for between 19% and 25% of daily food energy, with extrinsic sugars accounting for between 14% and 17%. In adults sugars account for between 16% and 28% of daily food energy, with extrinsic sugars accounting for between about 8% and 10%. The UK Department of Health Committee on Medical Aspects of Food (COMA) recommends that sugars should provide no more than 10-11% of food energy. From the above figures it is clear that children are at particular risk (Pan European Task Force on Dental Health, 1998).

- In Finland, as in the whole of Scandinavia, all children and adolescents are entitled to comprehensive, preventively oriented dental care and nearly all attend. In addition the population is homogenous in terms of social structure and ethnic background (Seppa 2001). Seppa *et al*., also point out that the inclusion of non-lifetime residents of the community in their analyses may have diluted the effect of water fluoridation (Seppa *et al*., 2000a & b).
- It is facile to assume that because the cessation of water fluoridation in one small region in Finland did not lead to an observed increase in caries that a similar result would be observed in other countries with much higher risk factors for dental caries. In a more recent publication Seppa has directly addressed this issue and has observed that '*although discontinuation of water fluoridation had no effect on caries in Kupio, Finland, water fluoridation is still effective in countries with a lower level of basic prevention and a less homogenous social structure*' (Seppa 2001).
- Similar observations to the above can be made concerning the external validity of the Kunzel *et al*.,(2000) study (also cited in the '*50 Reasons*' document). In this study it was observed that caries levels continued to decline in 12 year olds in two towns in East Germany following the cessation of water fluoridation. In East Germany the caries decline observed by Kunzel *et al*., (2000) took place over a 10 year period from 1985 – 1995, an era which included the significant social transformation in East Germany following reunification in 1990. Kunzel *et al*., (2000) note that during this period there was an increased use of topical fluoride, fluoridated salt became available after 1992 and there were also changes in the supply of food and luxury items and changes in many other environmental factors. In addition there was a complete restructuring of the pattern of dental care, with the adoption of a preventive approach by dental practitioners. It is impossible to appraise the impact of the cessation of water fluoridation when such changes in the dental care system occurred. None of these factors have been mentioned or discussed by the author of the '*50 Reasons*' document.
- The '*50 Reasons*' document also fails to acknowledge the totality of research evidence on the effects of the cessation of water fluoridation. A number of 'cessation studies' were assessed as part of the systematic review of water

fluoridation carried out by the University of York (McDonagh *et al*, 2000). Of 22 analyses of stopping water fluoridation, 14 found the direction of association to be negative (that stopping water fluoridation led to an increase in caries). Eight analyses found the direction of association to be positive (that stopping water fluoridation had not led to an increase in caries in the previously fluoridated areas). In many of the studies there was poor adjustment for potential confounding variables and the overall evidence was of moderate quality and limited quantity. In addition some of the studies did not provide a measure of the significance of the association observed and some did not provide standard error data. Whilst cognisant of these limitations, the review concluded 'the best available evidence on stopping water fluoridation indicates that when fluoridation is discontinued, caries prevalence appears to increase in the area that had been fluoridated compared with the control area. Interpreting from this data the degree to which water fluoridation works to reduce caries is more difficult'.

- Maupome *et al*., (2001) (cited in the '*50 Reasons*' document) compared the prevalence and incidence of caries between fluoridation-ended and still-fluoridated communities in British Columbia, Canada from a baseline survey and after three years. Maupome *et al*., (2001) reported that the availability of multiple sources of fluoride other than water fluoridation made it more difficult to detect changes in the epidemiological profile of a population with generally low caries experience, living in an affluent setting and with widely accessible dental services. The prevalence of caries assessed in the children reportedly decreased over time in the fluoridation-ended community while remaining unchanged in the fluoridated community. The reported decline in caries was postulated to be multifactorial in the fluoridation-ended community. With amenable dental services came the intervention of the dental profession and perhaps improved customs of oral health care at home. Very low levels of decay were found at baseline and at final recording of the data. The examiners were also different for each study site and the possibility of variations in the interpretations of the different examiners and examiner bias cannot be ruled out. Maupome *et al*., (2001) concluded overall that the

benefits of water fluoridation should be weighed against other preventive methods such as fissure sealing and concluded that the primary preventive measure of water fluoridation "*preserves the integrity of dental tissues overall, is cheaper and is more effective than other preventive measures*".

- The article by De Liefde (1998) (cited in the '*50 Reasons*' document) criticises the use of the DMF (Decayed Missing Filled) Index in recording caries prevalence as it '*does not identify the full magnitude of the change in caries prevalence*'. The index used in this study is, for all practical purposes, an F index determined by the treatment decisions of many uncalibrated operators. In New Zealand, the D and M components of the index are essentially negligible as the score provided only gives information regarding the fillings each child has received, instead of caries prevalence. It is therefore difficult to relate the findings in this study to other countries as the data refers to the service provided by the School Dental Service (SDS) rather than the caries experience of the population. Water fluoridation was introduced to a number of large urban areas in New Zealand in the mid-1960's. By the late 1960's, 54% of the population was using fluoridated water (De Liedfe *et al*., 1998). After 1982, fluoride toothpaste had an increasing impact on caries prevalence. Between 1988 and 1995, caries prevalence in 12-year-old children had almost halved (Hunter *et al*., 1992).

- Yiamouyiannis (1990) was not involved in the design and conduct of the US National Institute of Dental Research (NIDR) survey quoted in the '*50 Reasons*' document. Following the NIDR study, Yiamouyiannis obtained a printout of the dental records and a list of the 84 areas used in this survey through the United States Freedom of Information Act. Using this data Yiamouyiannis calculated the number of decayed and filled deciduous teeth (dft) and the number of decayed, missing and filled permanent teeth (DMFT) for each record. However, the "halo effect" of water fluoridation was ignored. That is, non-fluoridated communities located adjacent to geographic regions with fluoridated communities are more likely to receive the diffused benefits from water fluoridation as the number of fluoridated communities increases.

This “halo effect” arises out of the consumption of products like bread, milk, bottled beverages, processed foods and others that are manufactured in a fluoridated area and consumed in other non-fluoridated districts and from movement of people in and out of fluoridated areas.

- It has been hypothesised that as the proportion of the total US population receiving optimally fluoridated water increased from 43% in the early 1970’s to 56% in the early 1980’s (CDC 1970, CDC 1985), the diffusion of the benefits of water fluoridation also increased as a result of the “halo effect”. Thus as the diffusion effect increased in the US, the apparent direct contribution of fluoridated water to reducing caries, which was measured by the difference in mean DMFS between Non Fluoridated and Fluoridated communities, was probably underestimated because non-fluoridated communities were not true negative control groups since they were benefiting form the ‘halo effect’ of water fluoridation from nearby communities. Such a misclassification of fluoridation exposure status would lead to an attenuation of its apparent effect on dental caries.
- Griffin *et al* (2001) recently analysed data from the NIDR survey to estimate the total contribution of water fluoridation to caries reduction by including the benefit from the diffusion of fluoride from fluoridated communities to surrounding non-fluoridated communities via the export of bottled beverages and processed foods (Griffin *et al*., 2001). They found that U.S children residing in non-fluoridated areas with low diffusion exposure (DE) in 1986-1987 experienced higher levels of dental caries than did children living in fluoridated communities or children living in non-fluoridated (NF) areas with high diffusion exposure. They concluded that a failure to account for the diffusion effect may result in an underestimation of the total benefit of water fluoridation, especially in high diffusion exposure regions.

- Kumar and Green (1998) (cited in the “50 Reasons” document) discuss the significant role that fluoride has played in improving the oral health of Americans and advise that practitioners should prescribe fluoride therapy based on an understanding of patients’ total exposure to fluoride given the

increased availability of fluoride containing products over the counter in the U.S.

- A graph in the article by Kumar and Green (1998) shows the mean DMFT among 7-14-year-old lifelong residents of Newburgh (fluoridated) and Kingston (non-fluoridated) over a fifty-year period. Both communities exhibited a decline in DMFT from 1945 with a levelling off in differences in DMFT between the two communities from 1986 onwards.
- Kumar and Green discuss the caries decline in both the fluoridated and non-fluoridated communities as being attributable to the increased availability of fluoride in the form of fluoride toothpastes and consumption of beverages and foods processed in fluoridated areas –the "halo effect" of water fluoridation. Kumar and Green (1998) also note that although the difference in caries levels between fluoridated and non-fluoridated communities is lower today than it was in the early 1950's, fluoridation continues to be an ideal programme for fluoride delivery for several reasons, including its cost effectiveness.

- A study conducted in Co. Kerry by Creedon and O'Mullane (2001) investigated the factors associated with high caries levels in 5-year-old children in the Kerry Community Care Area of the Southern Health Board in Ireland. The mean dmfs of the 263 lifetime residents of fluoridated communities was 2.4 compared with 6.2 recorded for the 231 lifetime residents of non-fluoridated communities. Using multivariate logistic regression analysis the variables most significantly associated with the presence of caries were water fluoridation status, whether or not the child took the baby feeding bottle to bed, the age at which tooth brushing began and the number of sweet snacks and drinks taken in a day. While there was a wide variation in caries levels between nine geographic areas in Co. Kerry the only significant geographic variation found was between fluoridated and non-fluoridated areas. Some 61% of children in fluoridated areas were caries-free compared to 39% in non-fluoridated areas (see table 1 below). The authors concluded that the prevalence of caries amongst 5-year-old children in Co. Kerry was highest in those residing in non-fluoridated communities, in those who took a baby feeding bottle to bed, in those who did not commence tooth brushing until after two years of age and in those who consumed sweet snacks or sweets drinks between meals three or more times per day.

TABLE 1

Mean dmft, mean dmfs and percentage caries-free of 5-year-old children by fluoridation status (standard deviation in parenthesis)

Fluoridation Status	n	Mean dmft (SD)	Mean dmfs (SD)	% Caries Free	% dmft >/4
Fluoride	263	1.2(2.2)	2.4(5.0)	61	14
Non-Fluoride	231	2.9(3.9)	6.2(9.9)	39	31

Water fluoridation and ethical issues – statements 29 and 30

- The reader is referred to Chapter 13 in the final report of the Forum on Fluoridation in Ireland (Department of Health and Children 2002) where the ethical and legal dimensions of water fluoridation are discussed in detail.
- To consider the ethics of water fluoridation is to consider the balance between its benefits and risks. The issue of proportionality is at the heart of this question and is clearly dependent on the precise benefits that must be weighed against the precise debits which the process involves. Dr.Richard Hull, an expert in the area of ethics, was consulted by a sub-group in the Forum on Fluoridation (Department of Health and Children 2002) and the following paragraph is drawn from his deliberations:

> "It is also worth remembering that government, by its nature, is paternalistic. Health in general is seen as an area where paternalistic State intervention is justifiable, and in terms of oral health, the poor dietary habits of the Irish people could be seen as a justification for taking a paternalistic approach. The degree of infringement of bodily integrity by water fluoridation is relatively minor when compared to education, for example. This intervention could be seen to breach bodily and mental integrity in a much more serious manner. The idea of State intervention is with the aim of protecting health and perhaps life (dental decay may itself be responsible for a small number of deaths each year from anaesthesia), is far more compelling than is the idea of intervention with the aim of affecting more value-laden life-style choices. This points to an alternative approach – to place a very strong emphasis on the role of education, informing citizens on the importance of oral hygiene and dietary advice. However, it is all very well to emphasise the value of autonomy, but the desire to effectively safe-guard the health and safety of children (who are not yet autonomous) could be said to constitute a strong emphasis".

Fluorosis and other potential negative effects of water fluoridation – statements 7, 8, 9, 10, 19, 22, 23, 24, 25, 26, 28, 29, 30, 31, 32, 44, 45.

The following points should be noted in relation to some of the assertions made in the statements listed above:

- When the relationship between fluoride intake and decreased caries prevalence was first recognised it was assumed that the method of action was due to the incorporation of fluoride into the enamel during enamel formation: that in chemical terms it involved substitution of the hydroxyl ion with the fluoride ion in hydroxyapatite leading to the formation of fluorapatite (McClure, Likins 1951). Fluorapatite was deemed to be less soluble in acid and this reduction in acid solubility of enamel was attributed to larger apatite crystals, better crystallinity and the buffering action of fluoride released from enamel crystals during the early stages of acid attack. It was believed that in order for fluorapatite to be formed it was necessary for the fluoride ion to be present during amelogenesis and hence systemic fluoride was essential. However, later work using sophisticated enamel biopsy and fluoride analysis techniques revealed no simple relationship between enamel fluoride levels and caries experience. Further epidemiological evidence supported this view, in that caries reductions were found in teeth already erupted at the start of fluoridation programmes (Collins and O'Mullane 1970, Ast *et al.*, 1950). At about this time, understanding of how a carious lesion develops also began to change. Initially it was believed that the carious lesion developed as a slow, persistent ongoing process; that it started as a microscopic change leading to a white spot lesion, which inevitably progressed to a cavity. It is now known that this is not the case and that white spot lesions and other early carious lesions can remineralise (Holmen *et al*, 1987). A white spot lesion therefore, can behave in three different ways; it can progress to cavity, remain static, or reverse (remineralise). The carious process is a delicate balance between demineralisation and remineralisation and in the mouth there is a constant ‘see-saw’ between these two phenomena depending on the cariogenic challenge present. The presence of fluoride has been shown to promote the process of remineralisation and the ‘healed’ lesion has been found to be more resistant to caries attack than a similar unchallenged site.

- There is also evidence to show that low levels of fluoride in plaque affect plaque metabolism (including glycolysis) inhibiting the process in which cariogenic bacteria metabolise carbohydrates to produce acid. The persistence of fluoride levels in saliva, of the order of 0.04 – 0.2 ppm, appears to be critical for remineralisation. This origin of this salivary fluoride is from ingested fluoride; thus the "topical" effect is in part mediated through the "systemic" effect of ingestion and subsequent expression of fluoride in saliva.

- Whilst there is no doubt that frequent topical applications of fluoride will bring about a large reduction in dental caries for those who are willing to buy and use fluoride toothpaste or willing to regularly attend a dentist or hygienist for application of gels, compliance with these procedures may be problematic. This may be particularly true in the case of less well-off sections of the population who are most at risk of developing dental caries.
- The percentage of population in Ireland who attend regularly for dental care is low, again particularly amongst the less well-off sections of the population, hence fluoride gels and varnishes are not appropriate alternatives to water fluoridation (O'Mullane *et al*, 1999).

- Enamel opacities including fluorosis can be caused by local or systemic events. Local causes include dental trauma and local infections. A relatively common local cause of a marking or opacity on permanent teeth is trauma to the primary predecessor. Systemic events include infections (measles and generalised fevers), metabolic errors (such as phenylketonuria), neonatal disturbances (premature birth, hypocalcaemia and haemolytic anaemia), genetic conditions (amelogenesis imperfecta), endocrinopathies (hypothyroidism and diabetes mellitus) antibiotic consumption (classically, though now rarely, with tetracyclines), nutritional deficiencies (including all nutrients and general calorific intake) and asthma (Rugg-Gunn *et al*., 1999). From a clinical point of view, it is not always possible to distinguish between opacities caused by excessive intake of fluoride and opacities resulting from other reasons.
- The authors of the York Review (McDonagh *et al*., 2000) reported that the prevalence of fluorosis at a water fluoride level of 1ppm was 48% and for enamel

fluorosis of aesthetic concern it was 12.5%. The Review included 88 studies of dental fluorosis. They were largely cross sectional designs, with only four controlled before-after designs. All of the studies were of evidence level C (lowest quality), except one level B study. The authors also report that there was considerable heterogeneity between results of individual studies. Observer bias may be of particular importance in studies that assess fluorosis. Because assessment is subjective, unless the observer is blinded to the exposure status of the person being evaluated, bias can be introduced. Efforts to reduce potential observer bias were rarely undertaken in the included studies. The prevalence of fluorosis may be overestimated by the indices used in the included studies because enamel opacities not caused by fluoride may be included. The degree to which the estimated 48% prevalence of fluorosis at a water fluoride concentration of 1 ppm overestimates the true prevalence is unknown.

- Using data from the National Survey of US Schoolchildren, Heller *et al*., (1994) reported that children who consumed water with <0.3 ppm F and 0.7 – 1.2 ppm F have a fluorosis prevalence of 13.5% and 29.9% respectively. In a study conducted by Williams and Zwemer (1990), Tooth Surface Index of Fluorosis (TSIF) scores of 4-7 were present in 1.4% of the "county" children examined (water fluoridated at a level of 0.2-0.9 ppm F) and in 14% of the "city" children (water fluoridated at a level of 0.9-1,2 ppm F) in Augusta or adjoining Richmond County.
- The results of the National Survey of Children's Dental Health 2002 (Whelton *et al.*, 2004) provide a clear analysis of the prevalence of fluorosis in three age groups (8-, 12- and 15-year-olds) in Ireland. In all three age groups 80% or over of the children were in the normal or questionable categories. In fully fluoridated areas a score of normal was given to 76% of 8 year-olds, 71% of 12 year-olds and 61% of 15 year-olds. The authors reported 4% of 8 year-olds, 5% of 12 year-olds and 5% of 15-year-olds as having mild fluorosis. These data indicate that there has been a slight increase in the level of questionable, very mild and mild fluorosis in the past 20 years in Ireland. Strategies and recommendations to halt this trend are presented in detail in the Final Report in the Forum on Water Fluoridation in Ireland (www.fluoridationforum.ie). Work is in progress to determine the aesthetic impact of the recent increased levels of fluorosis in Ireland.

- Only three thyroid studies met the inclusion criteria for the "Systematic Review of Public Water Fluoridation" (McDonagh *et al*., 2000). No clear evidence of potential adverse effects was found. The subsequent Medical Research Council Report (2002) commissioned as a result of the York Systematic Review on Water Fluoridation by the U.K Department of Health discussed the two studies listed in the York Review in which goitre (hypothyroidism) was the outcome of interest. Two of these studies found no association with water fluoride level (Gedalia *et al*., 1963, Jooste *et al*., 1999). The third (Lin *et al*., 1991) found a significant positive association between combined high fluoride/low iodine levels and goitre. However, because this study looked at combined fluoride/iodine uptakes, and has not been published in a peer-reviewed journal, the findings should be "treated cautiously". The MRC report concluded that further work on the effect of water fluoridation on thyroid function is of low priority.
- Infant feeding practices including formula feeding and breast-feeding are discussed in Chapter 12 of the report of the Forum on Fluoridation (www.fluoridationforum.ie).
- The Forum on Fluoridation recommends that infant formula should continue to be reconstituted with boiled tap water in accordance with manufacturers' instructions or alternatively ready-to-feed formula may be used (www.fluoridationforum.ie).
- The use of bottled water to reconstitute infant formula is not recommended. Many of the brands of bottled water available in Ireland are not suitable for such use, due to the presence of salt and other substances, which may be harmful to infants and young children (www.fluoridationforum.ie).
- The Food Safety Authority of Ireland has investigated the overall contribution to the development of fluorosis attributable to infant formula. The subset of the infant population likely to receive the highest fluoride intake from infant formula reconstituted with fluoridated tap water is represented by those infants below the age of four months for whom infant formula is the sole food source and consumption is high relative to body weight. The Scientific Committee of the Food Safety Authority of Ireland (Department of Health and Children, 2002 www.fluoridationforum.ie) concluded that the maximum average intake of fluoride from infant formula reconstituted with fluoridated tap water over the first

four months of life was estimated to be in the range 0.105mg/kg b.w/day to 0.172mg/kg b.w/day, depending on body weight. This intake was calculated for infants residing in areas served by the 95% of water supplies that achieved an average yearly water fluoride level of below 1.03mg/l. The statutory upper limit in Ireland is 1mg/l. The remaining 5% of supplies exceeded the statutory limit on a consistent basis, however the highest average fluoride concentration calculated in any of these non-compliant supplies was 1.35mg/l.

- The Forum on Fluoridation contains the following conclusions about the possible risks to young infants from the consumption of infant formula reconstituted with fluoridated tap water at current levels of fluoride addition in Ireland:
    - There is no significant evidence that any adverse effect other than dental fluorosis is relevant to the assessment of the risk of fluoride intake at levels within the range estimated for young infants under 4 months of age.
    - The risk of moderate dental fluorosis of the primary or permanent dentition is very low in exclusively formula-fed infants aged 0-4 months residing in areas served by the 95% of supplies in which the level of fluoride in water does not exceed the statutory limit. For the remaining infants residing in areas served by the 5% of supplies that consistently exceed the statutory limit, the risk is also considered to be very low, but the safety margin is reduced.
- In a study by Harding *et al.*, (in press) in which 294 5-year-old children were examined for fluorosis in their primary teeth, 62.5% of mothers resident in a fluoridated community stated that they did not breast feed. The remaining 37.5% claimed to have breast-fed and formulae fed for various periods over the first year of life. The prevalence of dental fluorosis was similar in these two groups.

- In Ireland, Drinking Water Directives are adopted only on the basis of meticulous consideration by the EU Commission and Council, by the European Parliament and by appropriate technical experts from the member states. The Commission is also guided by an expert group – the Scientific Committee on Toxicity and the Environment – and takes into account the current medical opinions of the World Health Organisation. In the 1980 Directive the Community limit for fluoride in

drinking water was specified as 1.5mg/l. The 1998 Directive specified the same limit, after due consideration by the EU officials. However, in Ireland, the 1988 Regulations specified a limit of 1mg/l F, in line with the upper limit in the national Fluoridation Act. Fluoride is currently added to the water supplies at a level of 0.8-1ppm. An optimum level of 0.7ppm was recommended by the Forum on Fluoridation in 2002 (Department of Health and Children, www.fluoridationforum.ie) and arrangements to implement these new guidelines are now underway.

- McDonagh *et al*., (2000) examined possible adverse effects associated with water fluoridation including IQ. The authors concluded that the quality of these studies was low (evidence level C). The studies on IQ did not have a prospective follow-up and did not incorporate any form of blinding. In the case of the Down syndrome studies, for example, all six studies used designs that measured population rather than individual exposures to fluoridated water and, because of this were particularly susceptible to confounding. If the populations being studied differed in respect to other factors that are associated with the outcome under investigation, then the outcome may differ between these populations leading to an apparent association with water fluoride level (Treasure *et al*., 2002).
- The authors of the MRC report (2002) considered the two Chinese studies (Lu *et al*, 2000; Zhao *et al*., 1996) which have found a positive association between high levels of fluoride in drinking water and reduced children's intelligence IQ. However, the authors of the MRC report (2002) note that confounding factors were dismissed and their possible influence on the results of the study were not adequately explained. At lower fluoride concentrations (*e.g*. 0.91ppm) which would be more comparable to the levels in fluoridated water in the UK and Ireland, a reduction in children's IQ was not observed. The MRC concluded that further investigation of the impact of fluoride on intelligence (IQ) is considered to be of low priority.
- In 1999, the Ministry of Health in Ontario, Canada undertook a review of the literature published between 1994 and 1999 in relation to fluoride and health (Locker 1999). The author concluded that the studies from China claiming that children exposed to high levels of fluoride had lower IQs than children exposed to

low levels were deeply flawed and provided no credible evidence that fluoride obtained from water or industrial pollution affects the intellectual development of children.

- Endemic skeletal fluorosis in temperate climates is confined to individuals exposed continuously over many years to very high levels of fluoride. Not only are fluoride exposures very high in these climates but also nutrition is inadequate and high temperatures lead to greater consumption of water than in the UK and Ireland. These cases may be associated with industrial exposures or with unusually high fluoride levels in drinking water. Skeletal deformities may be associated with or accentuated by malnutrition and possible other conditions found in areas of long-term social and nutritional deprivation (WHO 1994).
- Studies in India (Jolly 1976) found an average daily fluoride intake of more than 9 milligrams in patients there with endemic fluorosis.
- Dietary fluoride intake by adults in optimally fluoridated (1 ppm) areas averages 1.4 to 3.4 mg/day, and in non-fluoridated areas averages 0.3 to 1.0 mg/day (Institute of Medicine, Food and Nutrition Board 1998).
- Crippling skeletal fluorosis has never been a clinically important problem in the United States, UK or Ireland even though for many generations there were many communities whose drinking water contained fluoride at levels which could have produced this disorder in the US (Whitford 1996). There was only one non-industrial case ever reported in the UK (Webb-Peploe and Bradley, 1966).
- In temperature climates in the developed countries, crippling skeletal fluorosis is not associated with water fluoridated to a level of 1ppm. Kaminsky *et al*., (1990) reported no evidence of skeletal fluorosis among the general US population exposed to drinking water fluoride concentrations lower than 4mg/l in their summary of the benefits and risks of fluoride ingestion.
- The York Review included 29 studies on the relation of fluoride in water to bone health (McDonagh et al 2000). The validity of the studies were generally assessed as low and all but one were classed at the lowest of the three levels of evidence that had been specified at the start of the review. A forest plot of all the bone studies was produced showing the measures of effect and the 95% confidence limits for all studies that provided sufficient data to allow calculation. The

majority of the measures of effect and their confidence intervals were distributed evenly around the line of no effect (1.0) suggesting no association with water fluoridation. A meta-regression of bone fracture studies also found no association with water fluoridation. The York review team concluded that 'the best available evidence on the association of water fluoridation and bone fractures (27 of 29 evidence level c) show no association' (McDonagh *et al*., 2000).

- In their systematic review of water fluoridation McDonagh *et al*., (2000), included seven studies of osteosarcoma, presenting twelve analyses. Seven of these found the direction of association to be positive (fewer cancers), three found a negative direction of association (more cancers) and two found no relationship (McDonagh *et al*., 2000). The study by Cohn (1992) (cited in the '*50 Reasons*' document), found a statistically significant association between fluoridation and increased prevalence of osteosarcoma in males. However, this study had the lowest validity score, 2.5 out of 8, of those included in the systematic review process. The review team concluded that, from the available research evidence, no association was detected between water fluoridation and mortality from any cancer, or from bone or thyroid cancers specifically (McDonagh *et al*., 2000).

- Challacombe (1996) has addressed the question of the potential effect of fluoridation on immune function. According to Challacombe (1996) there have been no confirmed cases of allergy to fluoride or of positive skin testing in humans or in animals and that there is no increased reporting of allergies of any type with increasing fluoride use. There are also no reports of reactions of an allergic nature to fluoride in other substances such as tea, tinned fish, salt water, where concentrations can be much higher than in water fluoridation programmes.
- Challacombe (1996) has concluded that there seems to be little doubt that ingestion of fluoride in high concentrations may result in perturbation of specific immune responses and can have various inhibitory effects on white cell function. However, no studies have reported such effects at physiological doses and most studies report effects at concentrations approximately 1000 times greater than

would be found due to water fluoridation. Thus there is no evidence of any deleterious effect on specific immunity following fluoridation.

- The Medical Research Council (2002) have concluded that further research on the possible effects of fluoride on immunological function and thyroid is "*considered to be of low priority*."

- Urbansky and Schock (2000) examined the chemodynamics of hydrofluorosilicic acid in water and demonstrated that there is complete dissociation of hydrofluorosilicic acid in drinking water. Whilst it is true that both fluoride ions and silicates form complexes with lead, the fluoride ions are more likely to complex with the more abundant ions (aluminium, iron, calcium, carbonate, sulphate) while lead will complex with the chloride, carbonate, bicarbonate and sulphate ions which are present in larger quantities than fluoride ions. Free lead 2+ ion is a very minor fraction of the soluble lead in most drinking water systems because lead forms complexes with higher concentrations than those associated with fluoridation so, the use of silicofluorides would have no significant effect on silica levels or lead hydroxide.
- The issue of possible increased blood lead levels and the use of hexafluorosilicic acid to fluoridate water have received much attention from several scientists in recent years. The work of Masters and Coplan forms part of the body of scientific literature on this subject (1999). In order to understand the significance or otherwise of the research by Masters and Coplan a full understanding of the wider role of lead in the environment is required. A short resume of lead and drinking water summarised from WHO Guidelines on Drinking Water for Human consumption follows (1996):
- In tap water, lead may be present as a result of dissolution from natural sources, but it is mainly as a result of domestic plumbing, from pipes, solder, fittings or service connections to homes, which may all contain lead. Human exposure can occur through inhalation of lead dust, drinking lead–contaminated water or consumption of lead–contaminated food. Lead may also be absorbed through the skin. Cigarette smoke also contains lead. More than 80% of the total daily intake of lead is from ingestion of food, dust and dirt. The average daily intake of lead from drinking water has been estimated as 3.8ug/ day for children and 10 ug/day

for adults (WHO 1996). This assumes an average concentration of lead in drinking water to be 5ug/litre.

- In young children a significant proportion of their total lead intake derives from the ingestion of soil, dirt and dust. Adults absorb approximately 10% of lead contained in food, but young children absorb 4 to 5 times as much. The gastrointestinal absorption of lead from ingested soil and dust has been estimated to be as high as 30% in young children. A provisional tolerable weekly intake of 25ug of lead per kilogram of body weight for infants and children has been established (intake of 3.5ug/kg per day). This is based on evidence that, in children, a lead intake of 3 – 4ug/ kg of body weight per day is cleared from the body, with no increase in blood lead levels or increased body burden of lead. For a 5kg infant with an average water consumption of 0.75 litres / day, the guideline value is 0.01mg/ litre. As this group is the most sensitive to the effects of lead, this value is protective for all other groups.
- A series of articles based on studies conducted by the authors, Masters and Coplan have attempted to show that certain approaches to fluoridating drinking water is linked to increased levels of lead (11) species in the blood. It has been suggested that certain adverse health or social conditions may be arising because of interactions between lead (11) species and inorganic fluoro – compounds, specifically, fluorosilicates and fluoride. Urbansky and Schock of the United States Environmental Protection Agency have investigated these assertions. They concluded that no credible evidence exists to show that water fluoridation has any quantifiable effects on the solubility, bioavailability, bioaccumulation, or reactivity of lead (0) or lead (11) species compounds (Urbansky and Schock 2000). They further state that the governing factors are the concentrations of a number of other species such as bicarbonate, hydroxide, or chloride whose effects far exceed those of fluoride or fluorosilicates under drinking water conditions. Urbansky and Schock (2000) were also of the view that statistical techniques used by Masters and Coplan were inappropriate and that many of the chemical assumptions were scientifically unjustified and contradicted by known chemistry data and principles.

References

Burt BA, Eklund SA (1999). Dentistry, dental practice, and the community. Philadelphia, Pennsylvania: WB Saunders Company, 204-20.

Buzalaf MA, Cury JA, Whitford GM (2001). Fluoride exposures and dental fluorosis: a literature review. V9, n.112, p.1-10.

Centres Disease Control Fluoridation Census (1985). Atlanta, Georgia: US Department of Health and Human Services, CDC. National Centre for Prevention Services, Division of Oral Health.

Centres for Disease Control (1970). Fluoridation Census 1969. Atlanta, Georgia: US Department of Health and Human Services, CDC. National Centre for prevention services, Division of Oral Health.

Challacombe SJ (1996). Does fluoridation harm immune function? Comm Dent Health, 13 (Suppl 2):69-71.

Chinoy NJ, Narayana MV (1994). In vitro fluoride toxicity in human spermatozoa. Fluoride, 27:4, 231-232.

Clarkson J, Hardwick K, Barmes D, Richardson L (2000). International Collaborative Research on Fluoride. J Dent Res 79(4):893-904.

Cohn, P (1992). A brief report on the association of drinking water fluoridation and the incidence of osteosarcoma among young males. Produced under an interagency agreement between the New Jersey Department of Environmental Protection and Energy and the New Jersey Department of Health. New Jersey Department of Health.

Collins C, O'Mullane DM (1970). Dental caries experience in Cork city school children aged 4-11 years after 4 ½ years of fluoridation. J Irish Dent Assoc. 16:130-134.

Commission of the European Communities (2000) Communication from the Commission on the precautionary principle. Brussels 02/02/2000. COM (2000) 1

Creedon MI and O'Mullane DM. (2001). Factors affecting caries levels amongst 5-year-old children in County Kerry, Ireland. Community Dental Health 18, 72-78.

De Liedfe B (1998). The decline of caries in New Zealand over the past 40 years. New Zealand Dental Journal 94: 109-113.

Department of Health and Children (2002). Forum on Fluoridation Ireland, www.fluoridationforum.ie.

DHHS (1991) Review of fluoride: Benefits and risks, Report of the Ad-Hoc Committee on Fluoride of the Committee to Co-ordinate Environmental Health and Related Programs. Department of Health and Human Services, USA.

Emsley J, Jones DJ, Miller JM, Overill RE, Waddilove RA. (1981). An unexpectedly strong hydrogen bond: Ab initio calculations and spectroscopic studies of amide-fluoride systems. J. Am. Chem. Soc. 103, 24-28.

European Committee for Standardisation. Chemicals used for treatment of water intended for human consumption – hexafluorosilicic acid. In Brussels; 1998.

European Communities (Drinking Water) Regulations S.I No.2000. In Dublin: Department of the Environment and Local Government; 2001. http://www.lenntech.com/drinking-water-standards.htm.

European Communities (Dangerious Substances). Regulations S.I. No. 12. In Dublin: Department of Environment and Local Government.

Forss H (1999). Efficiency of fluoride programmes in the light of reduced caries levels in young populations. Acta Odontol Scand., 57:348-351.

Foster HD (1993) Fluoride and its antagonists: implications for human health. Journal of Orthomolecular Medicine, 8, 149-153.

Freni SC (1994). Exposure to high fluoride concentrations in drinking water is associated with decreased birth rates. J Toxicology and Environmental Health, 42:109-121.

Friel S, MacGabhainn S, Kelleher C. The National Health and Lifestyle Surveys: (SLAN and HBSC): Centre for Health Promotion Studies , National University of Ireland, Galway; 2003.

Friel S, MacGabhainn S, Kelleher C. The National Health and Lifestyle Surveys: (SLAN and HBSC): Centre for Health Promotion Studies, National University of Ireland, Galway; 1999.

Gedalia I, Brand N (1963). The Relationship of fluoride and iodine in drinking water in the occurrence of goitre. Arch. Int. Pharmacodyn. 142, 312-315.

Griffin SO, Gooch BF, Lockwood SA, Tomar SL (2001). Quantifying the diffused benefit from water fluoridation in the United States. Community Dent Oral Epidemiol, 29:120-9.

Harding M, O'Mullane. Dental fluorosis in primary teeth of 5-year-old school children in Ireland. *In preparation.*

Heller KE, Stephen AE, Burt BA (1994). Dental caries and dental fluorosis at varying water fluoride concentrations. Journal of Public Health Dentistry 51(3);136-143.

Hodge HC, Smith FA (1965). Biological properties of inorganic fluorides. In: Fluorine chemistry. Simons HH, ed. New York: Academic Press; 1-42.

Holmen LA, Thylstrup A, Artun J (1987). Histological features observed during arrestment of active enamel carious lesions in vivo. Caries Res;21:546.

Hoover R. et al (1991 a). Fluoridation of drinking water and subsequent cancer incidence and mortality. In, review of fluoride: benefits and risks, report of the ad-hoc committee on fluoride of the committee on fluoride of the committee on fluoride of the committee in coordinate Environmental Health and Related Programmes. Department of Health and Human Services, USA, appendix E, E1-E51.

Hoover R et al (1991 b). In, Review of fluoride: benefits and risks, Appendix F. Time trends for bone and joint cancers and osteosarcomas in the surveillance epidemiology and end results (SEER) program, National Cancer Institute, Department of Health and Human Services, USA, Appendix F, F1-7.

Hunter PB, Kirk R, De Lidefe B (1992). The study of Oral Health Outcomes. The 1988 New Zealand Section of the WHO Second International Collaborative Study. Wellington: Department of Health.

Institute of Medicine, Food and Nutrition Board (1998). Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D and fluoride. Report of the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Washington, DC: National Academy Press.

Institute of Medicine (1997). Dietary reference intakes for calcium, phosphorous, magnesium, vitamin D and fluoride. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine, National Academy of Sciences, Washington DC: National Academy Press.

Jackson PJ, Harvey PW, Young WF (2002). Chemistry and bioavailability aspects of fluoride in drinking water. WRc-NSF Report July 2002.

Jackson RD, Kelly SA, Noblitt TW, Zhang W, Wilson ME, Dunipace AJ, Li Y, Katz BP, Brizendine EJ, Stookey GK (1997). Lack of effect of long-term fluoride ingestion on blood chemistry and frequency of sister chromatid exchange in human lymphocytes. Environ Mol Mutagen, 29(3):265-71.

Jolly SS (1976). Fluoride balance studies in endemic fluorosis. Fluoride 8, 138-147.

Jooste P, Weight M, Kriek J and Louw A (1999). Endemic goitre in the absence of iodine deficiency in school-children in the Northern Cape Province of South Africa. Eur J of Clinical Nutrition, 53, 8-12.

Kaminsky LS, Mahoney MC, Leach J, Melius J, Miller MJ (1990). Fluoride: benefits and risks of exposur. Critical Reviews IN oral Biology and Medicine; 1:261-281.

Kraus AS and Forbes WF (1992) Aluminum, fluoride and the prevemtion of Alzheimer's disease.

Kumar JV, Green EL, Wallace W, Carnahan T. (1989). Trends in dental fluorosis and dental caries prevalences in Newburgh and Kingston, NY. May: 79(5): 565-9.

Kunzel W, Fischer T, Lorenz R, Bruhmann S (2000). Decline of caries prevalence after the cessation of water fluoridation in the former East Germany. Community Dent Oral Epidemiol., 28(5):382-389.

Lepo JE, Snyder RA (2000). ECUA Fluoride Report: Impact of fluoridation on the municipal drinking water supply: Review of the Literature: The Centre for Environmental Diagnostics and Bioremediation, University of West Florida.

Lin F-F, Zhao H-X and Jian J-Y (1991). The relationship of a low iodine and high fluoride environment to subclinical cretinism in Xinjiang. Xinjiang Institute for endemic disease control and research, office of leading group for endemic disease control of Hetian prefectual committee of the Communist Party of China and county health and endemic prevention station, Yutian, Xinjiang.

Locker D (1999). Benefits and risks of water fluoridation. An update of the 1996 Ffederal-Provincial Sub-Committee Report. Toronto: Community Dental Health Services Research Unit, Faculty of Dentistry, University of Toronto.

Luke J. (2001). Fluoride Deposition in the Aged Human Pineal Gland. Caries Res. 35: 125-128.

Lu Y, Sun ZR, Wu LN, Wang X, Lu W, Liu SS (2000). Effect of high-fluoride water on intelligence of children. Fluoride, 33, 74-78.

Lyons G, Ahrens A, Salter-Green E (2000). An Environmentalist's Vision of Operationalizing the Precautionary Principle in the Management of Chemicals. Int J Occup Environ Health, 6: 289-295.

Masters RD, Coplan M (1999). Brain Biochemistry and the Violence Epidemic: Toward a 'Win-Win' Strategy for Reducing Crime Super-Optimising Examples: Across Public Policy Programmes. New York: Nova Science Publishers Inc.

Maupome G, Clark DC, Levy SM, Berkowitz J (2001). Patterns of dental caries following the cessation of water fluoridation. Community Dent Oral Epidemiol. 29: 37-47.

McClure FJ (1970). Water Fluoridation: The Search and the Victory. National Institute of Dental Research, Bethseda, Md.

McClure FJ, Likins RC (1951). Fluorine in human teeth studied in relation to fluorine in the drinking water. J Dent Res. 30:172-176.

McDonagh MS, Whiting PF, Wilson PM, Sutton AJ, Chestnut I, Cooper J, (2000).. A Systematic Review of Public Water Fluoridation. York: NHS Centre for Reviews and Dissemination, University of York; 2000.

McNeil DR (1957). The fight for fluoridation. New York: Oxford University Press.

Medical Research Council Working Group Report (2002): Water fluoridation and health (www.mrc.ac.uk)

Medical Research Council (2002). Water fluoridation and health. A Medical Research Council working group report. London: Medical Research Council.

Mihashi, Tsutsui T (1996). Clastogenic activity of sodium fluoride to rat-vertebral body-derived cells in culture. Mutat Res. 368(1):7-13.

Mullenix PJ, Denbesten PK, Schunior A, Kernan WJ (1995). Neurotoxicity of sodium fluoride in rats. Neurotoxicol Teratol. 17(2):169-77.

Olsen RE ed. (1986). Fluoride in food and water. Nutr Rev., 44(7):233-5.

Pan-European Taskforce on Dental Health. Dental Health in Europe: a problem for disadvantaged groups. Brussels; 1998.

Pendrys DG, Stamm JW (1990). Relationship of total fluoride intake to beneficial effects and enamel fluorosis. J Dent Res., 69(Spec Iss):529-38.

Ross JF, Daston GP (1995). Neurotoxicology and Teratology, 17(6):685-6. Letter to the editor.

Rugg-Gunn A, Nunn JH (1999). Nutrition, Diet and Oral Health: Oxford University Press.

Sandin P (1999). Dimensions of the precautionary principle, Human and Ecological Risk Assessment, 5: 889-907.

Seppa L, Karkkainen S, Hausen H (2000a). Caries in the primary dentition, after discontinuation of water fluoridation, among children receiving comprehensive dental care. Community Dent Oral Epidemiol., 28(4):281-288.

Seppa L, Karkkainen S, Hausen H (2000b). Caries trends 1992-1998 in two low-fluoride Finnish towns formerly with and without fluoridation. Caries Res., 34:462-468.

Seppa L (2001). The future of Preventive Programmes in countries with different systems for dental care. Caries Res., 35(Suppl 1):26-29.

Treasure ET, Chestnutt IG, Whiting P, McDonagh M, Wilson P, Kleijnen J (2002). The York Review- a systematic review of public water fluoridation: a commentary. British Dental Journal vol.192, 9, 495-497.

United Nations. UN Human Development Report 2004 – Cultural Liberty in Today-s Diverse World. United Nations 2001.

Urbansky, E and Schock, MR. (2000). Can fluoridation affect lead (II) in potable water? Hexafluorosilicate and fluoride equilibria in aqueous solution. International Journal Environmental Studies 57, 597-637.

Vanderzwaag, D (1999). Journal of Environmental Law Practice, 8: 355. See also http://www.ec.gc.ca/ceparegistry

Webb-Peploe MM, Bradley WG (1966). Endemic fluorosis with neurological complications in a Hampshire man. J Neurol Neurosurg Psychiat 29, 577-583.

Whelton H, Crowley E, O'Mullane D, Donaldson M, Kelleher V, Cronin M (2004). Dental caries and enamel fluorosis among the fluoridated and non-fluoridated populations in the Republic of Ireland in 2002. Community Dental Health, 21; 37-44.

Whitford GM (1996). The metabolism and toxicity of fluoride, 2nd rev. ed. Monographs in oral science, Vol. 16. Basel, Switzerland: Karger.

WHO Oral Health County/Area Profile Programme Department of Noncommunicable Diseases Surveillance/ Oral Health WHO Collaborating Centre, Malmo University, Sweden. http://www.whocollab.od.mah.se/euro.html.

World Health Organisation Expert Committee on oral health status and fluoride use. WHO Technical Report Series 846. Fluorides and Oral Health. Geneva: WHO; 1994.

Williams JE, Zwemer JD (1990). Community water fluoride levels, preschool dietary patterns, and the occurrence of fluoride enamel opacities. J Public Health Dent., 50:276-281.

World Health Organisation (2002). Health Behaviour among young people. Health Behaviour in school-aged children: a WHO Cross-National Study (HBSC) international Report. World Health Organisation.

World Health Organisation (1996). International Programme on Chemical Safety. Guidelines for drinking-water quality, 2nd ed. Geneva. http://www.who.int/water_sanitation_health/dwq/gdwp2v1/en/index1.html

Yiamouyiannis JA (1990). Water fluoridation and tooth decay: results from the 1986-1987. National Survey of US Schoolchildren. Fluoride: Journal of the International Society for Fluoride Research; 23(2); 55-67.

Zhao LB, Liang GH, Zhang DN, Wu XR (1996). Effect of high-fluoride water supply on children's intelligence. Fluoride, 29, 190-192.